SYNTHESIS OF SOME NEW OXADIAZOLE WITH ANTIMICROBIAL ACTIVITY

*Manish Kumar Mishra[1], A K Gupta[2], S Negi[2], Meenakshi Bhatt[1]

1. S.G.R.R.I.T.S. , Patel Nagar, Dehradun
2. S.G.R.R. (PG) College,Dehradun

ABSTRACT

6 – Methyl – 4 – aryl – 5 - (5- phenyl -1, 3, 4 – oxadiazol -2- yl) -1, 2, 3, 4-tetrahydropyrimidine-2(1*H*)-one have been synthesized and compound 3e has significant effect against Streptococcus *pneumonia*(+ve) and 3b has significant activity effect *Escheria coli* (-ve)

KEYWORDS

Dihydropyrimidines,Oxadiazole,Antibacterial

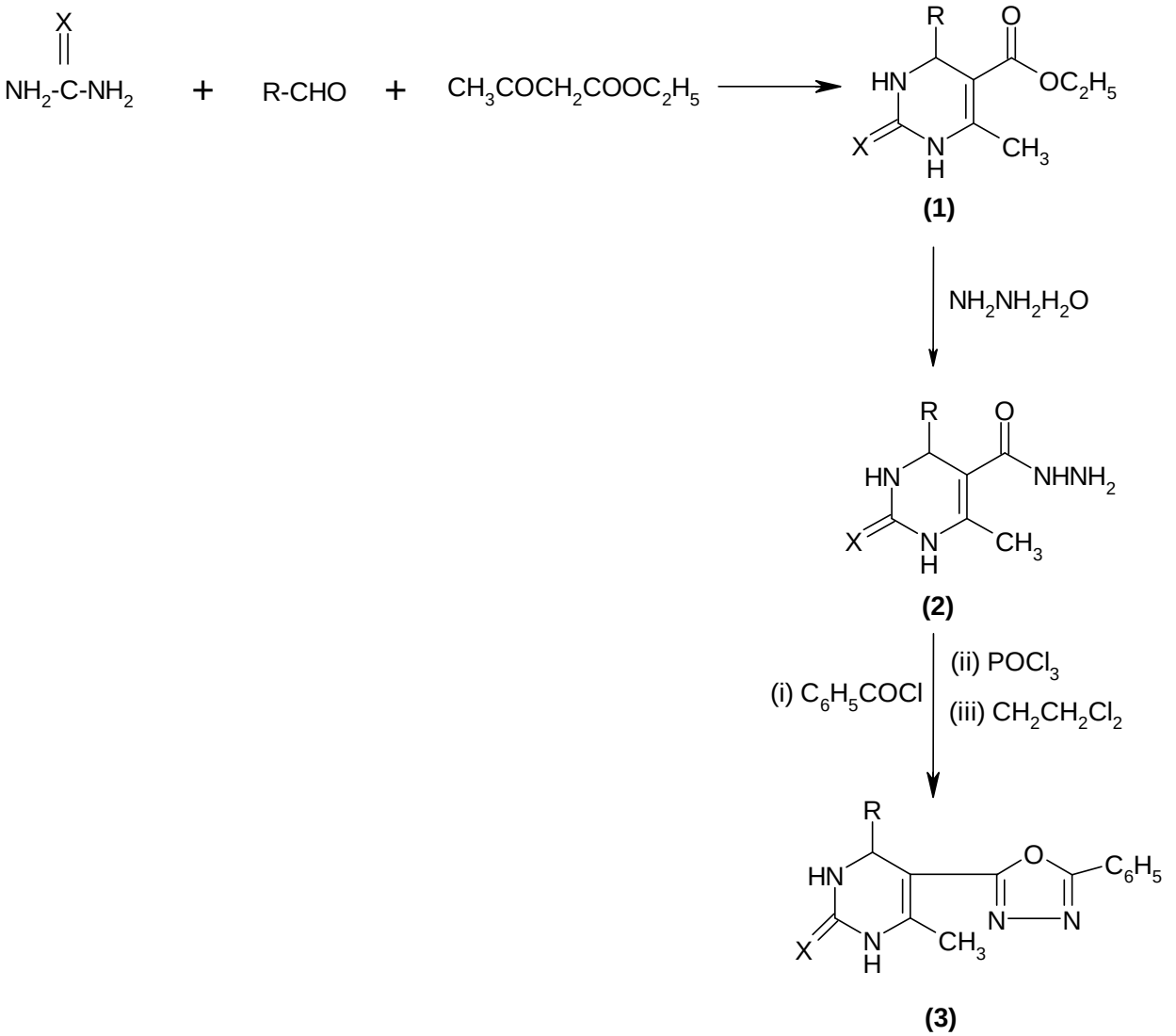
INTRODUCTION

Oxadiazole is important heterocyclic ring present in a large number of biologically active molecules of different pharmacological classes[1, 2]. It is known to have fungicidal, bactericidal and herbicidal activities. Compounds carrying the dihydropyrimidine ring have been reported to demonstrate a wide range of pharmacological activities[3-5], which include antibacterial, antifungal, antitubercular, anticonvulsant, analgesic[6], antihistaminic, and antihypertensive activity[7].

