Asian Journal of Chemistry Vol. 18, No. 1 (2006), 747–749

NOTE

Synthesis and Antimicrobial Activities of Some Substituted Pyrimidines and Pyrimidinothiocarbamides

S.U. PATIL† and P.B. RAGHUVANSHI*
Department of Chemistry, Brijlal Biyani Science College, Amravati, India

In this paper, guanidine carbonate was interacted with acetoacetic ester to synthesize 2-amino-4-hydroxy-6-methyl pyrimidine (I), which on further treatment with phenylisothiocyanate and methyl-isothiocyanate gave 1-(4-hydroxy-6-methyl pyrimidino)-3-phenyl thiocarbamide (Ia) and 1-(4-hydroxy-6-methyl pyrimidino)-3-methyl thiocarbamide (Ib). Similarly interaction of guanidine carbonate was carried out with ethyl-α-benzyl-β-keto butyrate to synthesize 2-amino-4-hydroxy-5-benzyl-6-methyl pyrimidine (II), which on further reaction with phenylisothiocynate and methylisothiocyanate gave 1-(4-hydroxy-5-benzyl-6-methyl pyrimidino)-3-phenyl thiocarbamide (IIa) and 1-(4-hydroxy-5-benzyl-6-methyl pyrimidino)-3-methyl thiocarbamide (IIb), respectively. The antimicrobial activities of these compounds were studied by using well diffusion assay method.

Key Words: Synthesis, Antimicrobial activities, Substituted, Pyrimidines and pyrimidinothiocarbamides.

Various forms of guanidine have their own identity and importance in organic chemistry. Different guanidine salts were used as intermediate for the synthesis of pyrimidino, triazino and different heterocyclic compounds. Heterocyclic compounds having pyrimidino nucleus and triazino nucleus possess medicinal, pharmaceutical, agricultural and industrial values[1–6]. Recently, some physico-chemical analyses of some triazino compounds were carried out[7]. Literature survey reveals that antimicrobial activities of the synthesized compounds are still lacking. In view of different applications of pyrimidino compounds it was thought interesting to study the antimicrobial activities of some synthesized pyrimidines and pyrimidinothiocarbamides.

All chemicals used were of AR grade (Merck, India) except guanidine carbonate (Lancaster, Germany). Ethyl-α-benzyl-β-keto butyrates[8] and phenyl-isothiocynate and methylisothiocynate[9] were prepared as described.

†Department of Chemistry, S.S.K.R. Innani Mv. Karanja (Lad), India.

2-Amino-4-hydroxy-6-methyl pyrimidine (I)

A reaction mixture of acetoacetic ester (0.1 M), guanidine carbonate (0.1 M) and absolute alcohol (50 mL) was refluxed on a water bath for 8 h to obtain **(I)**, (73%), m.p. 190°C. It gave red colouration with aqueous ferric chloride solution indicating presence of phenolic group. It gave dye test indicating presence of primary aromatic amino group. (Anal. $C_5H_7N_3O$: Found N 36.07%; Calcd. N 37.63%).

1-(4-Hydroxy-6-methylpyrimidino)-3-phenyl thiocarbamide (IIa)

A reaction mixture of **(I)** (0.1 M), phenylisothiocyanate (0.1 M) and acetone (50 mL) was refluxed on a water bath for 8 h; brown crystals of **(Ia)** separated out on cooling (78%), m.p. 168°C. It gave alkaline plumbite test for sulphur. It gave negative dye test indicating the absence of primary aromatic amino group.

PMR, $CDCl_3$ + DMSO, d_6: 2.5 {3H (CH_3), 7.2–7.6 {5H (Ar—H)}, 8.8 {2H (NH)}, 9.3 {1H (Ar—OH)}. The signal at 3.9 is due to moisture in DMSO-d_6.

Similarly 1-(4-hydroxy-6-methyl pyrimidino)-3-methyl thiocarbamide **(Ib)** was prepared by the interaction of **(I)** with methylisothiocyanate (69%), m.p. 159°C. **(Ib)** also gave negative dye test and positive alkaline plumbite test. Compounds **(Ia)** and **(Ib)** both gave satisfactory C, H, N, S analysis.

2-Amino-4-hydroxy-5-benzyl-6-methyl pyrimidine (II)

Interaction of guanidine carbonate (0.1 M), ethyl-α-benzyl-β-keto butyrates (0.1 M) was carried out in ethanol (50 mL) medium on a water bath for 16 h to obtain **(II)**, m.p. 216°C. Aqueous solution of product when treated with aqueous ferric chloride solution gave red colouration indicating presence of phenolic group. It also gave dye test indicating the presence of primary aromatic amino group. ($C_{12}H_{13}N_3O$: Found N 19.08%; Calcd. N 19.53%).

