International Journal of ChemTech Research
CODEN (USA): IJCRGG ISSN: 0974-4290
Vol.7, No.01, pp 275-278, 2014-2015

Synthesis and studies of some substituted pyrimidines

Hardik Mehta[1]*, Ranjan Khunt[2]

[1]M.M.Science college, Morbi, India
[2]Department of Chemistry, Saurashtra university,Rajkot, India

Abstract: The one keto group of amide was treated with various aromatic aldehydes and urea/ thiourea /guanidine to give corresponding pyrimidines[1]. The structures of newly synthesized compounds were confirmed by spectral analysis. The synthesized compounds were evaluated for antimicrobial activity. All the synthesized pyrimidines show good antimicrobial activity.
Keywords: Pyrimidines, amides, pentanoic acid, 4-chloro-2-methylaniline.

Introduction

Pyrimidine is the most important member of all the diazines as this ring occurs widely in living organisms. Purines, uric acid, barbituric acid and anti-malerial and anti-bacterial agents also bears the pyrimidine skeleton.[2-6]

Pyrimidine derivatives have been reported to possess various pharmacological activities like antifungal, insecticidal etc.[7-12] in order to achive batter drug potency, we have synthesized pyrimidine derivetives by the condensation of aryl aldehydes, *N*-(4-chloro-2-methylphenyl)-4-methyl-3-oxopentanamide and Urea/thiourea/ guanidine.

The constitution of the synthesized products have been supported by using IR, NMR and Mass spectral analysis.

Experimentals

Materials and Methods

All the melting points are uncorrected. TLC method was used to check reaction progress.

1} Preparation of *N*-(4-chloro-2-methylphenyl)-4-methyl-3-oxopentanamide:

Take 4-chloro-2-methylaniline (0.1 mole) in 40 mL Toluene. Add Methyl isobutyryl acetate (0.1 mole), add slury of NaOH(2 gm NaOH + 6 mL H_2O). reflux for 8-10 hr. at 108^oC.

The solution is allowed to stand for 12 hr. at room temperature and the resulting solid mass separated was filtered and crystallized from methanol. M.P. 110^oC, Yield 48%.

2} Preparation of *N*-(4-chloro-2-methylphenyl)-2-oxo/thioxo/imine-4-aryl-6-(propan-2-yl)-1,2,3,4–tetra hydro pyrimidine-5-carboxamide:

A mixture of *N*-(4-chloro-2-methylphenyl)-4-methyl-3-oxopentanamide (0.01 mole), urea/thiourea/guanidine (0.01 mole) and aromatic aldehyde (0.01 mole) in 15 mL of ethanol containing catalytic amount of con.HCl was refluxed for 24-25 hrs. The solution was allowed to stand for 12 hrs. at room temperature and the resulting solid mass separated was filtered and crystallized from methanol. M.P. 192^oC, Yield 40%. Similarly other derivatives were synthesized. Physical data are recorded in (Table-1).

3} Antimicrobial activity of the synthesized compounds:

Antimicrobial activity was carried out by cup-plate agar diffusion method which has been described as under.

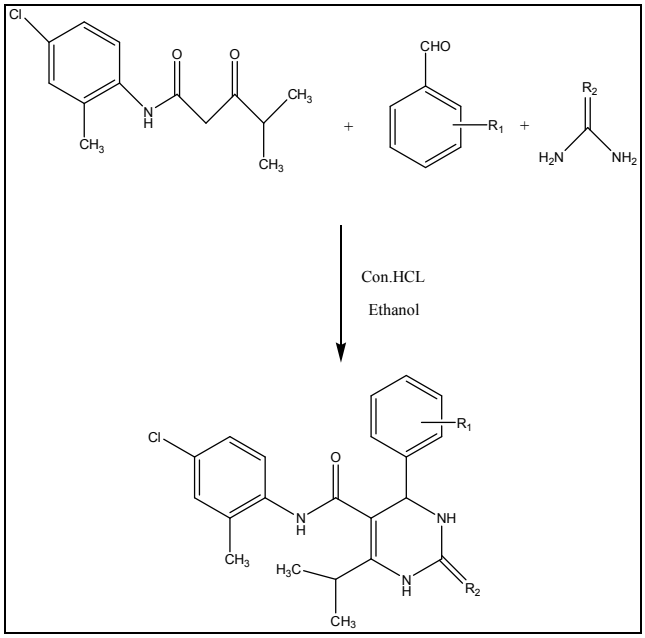
The purified products were screened for their antibacterial activity. The nutrient agar broth prepared by the usual method, was inoculated aseptically with 0.5mL of 24 hrs. old subcultures of *B.subtillis, S.aureus, P.aerougenosa, E.coli* in separate conical flasks at 40-50 ^{o}C and mixed well by gentle shaking. About 25mL content of the flask were poured and evenly spreaded in a Petridis (13 cm in diameter) and allowed to set for 2 hr.

