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Synthesis and biological evalution of some novel 1, 4-dihydropyridines

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ABSTRACT

4-(1′-N-Phenyl-3′-methyl-5′-chloro-pyrazol-4-yl)-2,3,5,6-substituted 1,4-dihydro pyridines**(1a-f)** have been synthesized by hantzsch reaction of 1-N-phenyl-3-methyl-5-chloro-pyrazole-4-carboxaldehyde,ethylacetoacetate/ acetylactone/methyl acetoacetaete and liq.ammonia.

KEYWORDS

1,4-Dihydropyridines;
Antimicrobial activity.

INTRODUCTION

1,4-Dihydropyridine contribute as an important class of compounds in medicinal chemistry, leading to several new drugs currently widely used especially as calcium channel antagonist[1], and other cardiovascular diseases also.1,4-dihydro pyridine derivatives are also associated with diverse pharmacological activities viz., antiinflammatory[2], antiallergic[3], coronary vasodilator[4], antitumer[5], cardiovascular[6], antihypertensive[7] etc.The Purity and structures of the final-products **(1a-f)** were established on the basis of their TLC and spectra (IR, ^{1}HNMR, Mass) data. In the view of potent pharmacological activities of 1, 4-dihdropyridins, it was contemplated to synthesized 1,4-dihdropyridines**(1a-f)** by hantzsch synthesis of 1-N-phenyl-3-methyl-5-chloropp-yrazole-4-carboxaldehyde, ethylacetoacetate/ acetylactone / methylacetoacetaete and liq.ammonia.

Biological activity

The compounds **(1a-f)**were screened for their antimicrobial activity against *S.pyogens* MTCC-442, *S. aureus* MTCC-96, *E.coli* MTCC-443, *B.subtillis* MTCC-441 and anti-fungal activity against *C.albicans* MTCC-227, *A.niger* MTCC-282 by using cupplate method[8]. The minimum inhibitory concentratio[9] (MIC)value were recorded at a concentration(μg/ml):O(control),25.50,100,200,500,800. Most of the compounds were found to be moderately active against different strains of bacteria and fungal. Compound 1e were found to have higer biological activity against *S. aureus* MTCC-96 and *S.pyogens* MTCC-442 and compound 1c were also found to have higer biological activity against *S.pyogens* MTCC-442, *E.coli* MTCC-443. The MIC value are summarized in TABLE 2.

EXPERIMENTAL

Melting points are uncorrected. IR Spectra (ν max in cm^{-1}) were recorded in KBr on a SHIMADZU-FT-IR-8400 Spectrophotometer and 1HNMR Spectra on a BRUCKER SPECTROMETER at 300 MHz using DMSO-d6 as solvent and TMS as an reference standard(chemical shift in δ,ppm).

Preparation of 4-(1'-N-Phenyl-3'-methyl-5'-chloro-pyrazol-4'-yl)-2,6-dimethyl-3,5-dicarbethoxy-1,4-dihydro pyridine(1a)

A mixture of ethylacetoacetate (2.60 ml,0.02M), 1-N-Phenyl-3-methyl-5-chloro-pyrazol-4-carboxal dehyde(2.21 gm,0.01M) and ammonia (25 ml) in ethanol (25 ml)was refluxed for 12 hrs. Then the reaction

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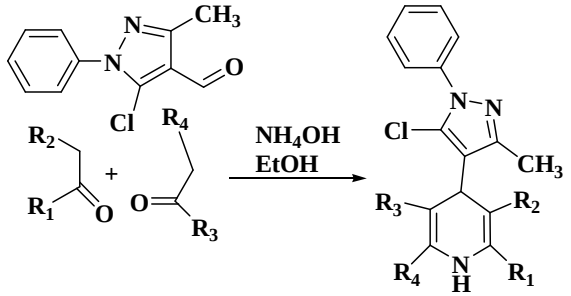
TABLE 1 : Physical data of 4-(1'-N-Phenyl-3'-methyl-5'-chloro-pyrazol-4'-yl)-2,3,5,6-substituted 1,4-dihydro pyridines(1a-f)

Sr. no.	R_1	R_2	R_3	R_4	M.F.	Yield%	M.P. ^{0}C
(1a)	CH_3	$COOC_2H_5$	$COOC_2H_5$	CH_3	$C_{23}H_{26}ClN_3O_4$	62	141
(1b)	CH_3	$COOCH_3$	$COOCH_3$	CH_3	$C_{21}H_{22}ClN_3O_4$	58	151
(1c)	CH_3	$COCH_3$	$COCH_3$	CH_3	$C_{21}H_{22}ClN_3O_2$	55	162
(1d)	CH_3	$COOCH_3$	$COOC_2H_5$	CH_3	$C_{23}H_{26}ClN_3O_4$	64	139
(1e)	CH_3	$COCH_3$	$COOC_2H_5$	CH_3	$C_{22}H_{24}ClN_3O_3$	53	147
(1f)	CH_3	$COCH_3$	$COOCH_3$	CH_3	$C_{21}H_{22}ClN_3O_3$	57	157

TABLE 2: Antimicrobial activity of 4-(1'-N-Phenyl-3'-methyl-5'-chloro-pyrazol-4'-yl)-2,3,5,6-substituted 1,4-dihydro pyridines(1a-f, minimum inhibitory concentration in μg/ml)

Sr.no.	Antimicrobial activity				Antifungal activity	
	S.Pyogens MTCC-442	*S.aureus* MTCC-96	*E.coli* MTCC-443	*B.subtillis* MTCC-441	*C.albicans* MTCC-227	*A.niger* MTCC-282
(1a)	50	100	100	50	200	500
(1b)	100	500	50	100	50	800
(1c)	50	500	25	50	500	800
(1d)	500	50	50	100	100	50
(1e)	50	25	100	500	200	200
(1f)	100	100	200	500	-	500



SCHEME 1

mass was kept at room temperature for 10hrs. The product was isolated and recentralized from ethanol. Yield 62% m.p 141 ^{0}C (Required: C;62.23%; H,5.86%; N,9.47%; For $C_{23}H_{26}ClN_3O_4$: Found:C;62.9%;H, 5.83%;N,9.43 %).

IR(KBr): 3413 (N-H Str.), 3070 (C-H Str., aromatic); 2925, 2852 2963 (C-H Str., alkane), 1596(N-H def.), 1676 (C=O str.)

^{1}HNMR:-1.23 (t,3H,C<u>H</u>$_3$-CH$_2$), 2.3(s, 3H,C<u>H</u>$_3$), 3.92-4.18(q,2H, 2H,CH$_3$-C<u>H</u>$_2$),5.08(s, 1H,C<u>H</u>),7.27-7.50(m, 5H,Ar-<u>H</u>),7.75(s,1H,N<u>H</u>).

Mass:- m/e = 444 corresponding to MF= $C_{23}H_{26}ClN_3O_4$.

Similarly other 1,4dihydro pyridines **(1a-f)** were synthesized. The physical data are recorded in TABLE 1.

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