1-(4-Hydroxy-5-benzyl-6-methyl pyrimidino)-3-phenyl thiocarbamide (IIa)

A reaction mixture of **(II)** (0.1 M), phenylisothiocyanate and acetone (50 mL) was refluxed on a water bath for 8 h to obtain needle-shaped yellowish crystals of **(IIa)** (68%), m.p. 198°C. It gave alkaline plumbite test. It did not give dye test, indicating absence of primary aromatic amino group.

PMR, $CDCl_3$ + $DMSOd_6$: {3H (CH_3)}, 4.5{(2H (CH_2)}, 6.2 {2H (NH)}, 7.2–7.6 {10H (Ar—H)}, 10.7 {1H (Ar—OH)}. The signals at 2.2–2.5 and 1.2–1.4 due to DMSO-d_6.

Similarly, 1-(4-hydroxy-5-benzyl-6-methyl pyrimidino)-3-methyl thiocarbamide **(IIb)** was prepared by interaction of **(II)** with methylisothiocyanate in acetone medium to obtain **(IIb)** (72%), m.p. 183°C.

Antimicrobial Activity

All the above compounds were tested against pathogenic bacteria for their antimicrobial activities by using well diffusion assay method[10]. The organisms tested were *Pseudomonas aeruginosa, Staphylococcus aureus, Proteus vulgaris* and *Escherichia coli*. The sizes of the zones of inhibition were measured by

antibiotic zone reader (Metzer make) and reported in cm. The results are cited in Table-1.

TABLE-1
SIZE OF ZONES OF INHIBITION USING ANTIBIOTIC ZONE READER

Compound No.	*P. aeruginosa* (cm)	*S. aureus* (cm)	*P. vulgaris* (cm)	*E. coli* (cm)
I	0.48	—	0.42	1.03
Ia	1.01	0.52	0.87	1.31
Ib	0.83	0.43	0.83	1.21
II	0.98	0.58	0.68	1.30
IIa	1.12	0.72	1.01	2.10
IIb	1.02	0.68	0.98	1.48

All the four organisms studied were human pathogens. From Table-1, it is clear that the following compounds were effective against the said organisms. It is also clear that all compounds showed remarkable antimicrobial activities against *E. coli*. Compounds **II, IIa** and **IIb** showed more activities than **I, Ia** and **Ib.** More activity of these compounds may be due to the presence of benzyl group in pyrimidino nucleus which activates these compounds.

It is also observed that **Ia** and **IIa** show more activity. This may be due to presence of phenyl group in thiocarbamidino group in the compound.

ACKNOWLEDGEMENTS

The authors are thankful to Dr. Lohiya, Principal, Brijlal Biyani Science College, Amravati; Dr. Deshpande, Principal and Dr. A.Y. Deshmukh, S.S.R.K. Innani Mv., Karanja (Lad); Dr. D.T. Tayade, Department of Chemistry, S.R.R.L. Science College, Morshi; R.S.I.C, Chandigarh for spectral analysis; Dr. Mrs. Keerti Dubey and Dr. V.S. Dubey for counting antimicrobial activities.

REFERENCES

1. Park Davis and Co., British Patent, 48, 245 (1960).
2. M. Seidel and F.E. Betiver, *S. African Patent*, 68, 03, 47 (1964).
3. A.G. Ghaigh (Jr.), Siess Patent, 393, 344 (1965).
4. S. Richard, S. Robi and P. Jackson, *J. Am. Chem. Soc.*, **84**, 589 (1951).
5. P. Jackson, A. Joseph and T. Podell, *J. Am. Chem. Soc.*, **123**, 169 (1961).
6. E.A. Fako, S. DDu Breuil and G.H. Hitching, *J. Am. Chem. Soc.*, **73**, 3758 (1951).
7. D.T. Tayade, S.P. Dhakite and S.U. Patil, *Asian J. Chem.*, **15**, 379 (2003).
8. R.G. Weginwar, Project Report, M.Sc., Nagpur University (1987).
9. A.I. Vogel, Text Book of Practical Organic Chemistry including Qualitative Organic Analysis, ELBS and Longman Green and Co. Ltd., p. 615 (1954).
10. D.T. Tayade, Ph.D. Thesis, Amravati University, Amravati (1998).

(*Received*: 21 March 2005; *Accepted*: 27 October 2005) AJC-4479