Asian Journal of Chemistry Vol. 9, No. 3 (1997), 395–398

Synthesis and Antibacterial Screening of some Pyrazine-carboxamidomethyl Derivatives

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Some pyrazinecarboxamidomethyl derivatives were synthesized and screened for their antibacterial activity against some gram positive and gram negative bacteria.

INTRODUCTION

A number of pyrazinecarboxamide derivatives have been reported to have good biological activities[1–5] and a few derivatives are reported to have antiseptic properties.[6] The compounds of present study have been synthesized by condensing N-hydroxy-methyl-pyrazinecarboxamide with selected compounds with a view to obtain more active compounds.

EXPERIMENTAL

N-Hydroxymethyl pyrazinecarboxamide (I)[7]

Pyrazinecarboxamide (I) (12.3 g) was warmed with formaldehyde (30 mL, 37% v/v) and potassium carbonate solution (20 mL, 11% v/v) on a water bath till a clear solution was obtained. The reaction mixture was allowed to cool and set aside for three days at room temperature. A white amorphous powder appeared. The powder was collected, washed with small quantities of icecold distilled water and crystallised from ethanol (yield 70%, m.p.118°C).

Pyrazinecarboxamidomethyl derivatives (II–IV)

Using Tscherniac procedure[8], compound (Ia) and the selected compounds (salicylic acid, nitrofurazone and thymol), in equimolar quantities, were dissolved in concentrated sulfuric acid (20 mL) separately and kept at 25°C for 2 days. Then the reaction mixture was poured on crushed ice to obtain the crude product, which was filtered and washed with water and crystallised from appropriate solvent.

Pyrazinecarboxamidomethyl derivatives (V–VII)

Using Einhorn procedure,[8] compound (Ia) and the selected compounds (resorcinol, β-naphthol and β-resorcylic acid) in equimolar quantities, were dissolved in minimum quantity of ethanol separately. Then 2 mL concentrated hydrochloric acid was added and contents were refluxed for 2 h on a water bath. The product separated out simply on cooling or diluting with cold water, which was filtered and washed with water and crystallised from appropriate solvent.

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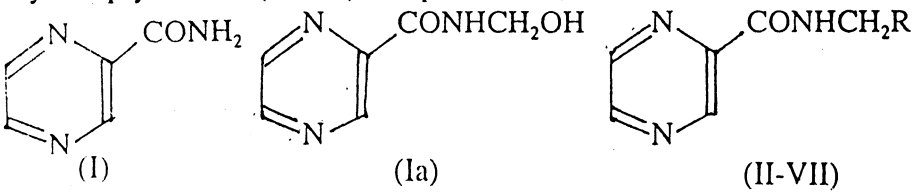
RESULTS AND DISCUSSION

In order to synthesize pyrazinecarboxamidomethyl derivatives (II–VII), N-hydroxymethyl-pyrazinecarboxamide (Ia) was condensed with selected compounds using either Tscherniac or Einhorn method with minor modifications in the quantities of acids used or in the reflux temperature, to get better yields.

The purity of the synthesized compounds was checked by TLC using benzene: methanol (2 : 3) solvent system. The structures of these compounds are supported by their physical data (Table-1) and spectral data (Table-2).



(I) (Ia) (II-VII)

(II) R = —$C_6H_3(OH)COOH$
(III) R = —$HNCOHNN{=}CH(C_4H_2O)NO_2$
(IV) R = —$C_6H_2(OH)(CH_3)(CH(CH_3)_2)$
(V) R = —$C_6H_3(OH)_2$
(VI) R = —$C_{10}H_6OH$
(VII) R = —$C_6H_2(OH)_2COOH$

