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Synthesis and Evaluation of Antimicrobial Activity of 1-Phenylpyrazolo[4,5-*c*]quinolin-4-one

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A series of 1-phenylpyrazolo[4,5-*c*]quinolin-4-ones, carrying appropriate substituents at the quinoline ring have been synthesized in good yields involving the condensation of 4-chloro-3-formylquinolin-2[1*H*]ones with phenylhydrazine using triethylamine as a base. All the synthesized compounds were evaluated for their antibacterial activities.

Key Words: 2,4-Dichloroquinolines, Pyrazolo quinolone, 4-Chloro-3-formylquinolin-2-[1*H*]ones, Antimicrobial activity.

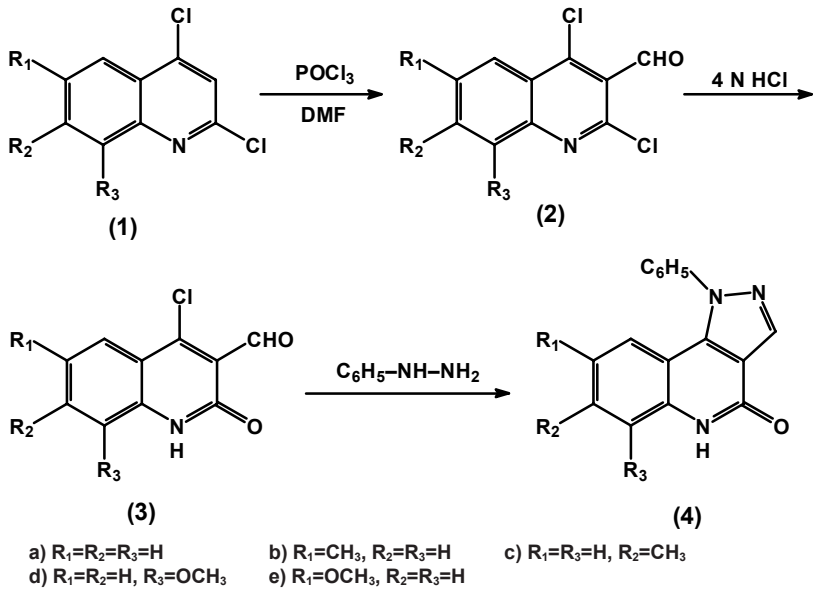
INTRODUCTION

Pyrazoloquinolines and their derivatives are important constituents of biological active compounds[1-3] as they have been associated with biological activities such as antimalarial[4,5], antibacterial[6,7], antiviral[8] and antitumour[9,10] activities. Synthesis of the title compound and its derivatives is reported by the condensation of 4-chloro-3-formylquinolin-2[1*H*]ones with phenylhydrazine and to screen them for antimicrobial activities (**Scheme-I**).

EXPERIMENTAL

Melting points were determined using melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer-597 infrared spectrophotometer as KBr Pellets. ^{1}H NMR spectra were recorded on an AMX 400 spectrometer in $CDCl_3$ unless otherwise specified. Mass spectra were recorded on a Jeol D 300 mass spectrometer.

Synthesis of 1-phenylpyrazolo[4,5-*c*]quinolin-4[5*H*]one (4a-c): 4-Chloro-3-formylquinolin-2[1*H*]one[11] (**3**) was prepared from 2,4-dichloroquinoline[11] (**1**). To a solution of 4-chloro-3-formylquinolin-2[1*H*]one (**3**) in absolute ethanol was added phenyl hydrazine and refluxed for 5-6 h in presence of catalytic amount of triethylamine. After completion of the reaction, the mixture was poured into crushed ice with stirring and kept aside for 4-5 h. The resulting solid was filtered, dried and purified using column chromatography.