Pyrimidines are considered to be important not only because they are integral part of genetic material viz. DNA and RNA as nucleotide and nucleoside but they are also important in numerous biological activities such as bactericidal, fungicidal, insecticidal etc. Biodynamic property of pyrimidine ring system prompted us to account for their pharmacological properties, especially as antibacterial agents[8].

By the literature survey both dihydropyrimidines and oxadiazole have different activities. In present work compound synthesized having both the rings and evaluate for antimicrobial activity.

SCHEME



EXPERIMENTAL:

Ethyl -6- methyl- 2- oxo- 4- substituted phenyl- 1,2,3,4-tetrahydropyrimidine-5- carboxylate:-To a mixture of urea (0.15mole), substituted aldehyde (0.10mole) and ethylacetoacetate (0.10mole) in ethanol (75 ml), 4 drops of concentrated hydrochloric acid was added and heated for 1.5 hrs at 70^0C . The reaction mixture was poured in to ice water (100ml) with stirring and left overnight at room temperature .Filtered and residue dried at room temperature, recrystallised from ethanol.

The compounds prepared in this manner (1a-e) are listed in table no: 1

IR (KBr) 1650cm^{-1} (amide C=O), 1730cm^{-1} (ester C=O), 3250cm^{-1}(-NH), Two bands in between1230 cm^{-1} and 1030cm^{-1} (tert. amine).

6- methyl- 2- oxo- 4- substituted phenyl- 1,2,3,4-tetrahydropyrimidine-5- carbohydrazide:-To a hot solution of (0.01 mole) in ethanol (150 ml) was added hydrazine hydrate (0.99%, 0.015 mole) and the reaction mixture was heated under reflux for 3hrs. The solvent was removed to possible extent by distillation and the product thus separated was filtered and purified by recrystallization from ethanol to get a colorless crystalline solid.

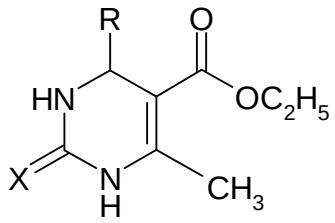
The compounds prepared in this manner (2a-e) are listed in table no: 2

IR (KBr) 1650cm^{-1} (amide C=O), 3250cm^{-1}(-NH), Two bands in between1230 cm^{-1} and 1030cm^{-1} (tert. amine).

6 – Methyl – 4 – aryl – 5 - (5- phenyl -1, 3, 4 – oxadiazol -2- yl) -1, 2, 3, 4-tetrahydropyrimidine-2(1*H*)-one:- To a solution of benzoyl chloride (0.01 mole) in dichloroethane (10 ml) and compound 2 (0.01 mole), phosphorous oxychloride (5ml) was added and content were refluxed for 8 hrs on an oil bath. After the reaction, excess of solvent

and $POCl_3$ were distilled at reduced pressure. Reaction mass was cooled and poured into ice, left overnight. The product was obtained by filtration and purified by recrystallization from aqueous ethanol.
The compounds prepared in this manner (3a-e) are listed in table no:3
IR (KBr) 1689 cm^{-1} (amide C=O), 1026 cm^{-1} (C-O-C), 1603 &1582 cm^{-1} (C=N).

TABLE-1



COMPOUND-1

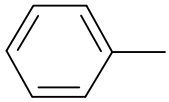
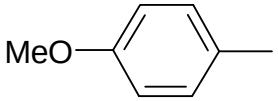
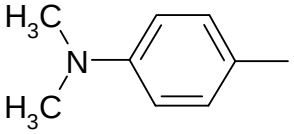
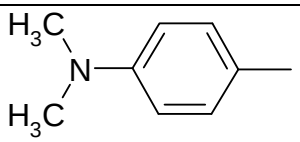
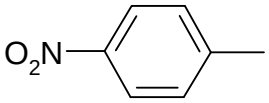
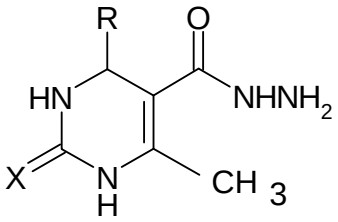
SL. NO.	R	X	%YIELD	M.P. °C	MOLECULAR FORMULA
1a		O	89%	200	$C_{14}H_{16}O_3N_2$
1b		O	90%	198	$C_{15}H_{18}O_4N_2$
1c		O	82%	250	$C_{16}H_{21}O_3N_3$
1d		O	80%	148	$C_{16}H_{21}O_3N_3$
1e		O	92%	208	$C_{14}H_{15}O_5N_3$