The cup (8mm in diameter) were formed by the help of borer in agar medium and filled with 0.04mL(40mg) solution of sample in DMSO. The plates were incubated at 37^{o}C for 24 hrs. The control was also maintained with 0.04mL of DMF in a similar manner and the zones of inhibition of the bacterial growth were measured in millimeter and are recorded in (Table-2).

The antibacterial activity data of the synthesized compounds have been compared with standard antibiotics like Benzylpenicilline, Ciprofloxacine, Sparfloxacine, and Ampicilin.

Results and Discussion:

Reaction Scheme:



Discussion

It has been observed from the experimental data that all the compounds were moderately active against Gram positive and Gram negative bacterial strains.

In case of Gram positive bacterial strain maximum activity was observed in compounds bearing R=2-chloro , urea and 4-methoxy, thiourea have fairly inhibit the growth of *B.subtillis*. Almost all the compounds have least active against *S.aureus*, while the compounds having R= 4-Fluorophenyl, urea displayed significant activity.

In case of Gram negative bacterial strain compounds bearing R=2-chloro, guanidine and 3,4-dimethoxy, guanidine have shown maximum activity against *E.coli* and R= 2-Chloro, guanidine has shown

maximum activity against *P.aerougenosa*.

Table 1. Physical data

Sr. No.	R_1	R_2	Molecular Formula	M. Mass	M.P. ^oC	$R_f^{\#}$ value	Yield %	Nitrogen %
1	4-F	=O	$C_{21}H_{21}ClFN_3O_2$	401	182	0.61	22	10.46
2	4-F	=S	$C_{21}H_{21}ClFN_3OS$	417	192	0.79	40	10.50
3	4-F	=NH	$C_{21}H_{22}ClFN_4O$	400	204	0.84	54	13.98
4	2-Cl	=O	$C_{21}H_{21}Cl_2N_3O_2$	418	201	0.13	32	09.24
5	2-Cl	=S	$C_{21}H_{21}Cl_2N_3OS$	434	225	0.77	41	08.92
6	2-Cl	=NH	$C_{21}H_{22}Cl_2N_4O$	417	187	0.54	39	12.35
7	3,4-$(OCH_3)_2$	=O	$C_{23}H_{26}ClN_3O_4$	444	255	0.45	72	09.47
8	3,4-$(OCH_3)_2$	=S	$C_{23}H_{26}ClN_3O_3S$	460	232	0.23	62	09.14
9	3,4-$(OCH_3)_2$	=NH	$C_{23}H_{27}ClN_4O_3$	443	114	0.66	33	12.65
10	4-OCH_3	=O	$C_{22}H_{24}ClN_3O_3$	414	198	0.21	52	10.15
11	4-OCH_3	=S	$C_{22}H_{24}ClN_3O_2S$	430	168	0.68	41	09.77
12	4-OCH_3	=NH	$C_{22}H_{25}ClN_4O_2$	413	112	0.31	49	13.57

Table-2 Antimicrobial activity

Sr. No.	Compound	*B.subtillis*	*S.aureus*	*E.coli*	*P.aerougenosa*
1	$C_{21}H_{21}ClFN_3O_2$	16	18	10	15
2	$C_{21}H_{21}ClFN_3OS$	10	19	13	08
3	$C_{21}H_{22}ClFN_4O$	09	21	14	09
4	$C_{21}H_{21}Cl_2N_3O_2$	11	26	12	09
5	$C_{21}H_{21}Cl_2N_3OS$	14	09	18	16
6	$C_{21}H_{22}Cl_2N_4O$	13	11	22	28
7	$C_{23}H_{26}ClN_3O_4$	16	14	12	24
8	$C_{23}H_{26}ClN_3O_3S$	18	13	16	16
9	$C_{23}H_{27}ClN_4O_3$	20	16	18	13
10	$C_{22}H_{24}ClN_3O_3$	21	18	20	12
11	$C_{22}H_{24}ClN_3O_2S$	28	15	21	16
12	$C_{22}H_{25}ClN_4O_2$	12	08	28	18
	Benzylpenicillin	17	18	16	16
	Ciprofloxacin	35	34	12	12
	Sparfloxacine	30	30	10	36
	Ampicilline	22	16	10	18

