Asian Journal of Chemistry Vol. 19, No. 1 (2007), 821–822

NOTE

Synthesis and Antimicrobial Activity of 2,3-(Substituted Phenyl) Pyrazine Dicarboxamide

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Pyrazine derivatives are synthesized from quinoline and screened for their antimicrobial activity against *Eschericia coli, Bacillus subtilis, Trichoderma* sp. and *Aspergillus niger.*

Key Words: 2,3-(Substituted phenyl) pyrazine dicarboxamide, Antimicrobial activity.

Pyrazine[1] or 1,4-diazine is a symmetrical molecule as the nitrogen atoms occupy the 1,4-positions. Pyrazine and several polyclinics such as pteridine and phenazine occur in nature. Pyrazines have long been of interest for medicinal chemists[2]. Their derivatives are found to be useful as antibiotics, diuretics and anti-tumor agents[3].

2-3-Pyrazine dicarboxylic acid

Quinomaline (1.2 mol) and demineralized water 1000 mL is taken and temperature raised to 90°C. $KMnO_4$ (6.6 mol) is slowly added during 1½ h. The reaction mixture is cooled to room temperature and recrystallized from water.

2,3-Pyrazine dimethyl ester

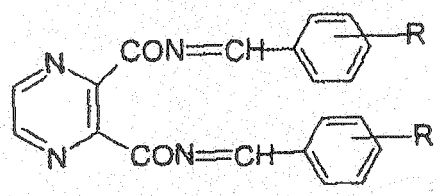
Pyrazine dicarboxylic acid (0.01 mol) and 5 g H_2SO_4 in methanol (100 mL) are mixed and the mixture is refluxed for 20 h, cooled to room temperature and filtered. The mixture is neutralized with Na_2CO_3 solution. and then extracted with 100 mL toluene. The toluene layer is then distilled completely under vacuum at below 60°C.

2,3-Pyrazine dicarboxamide

Methanol (100 mL) is taken in a three-necked flask. Ammonia is passed through one neck and one neck is placed outside such that excess ammonia goes out. The percentage of solution to be 20–25%. The reaction mixture is cooled to 0–5°C. 2,3-Pyrazine dimethyl ester is added during 1 h. The mixture is stirred for 2–3 h, then filtered and washed with methanol and water.

2,3-(Substituted phenyl) pyrazine dicarboxamide

A reaction mixture containing aromatic aldehyde (0.02 mol) and 2,3-pyrazine dicarboxamide (0.01 mol) in glacial acetic acid (40 mol) is refluxed for 4 h. The resulting mixture is washed with water and recrystallized from glacial acetic acid (Fig. 1).



R = C_6H_5, 4-$OCH_3C_6H_4$, 4-ClC_6H_4, 2-furyl, 4-OH-C_6H_5, 4-OH-3-$OCH_3C_6H_3$

Fig. 1

Antimicrobial activity

The antimicrobial activity is determined by using filter paper disc diffusion method[4] by measuring in mm. All the compounds are screened *in vitro* for their antimicrobial activity against bacteria and fungi. The activity is to be determined by using 4% solutions. All the compounds show much higher activity than the standard solutions of the standard drugs griseofluvin (for fungi) and streptomycin (for bacteria).

TABLE-1
ANTIMICROBIAL ACTIVITY OF COMPOUNDS

Compd.	R	Antibacterial activity		Antifungal activity	
		E. coli	*B. subtilis*	*Trichoderma sp.*	*Aspergillus niger*
1a	—C_6H_5	24	24	22	21
1b	4-OCH_3-C_6H_4	20	19	23	20
1c	4-Cl-C_6H_4	22	21	20	21
1d	2-Furyl	19	22	19	22
1e	4-OH-3-OCH_3-C_6H_3	23	22	22	20
Streptomycin (standard)		10	8		
Griseofulvin (standard)				12	10

ACKNOWLEDGEMENT

The authors are thankful to the Head, Department of Chemistry, Dr. H.S. Gour University for providing laboratory facilities. The authors are also thankful to Dr. Mrs. Archana Mehta and Mr. Vivek Agnihotry of Botany Department for their help in carrying out antimicrobial activities.

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(*Received*: 21 April 2006; *Accepted*: 24 June 2006) AJC-5022