Scheme-I

RESULTS AND DISCUSSION

1-Phenylpyrazolo[4,5-*c*]quinolin-4[5*H*]one (**4a**) was synthesized by the condensation reaction of 4-chloro-3-formylquinolin-2[1*H*]one (**3a**) with phenyl hydrazine in absolute ethanol and in presence of catalytic amount of triethylamine. IR spectrum of **4a** revealed the disappearance of the peak at 1670 cm^{-1} indicating the loss of carbonyl group of aldehyde. The ^1H NMR spectrum showed signals at δ 7.20-7.70 (m, 8H, Ar-H), 7.90 (d, 1H, C_6-H), 8.20 (s, 1H, C_3-H), 12.01 (s, 1H, NH). The molecular ion peak at m/z 261 in its mass spectrum confirmed the formation of 1-phenylpyrazolo-[4,5-*c*]quinolin-4[5*H*]one (**4a**). The derivatives **4b-e** were synthesized using differently substituted quinolines (Table-1, **Scheme-I**).

Antibacterial activity: All the synthesized compounds were screened for their antibacterial activity by disc diffusion method[12]. *Staphylococcus aureus*, *Escherichia coli* and *Bacillus subtilis* were used as test organism. The discs (6 mm in diameter) impregnated with 10 µL of the test compounds (500 µg/disc) at the concentration of 50 mg/mL were placed on the inoculated agar. DMF was employed as the solvent to dissolve the test compound and negative control. Oflaxacin (5 µg/disc) were used as positive reference standards to determine the sensitivity of each microbial species tested. The inoculated plates were incubated at 37 ºC for 24 h. Antimicrobial activity was evaluated by measuring the diameter of zone of inhibition against test organisms. Based on the results (Table-2), it is concluded that

compound **4d** and **4e** have significant inhibition effect on the growth of bacteria like *Escherichia coli*, *Bacillus subtilis* and *Staphylococcus aureus*. The compound **4a** and **4b** were active against *Escherichia coli* and *Bacillus subtilis* whereas compound **4c** registered good antibacterial against *Escherichia coli* and *Staphylococcus aureus*.

TABLE-1
PHYSICAL AND SPECTROSCOPIC DATA OF COMPUND **4a-e**[a]

Compd.	m.p. (ºC)/ Yield (%)	IR[b] (ν_{max}, cm^{-1})	^1H NMR[c] (δ) ppm	MS m/z M^+
4a	>300 (80)	3200-3000 (NH), 1650 (NHC=O), 1590 (C=N)	7.20-7.70 (m, 8H, Ar-H), 7.90 (d, 1H, C_6-H, 8.20 (s, 1H, C_3-H), 12.01 (s, 1H, NH)	261
4b	>300 (80)	3200-3000 (NH), 1650 (NHC=O), 1590 (C=N)	2.35 (s, 3H, C_8-CH_3), 7.20-7.70 (m, 7H, Ar-H), 7.90 (d, 1H, C_6-H), 8.20 (s, 1H, C_3-H), 12.01 (s, 1H, NH)	275
4c	292-294 (70)	3250-3100 (NH), 1655 (NHC=O), 1600 (C=N)	2.51 (s, 3H, C_7-CH_3), 7.21-7.95 (m, 7H, Ar-H), 8.01 (s, 1H, C_6-H), 8.25 (s, 1H, C_3-H), 12.14 (s, 1H, NH)	275
4d	295(d) (73)	3300-2900 (NH), 1640 (NHC=O), 1610 (C=N)	3.90 (s, 3H, C_6-OCH_3), 7.91-8.01 (m, 8H, Ar-H), 8.21 (s, 1H, C_3-H), 12.10 (s, 1H, NH)	291
4e	286-288 (73)	3300-3000 (NH), 1655 (NHC=O), 1620 (C=N)	3.91 (s, 3H, C_8-OCH_3), 7.30-8.44 (m, 8H, Ar-H), 8.25 (s, 1H, C_3-H), 11.92 (s, 1H, NH)	291

(a) Ethanol (b) KBr pellet (c) $CDCl_3$

TABLE-2
ANTIBACTERIAL ACTIVITY (**4a-e**)

Compd.	Organisms		
	Diameter of inhibition zone (mm) at µg/disc		
	E. coli	*B. subtilis*	*S. aureus*
4a	8	9	–
4b	8	8	–
4c	9	–	8
4d	9	8	8
4e	10	7	7
Oflaxacin (standard)	22	21	23

In conclusion, 1-phenylpyrazolo[4,5-c]quinolin-4-one (**4a-e**) were synthesized and evaluated for their antimicrobial activities. All the compounds were found to possess moderate antibacterial activity when compared to the standard.

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