Original Research Paper

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Synthesis, Characterization and Antimicrobial activity of 4-(substituted phenyl)-1-(2,4-dinitrophenyl)-3-methyl-4,5-dihydro-pyrazolo[3,4-d]pyrimidine-6-thiol

Chemistry

KEYWORDS: Aldehyde, methanol, thiourea and hydrochloric acid .

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ABSTRACT

4-(substituted phenyl)-1-(2,4-dinitrophenyl)-3-methyl-4,5-dihydro-pyrazolo[3,4-d]pyrimidine-6-thiol $_{z=1,x=y}$ synthesized by reaction between 2-(2,4-dinitrophenyl)-5-methyl-2,4-dihydro-pyrazol-3-one and different aldehyde in presence of thiourea ,hydrochloric acid and methanol The synthesized compounds were characterized by means of their IR, 1H-NMR spectral data and elemental analysis. All the synthesized products were evaluated for their antimicrobial activities by Cupborer method.

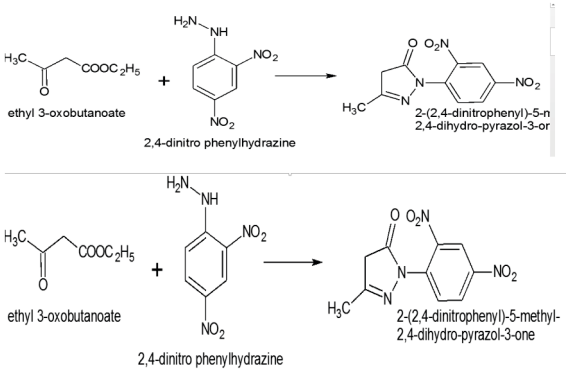
INTRODUCTION

Pyrimidine is a six-membered heterocyclic compound consisting of two nitrogen atoms at 1 and 3 position of heterocyclic ring. Pyrimidine derivatives generally studied are 2-hydroxy pyrimidine, 2-mercapto pyrimidine and 2- amino pyrimidine.

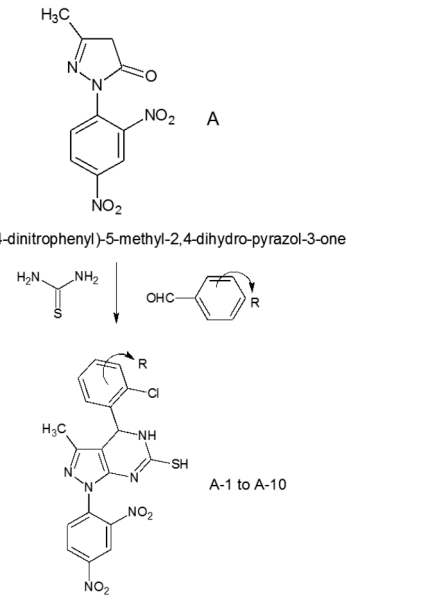
A general important method for preparing pyrimidines is the condensation between a three carbon compounds of the type YCH_2Z, where Y and Z = COR, CO_2R, CN, and compounds having the amidine structure $R(C=NH)NH_2$, where R = R (an amidine), SH or SR (thiourea or its s-derivative), NH_2 (guanidine). The condensation is carried out in the presence of sodium hydroxide or sodium ethoxide. This general reaction may be illustrate by the condensation of acetamidine with ethylacetoacetate to form 4-hydroxy-2,6-dimethylpyrimidine.

Abd-El-gali E. Amr**[1]** synthesised 2-aminopyrimidines by the reaction of chalcones with guanidine hydrochloride in the presence of NaOH.The reaction of chalcone with guanidine hydrochloride in presence of potassiumbutoxide in t-butanol yielded corresponding 2-amino pyrimidine derivatives**[2]**.Pyrimidine can conveniently be prepared by the reaction of melonic ester and urea. **[3]**.4-amino-5-cyano-2-mercapto-6-aryl pyrimidine can be synthesized by the condensation of aromatic aldehyde, urea, thiourea and 1-1-dicyano methane. **[4]**.Gangjee Aleen *et al.***[5]** Synthesised aminopyrimidines which possess antitumor activity. Pan Senliang *et al.***[6]** prepared 2-methylthio-4-amino-6-(3,5-diacetylphenylamino) pyrimidines which show anti HIV activity in Hq cell cultures. Ugarkar Bheemarao G *et al.*[7] found aminopyrimidines in the inhibition of cardiovascular and ceribrovascular disorders. Some aminopyrimidines have been studied for their antimicrobial activity**[8]**. Bargiotti Alberto *et al.***[9]** prepared aminopyrimidine derivatives for their therapeutic use as telomerase inhibitors and anticancer agent. Jden and Juan**[10]** synthesised some new aminopyrimidines for the treatment of cytomegalovirus infections.