Table-3

Signal No.	Signal Position	Intensity	Multiplicity	Interference
1	**1.51**	**3H**	**Singlet**	**-CH_3**
2	**1.66**	**3H**	**Singlet**	**-CH_3**
3	**2.48**	**3H**	**Singlet**	**-CH_3**
4	**3.45**	**1H**	**Multiplaet**	**-CH=**
5	**4.99**	**1H**	**Singlet**	**-CH=**
6	**7.159-7.263**	**5H**	**Multiplaet**	**Ar-H**
7	**7.33-7.32**	**1H**	**Doublet**	**Ar-H**
8	**7.424-7.402**	**1H**	**Doublet**	**Ar-H**
9	**8.96**	**2H**	**Singlet**	**NH-(C=S)-NH**
10	**9.049**	**1H**	**Singlet**	**Amide**

Acknowledgements

The authors are thankful to Dr. P. H. Parsania, Prof. and Head, Department of Chemistry (SAP & FIST Sponscered), Saurashtra University, Rajkot, for providing research facility. Authors are also thankful to RSIC-Chandigarh, CDRI-Lucknow for spectral analyses.

References

1. G. shaw and G. Saugowdz, The hydrogenation of 5-amino*iso*oxazoles. A new synthesis of pyrimidines,J. Chem. Soc 1954; 665-668.
2. 2.R.L. Miller,P.G. Lycos, and H.N. Schmeising, A Quantum Theoretical Study of Some N-Heteroaromatic Compounds,J.Am.Chem.Soc. 1962,84, 4623-4627.
3. I.J.Rinkes, R.T.Caim, Buehrer, the action of sodium hypochlorite on amides, Pays-bas. 1927, 46,268.
4. G.A. Howard, B.Lythgog and A.R.Todd, Experiments on the synthesis of purine nucleosides, J. Chem. Soc. 1944.476.
5. C.W.Whitehead and J.J.Traversol, Alkoxymercuration by Mixed Anion Salts of Mercury,J. Am.Chem. Soc. 1958,80, 2185.
6. H.Bredereck, F.Effenberger and H.J.Treiber, Trisacylaminomethane: Synthesen und Umsetzungen, Chem. Ber. 1963, 96, 1505.
7. D.J.Brown, Chem.Hetero. compounds;1970, 20, 16-51.
8. S.inoue,A.J. saggimoto and E.A.Nodiff, Fluorine-Containing Potential Anticancer Agents. I. Synthesis of Some Trifluoromethylpyrimidines ,J.org.chem. 1961, 26, 4504.
9. J.A. Van allan, 2,4-DIAMINO-6-HYDROXYPYRIMIDINE. Org.Synth. 1952, 32, 45 .
10. E.C.Taylor and R.W.Morrison.Jr., An unusual molecular rearrangement of an N-aminopyrimidine ,J.org.Chem. 1967, 32, 2379.
11. P.B.Rusell, G.H.Hitchings, Some 2,4,6-Triamino-5-alkyl- and 5-Benzylpyrimidines, J.Am. Chem. Soc. 952, 74, 3443.
12. P.Krohnke, E.Schmidt, W.Zoecher, Neue Pyrimidin-Synthesen, Chem.Ber, 1964, 97, 1163.
13. A.Dornow, H.Hell, Die Darstellung von 5-Acetyl-oxazolen und deren Umwandlung in 5-Hydroxy-pyrimidine Chem. Ber,1960, 93, 1998-2001 .
14. J.W.Streef, H.J.Denhertog, Action of potassium amide on 6-substituted derivatives of 2-bromopyridine in liquid ammonia, Rec.Trav.Chem.Pays-Bas;1969, 88, 1391.
15. W.D.Crow, C.Wentrup, Reactions of exited molecules v. Thermal decomposition of pyrazine, Tetrahedron Lett. 1968, 7, 3115.
16. F.C.Schaefer, K.R.Huffman, G.A. Peters, Pyrimidine Syntheses. I. Reaction of s-Triazine with Imidates and Amidines Containing an Acidic α-Methylene Group, J.org.Chem. 1962, 27, 548.
17. F.Eiden, B.S. Nagar, Oxazin- und Pyrimidinderivate aus Enamiden, Naturwissen Schaften;1963, 50, 403.

*****