Fig. 1

TABLE-1
PHYSICAL AND BACTERICIDAL DATA OF
PYRAZINECARBOXAMIDOMETHYL DERIVATIVES

Compod. No.	Molecular formulae/Colour	m.p. (°C)	Yield %	Antibacterial activity (Average, zones of inhibition in mm)							
				B.p.	*B.s.*	*St.al.*	St.au.	P.m.	Sa.p.	Sa.t.	V.c.
I	$C_5H_5N_3O$ White	191	—	11	8	9	11	9	9	10	9
II	$C_{13}H_{11}N_3O_4$ Yellow	85	75	14	10	12	13	10	11	12	11
III	$C_{12}H_{11}N_7O_5$ Chocolate	230	55	16	16	13	12	14	23	14	11
IV	$C_{16}H_{19}N_3O_2$ Black	82	60	13	10	14	12	11	10	9	11
V	$C_{12}H_{11}N_3O_3$ Turmeric yellow	148	65	12	11	13	14	11	10	11	12
VI	$C_{16}H_{13}N_3O_2$ Pinkish brown	147	70	12	12	13	11	14	11	12	13
VII	$C_{13}H_{11}N_3O_5$ Dirty brown	118	50	12	10	13	12	12	13	11	12

D—Decomposition temperature. All the compounds gave satisfactory C, H and N analysis.
B.p.—Bacillus pumilus, B.s.—Bacillus subtilis, St.al.—Staphylococcus albus, St.au.—Staphylococcus aureus, P.m.—Pseudomonas mangiferae, Sa.p.—Salmonella paratyphi, Sa.t.—Salmonella typhi, V.c.—Vibrio cholerae.

TABLE-2
IR SPECTRAL DATA OF SYNTHESIZED COMPOUNDS (II–VII)

Compound No.	Absorption bands (cm^{-1})	Assignments*[9]
(II and IV–VII)	3610	CO stretching of phenolic OH
(II and VII)	1680	C==O vibrations of aryl COOH
(II—VII)	1640	C==N stretching of pyrazine nucleus
(II—VII)	1630	CO stretching (amide I band)
(II and IV–VII)	1622	Vibrations of phenyl ring
(II–VII)	1600	NH stretching of secondary amides
(III)	1580 1543	C—NO_2 vibrations C—NO_2 vibrations
(II and IV—VII)	1505	Vibrations of phenyl ring
(III)	1350	C—NO_2 vibrations
(II and IV-VII)	1300	CO stretching of phenolic OH
(II–VII)	1290	Combination of OCN and NH deformation
(II and IV–VII)	1200	CO stretching of phenolic OH
(IV)	1175 1140	Skeletal vibration of *gem* dimethyl group Skeletal vibration of *gem* dimethyl group
(III)	1015 800	Vibration of furan nucleus Vibration of furan nucleus
(II–VII)	700 620—600	NH deformation (amide V band) NH stretching (amide IV and VI bands)

*The absence of CO stretching and OH deformation near 1075–1010 cm^{-1} shows that methylene carbon of side chain of (Ia) is attached to the active hydrogen site of the selected compounds. This attachment is further supported by negative test of primary OH group.[10]

All these compounds (II–VII) were screened for their antibacterial activity against some gram positive and gram negative bacteria (Table 1).

Screening for Antibacterial Activity

The synthesized compounds (II–VII) (0.2% w/v in 10% v/v DMF) were tested against *Bacillus pumilus (B. p.), Bacillus subtilis (B. s.), Staphylococcus albus (St. al.)* and *Staphylococcus aureus (St. au.)* (all gram positive) and *Pseudomanas mangiferae (P. m.), Salmonella paratyphi (Sa. p.), Staphylococcus typhi (Sa. t.)* and *Vibrio cholerae (V. c.)* (all gram negative). Filter paper disc method[11] was applied using nutrient agar medium[12], for antibacterial screening. The compound (I) was tried as standard (0.2% w/v in 10% v/v DMF).

All the six compounds (II–VII) showed improved antibacterial activity with a remarkable activity in compound (III).

ACKNOWLEDGEMENT

The authors are thankful to the Head, Department of Pharmaceutical Sciences, Dr H.S. Gour Vishwavidyalaya, Sagar for providing necessary facilities.

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(*Received:* 17 September 1996; *Accepted*: 21 January 1997) AJC-1217