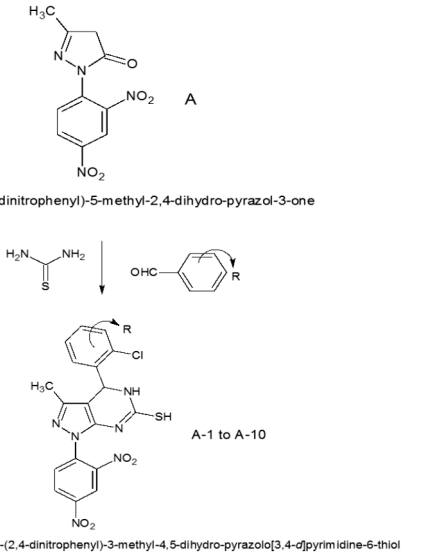
EXPERIMENT REACTION



Reaction Scheme



Reaction Scheme



EXPERIMENTAL WORK

For synthesis of 2-(2,4-dinitrophenyl)-5-methyl-2,4-dihydro-pyrazol-3-one mix 0.4 M of ethyl acetoacetate and 0.44 M of 2,4-dinitrophenyl hydrazine in a evoparating dish and heat it for two hours in water bath in fume cupboard with continuous stir then cool it and add 100 ml of ether and stir the mixture vigorously the product 2-(2,4-dinitrophenyl)-5-methyl-2,4-dihydro-pyrazol-3-one is obtain in 15 minute then filter it and wash with eather to remove coloured impurities.Recrystalise product of 2-(2,4-dinitrophenyl)-5-methyl-2,4-dihydro-pyrazol-3-one from hot water the yield of product was 76 % and product was melt at 95 ^{o}C Found: C(45.42%) H(3.03%) N(21.19%), Calcd. for C10H8N4O5: C(45.46%) H(3.05%) N(21.21%) IR; (cm-1):3079(=CH), 2912(-CH, Stretch),1720(>C=O), 1600(>C=N Stretch),1499(>C=C<,aromatic ring),1557(-N=O),1463(-CH3 bend),1343(-C-N<), 1245(>N-N<).1H NMR (DMSO);: 2.55, singlate (3H) (-CH3),2.30,singlate (2H)(-CH2-), 8.16- 9.10, multiplate (3H) (Ar-H).

Preparation of 4-(2-chlorophenyl)-1-(2,4-dinitrophenyl)-3-methyl-4,5-dihydro-pyrazolo[3,4-d]pyrimidine-6-thiol (A-1 to 10)

A mixture of 2-(2,4-dinitrophenyl)-5-methyl-2,4-dihydro-pyrazol-3-one (0.01M), thiourea (0.01M) and different aldehyde (0.01M) in methanol (30ml) was refluxed for 7 hours in presence of hydrochloric acid. Then the reaction mixture was poured on to crushed ice and the obtained product was filtered and crystallized from ethanol. The yield of the product was 77% and Melting points were taken in open capillary tube and were uncorrected. used for NMR Spectroscopy was recorded in DMSO on Bruker Advance II 400 MHz spectrometer using TMS as an internal standard. IR spectra were recorded on I.R. Spectrophotmeterof Bruker scientific Model No. Alpha E and instrument Purity of the compounds were checked by TLC on silica-G plates.and Antimicrobial activity were checked by cupboard method

IR :(A-6) cm^{-1} , >N-H : 3370, -OH : 3250, =C-H : 3070, -C-H (Stretch) : 2905 , -S-H : 2475 , >C=N- (Stretch) : 1590, >C=C< aromatic : 1500 , -N=O : 1550 , -CH_3 (bend) : 1415, C-N : 1310 , N-N : 1265, -C-O : 1200, C-O-C : 1200

^{1}HNMR (DMSO) A-7: =1.5287ppm singlet (1H)(-SH) , =1.993 ppm singlet (1H)(-NH-) , =2.5885 ppm singlet (3H)(-CH_3) , =4.9987 ppm singlet (1H)(Ar-OH) , =5.1889 ppm singlet (1H)(>CH-) , =6.8783-9.0457 ppm (7H)(Ar-H)

TABLE NO. 1

Physical constant of 4-(substitutedphenyl)-1-(2,4 -dinitrophenyl)-3-methyl-4,5- dihydro-pyrazolo[3,4-d]pyrimidine-6-thiol