TABLE-2



COMPOUND-2

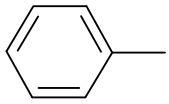
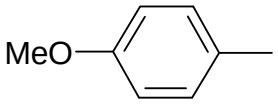
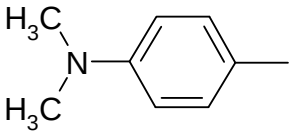
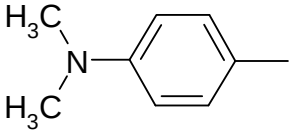
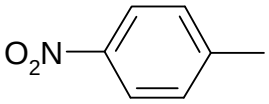
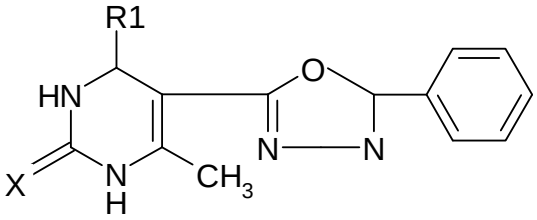
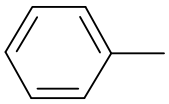
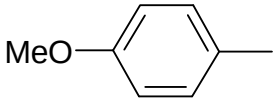
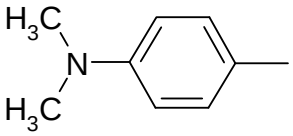
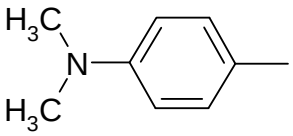
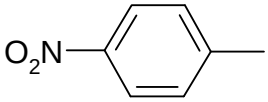
SL. NO.	R	X	%YIELD	M.P. °C	MOLECULAR FORMULA
2a		O	88%	210	$C_{12}H_{14}O_2N_4$
2b		O	86%	206	$C_{13}H_{16}O_3N_4$
2c		O	82%	268	$C_{14}H_{19}O_2N_5$
2d		O	80%	198	$C_{14}H_{19}O_2N_5$
2e		O	87%	224	$C_{12}H_{13}O_4N_5$

TABLE-3



COMPOUND-3

SL. NO.	R1	X	%YIELD	M.P. ^{o}C	MOLECULAR FORMULA
3a		O	72%	200	$C_{14}H_{16}O_3N_2$
3b		O	78%	116	$C_{15}H_{18}O_4N_2$
3c		O	71%	115	$C_{16}H_{21}O_3N_3$
3d		O	69%	117	$C_{16}H_{21}O_3N_3$
3e		O	72%	121	$C_{14}H_{15}O_5N_3$

STUDY OF ANTIMICROBIAL ACTIVITY

The synthesized compounds are screened for antibacterial activity three species were selected, *Streptococcus aureus* for gram positive and *Escheria coli* for gram negative activities respectively.

Antibacterial activity: The antibacterial activity are performed by cup and plate method (Disc diffusion technique) 40-45 fresh cultures of bacteria are obtained by inoculating bacteria in Muller-Hinton broth and incubated at 37^0 $\pm 2^OC$ for 18-24 hours in B O D incubator. This culture is mixed with nutrient agar 20% (High Media) and poured into petri dishes aseptically. After solidification of the media five bores are made at equal distance by using sterile cork borer (8mm diameter), different concentrations of standard drug and synthesized compounds are introduced into these cups. Dimethyl formamide (DMF) is used as a control.

Table no-4

Antibacterial activity of synthesized oxadiazoles

S.No.	Name of the compound	Mean zone of inhibition (in mm)	
		Streptococcus pneumonia (+ve)	***Escherichia coli (-ve)***
1	OFLOXACIN	19	16
2	LEVOFLOXACIN	20	17
3	3a	11	12
4	3b	12	15
5	3c	13	13
6	3d	10	10
7	3e	15	12

Result and Discussion

Antibacterial activity of synthesized 6 – Methyl – 4 – aryl – 5 - (5- phenyl -1, 3, 4 – oxadiazol -2- yl) -1, 2, 3, 4-tetrahydropyrimidine-2(1*H*)-one were tested against gram +ve (*Streptococcus pneumonia*) and gram –ve (*Escheria coli*) bacteria, the tested compound 3e showed promising antibacterial activity against gram +ve (*Streptococcus pneumonia*) bacteria and compound 3b showed promising antibacterial activity against gram -ve (*Escheria coli*) compared to standard drugs ofloxacin and levofloxacin

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