No	Sub No	R	Molecular Formula	Mol. Wt	Yield %	M.P.	C (%)		H (%)		N (%)	
							Found	Req	Found	Req	Found	Req
1	A-1	-4 Cl	$C_{18}H_{13}ClN_6O_4S$	444.85	77	112	48.54	48.60	2.92	2.95	18.83	18.89
2	A-2	-2 Cl	$C_{18}H_{13}ClN_6O_4S$	444.85	75	146	48.56	48.60	2.90	2.95	18.85	18.89
3	A-3	-3-OCH_3 , -4-OCH_3	$C_{18}H_{14}N_6O_4S$	470.45	72	109	51.00	51.06	3.82	3.86	17.83	17.86
4	A-4	-H	$C_{18}H_{14}N_6O_4S$	410.40	69	122	52.60	52.68	3.41	3.44	20.45	20.48
5	A-5	-2 -OH	$C_{18}H_{14}N_6O_5S$	426.40	86	142	50.62	50.70	3.27	3.31	19.65	19.71
6	A-6	-3-OCH_3, -4-OH	$C_{19}H_{16}N_6O_6S$	456.43	83	157	49.94	50.00	3.50	3.53	18.35	18.41
7	A-7	-4-OH	$C_{18}H_{14}N_6O_5S$	426.40	71	185	50.64	50.70	3.26	3.31	19.65	19.71
8	A-8	-4-$N(CH_3)_2$	$C_{20}H_{19}N_7O_4S$	453.47	80	168	52.92	52.97	4.17	4.22	21.56	21.62
9	A-9	-4-OCH_3	$C_{19}H_{16}N_6O_5S$	440.43	78	153	51.75	51.81	3.60	3.66	19.01	19.08
10	A-10	-3-NO_2	$C_{18}H_{13}N_7O_6S$	455.40	74	195	47.44	47.47	2.85	2.88	21.50	21.53

ANTI BACTERIAL CTIVITY:

synthesized compounds suggests their moderate antibacterial and antifungal activity as compared to the standard drugs Penicillin, Chloramphenlcol, Streptomycin, Tetracyclin and Amphotericin using cupboar method. Antibiotic solution is prepared in sterile distilled water.Penicillin: 12 units , Chloramphenicol: 30 µg/ml , Streptomycin: 30 µg/ml,Tetracycline: 30 µg/ml , Fluconazole: 30 µg/ml

Culture activation:

The culture was activated in nutrient broth and potato dextrose broth for bacteria and yeast respectively. One colony of each organism was inoculated and incubated at 37^{0}C (bacteria) and 28^{0}C (yeast) temperature for 24 hours. 200 µl of activated culture was inoculated in 25 ml of molted Nutrient agar and Yeast peptone agar for bacteria and yeast respectively. After proper mixing of culture it was poured in sterile 100mm Petri dish.

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Over all analysis of the results suggest that,A-9 showed good anti-bacterial activity against E.coli NCIM 2066.A compounds A-5,A-9 and A-10 have good anti-bacterial activity then standard tested drugs Chloramphenicol and streptomycine and other all have less anti-bacterial activity then standard tested all drugs against S.aureus MTCC 737A. A compounds A-10 have good and A-2 have equal anti-bacterial activity then streptomycine and Chloramphinicol against B.spizinzenii MTCC 441. And also A-1,A-6,A-8,A-9,A-10 all most compound showed very good anti-bacterial activity against P.aeruginosa MTCC 1688. A-8 is showed high anti-bacterial activity then the standard tested drugs used for bio-assay for S.paratyphi A. A-6 and A-9 are equal anti-bacterial activity then the standard tested drugs against S.paratyphi A MTCC 735 and A-1,A-2,A-3, A-5,A-6,A-7 and A-10 High anti-bacterial activity then other standard drugs Penicillin,streptomycine and Chloramphenicol against B.pumilusMTCC 1607 and A-1,A-8,A-9 are showed High anti-bacterial activity for K.pneumoniae MTCC 432 than the standard tested drugs used for bio-assay. And A-5 is equalanti-bacterial activity for K.pneumoniae than the standard tested drug Chloramphenicol .

TABLE-2

	A-1	A-2	A-3	A-4	A-5	A-6	A-7	A-8	A-9	A-10	SD 1	SD 2	SD 3	SD 4	SD 5
E.Coli	18	17	18	14	18	18	17	17	20	16		12	18	17	
S.aureus	21	22	17	17	0	18	22	20	0	0	22	16	16	22	
B.spizinzenii	23	21	17	16	16	14	20	15	18	22	23		21	22	
P.aeruginosa	16	12	0	11	11	16	14	15	15	17			12		
S.paratyphi A	16	16	16	14	16	19	17	20	19	16	19	18	12	18	
B.pumillus	17	20	20	0	21	17	17	16	15	18	15		16	22	

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K.pneumoniae	22	18	16	16	19	17	18	20	20	0		19	13	17	
C.albicans	23	20	17	16	18	19	18	23	20	19					21

Whwre, SD1=Penicillin, SD2=Chloramphenicol, SD3=Streptomycin, SD4=Tetracyclin SD5= Fluconazole.

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