Synthesis of 1-Carboxamido-3,5-Diaryl-Δ^2-Pyrazolines and Their Antimicrobial Study

R.M. KEDAR
Department of Chemistry
Shri Shivaji Science College, Amravati-444 603, India

Nine chalcones were obtained by condensing acetophenones with aromatic aldehydes in ethanolic NaOH. Their structures were confirmed by physical as well as chemical methods. These chalcones were then reacted with semicarbazide hydrochloride in presence of aqueous alkali in ethanol to get 1-carboxamido-3,5-diaryl-Δ^2-pyrazolines. The structures of these compounds were established on the basis of chemical properties and spectral analysis. These compounds were subjected to antimicrobial tests against the test organisms: *Klebsiella pneumoniae, Escherichia coli, Proteus mirabilis, Staphylococcus aureus, Shigella dysentery and Salmonella typhi.* It has been found that the compounds containing chloro and dimethylamino groups as substituents enhance the antimicrobial activity.

INTRODUCTION

Pyrazolines are known to possess fungicidal[1], insecticidal[2] and bactericidal[3] properties. The synthesis of 1-carboxamido-Δ^2-pyrazolines from epoxy ketones and semicarbazide has been reported by El Hashash[4]. Saraf[5] reported the formation of 5-phenyl-3-(2-methyl-4-oxo-4H-1-benzopyran-3-yl)-Δ^2-pyrazoline-1-carboxamides from 3-cinnamoyl-2-methylchromone and semicarbazide in ethanol containing little acetic acid. Thakare[6] synthesised 1-carboxamido--3-(2-hydroxyphenyl)-5-aryl-Δ^2-pyrazolines by the reaction between 2′-hydroxychalcones and semicarbazide hydrochloride in ethanol.

The work presented here describes the synthesis of 1-carboxamido-3,5-diaryl-Δ^2-pyrazolines obtained from newly synthesised chalcones and their antimicrobial study.

EXPERIMENTAL

Nine chalcones **(Ia–i)** were prepared by reacting acetophenones (0.1 mol) with aromatic aldehydes (0.1 mol) in ethanolic NaOH. They were filtered, washed with water and recrystallised from ethanol to obtain bright orange coloured crystalline solids. Their structures were confirmed by chemical as well as physical methods.

These chalcones **(Ia–i)** were then reacted with semicarbazide hydrochloride in presence of aqueous alkali in ethanol to get 1-carboxamido-3,5-diaryl-Δ^2-pyrazolines. The structures of these compounds were established on the basis of chemical properties and spectral analysis. Their melting points are shown in Table-1.

TABLE-1
COMPOUNDS SYNTHESISED AND THEIR MELTING POINTS

No.	Compound	m.p. (°C)
1.	1-Carboxamido-3-(2-hydroxy-5-chlorophenyl)-5-(4-dimethyl-aminophenyl)-Δ^2-pyrazoline	232
2.	1-Carboxamido-3-(2-hydroxy-5-chlorophenyl)-5-(phenyl)-Δ^2-pyrazoline	194
3.	1-Carboxamido-3-(2-hydroxy-5-chlorophenyl)-5-(4-methoxyphenyl)-Δ^2-pyrazoline	207
4.	1-Carboxamido-3-(2-hydroxy-5-chlorophenyl)-5-(2-furyl)-Δ^2-pyrazoline	196
5.	1-Carboxamido-3-(2-hydroxyphenyl)-5-(4-dimethyl-aminophenyl)-Δ^2-pyrazoline	227
6.	1-Carboxamido-3-(2-hydroxy-5-methylphenyl)-5-(4-dimethyl-aminophenyl)-Δ^2-pyrazoline	235
7.	1-Carboxamido-3,5-(diphenyl)-Δ^2-pyrazoline	240
8.	1-Carboxamido-3-phenyl-5-(5-dimethylaminophenyl)-Δ^2-pyrazoline	229
9.	1-Carboxamido-3-phenyl-5-(4-methoxyphenyl)-Δ^2-pyrazoline	212

Spectral data

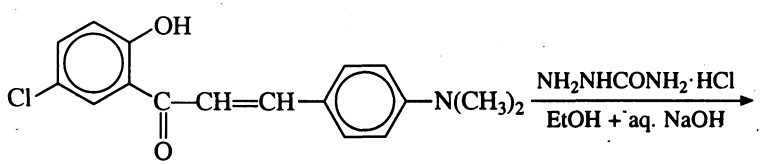
(I) IR (KBr): 3438 cm^{-1} ν(—OH phenolic), 1640 ν(C=O), 1546 ν(—CH=CH), 1172 ν(C—O stretching in phenols), 727 ν(C—Cl), 1025 ν[(C—N—$(CH_3)_2$)].

PMR ($CDCl_3$): 3.06 (S, 6H, $N(CH_3)_2$), 6.67–7.85 (m, 7H, Ar—H), 7.30 (d, 1H, =CH—), 7.90 (d, 1H, =CH—), 13.17 (S, 1H, —OH).

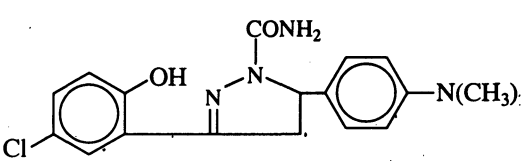
The compound is 2′-hydroxy-5′-chloro-4-dimethylamino chalcone **(Ia)**.

(II) IR (KBr)-3461 ν(phenolic OH), 3291 ν(—$CONH_2$), 1605 ν(> C=N), 1642. ν(—CH_2), 1019 ν(N<$^{CH_3}_{CH_3}$), 761 ν(C—Cl), 3.60 (dd, 1H, >CHBH), 4.90 (t, 1H, >CHX), 5.9–6.05 (s, 2H, —$CONH_2$), 6.65–7.86 (m, 7H, AR—H), 9.88 (s, 1H, Ar—OH).

Reaction:



(Ia)



(IIa)

The compound is: 1-Carboxamido-3-(2-hydroxy-5-chlorophenyl)-5-(4-dimethylaminophenyl)-Δ^2-pyrazoline **(IIa)**.

Antimicrobial Activity of the compounds

These compounds were assayed for their antimicrobial activities[7] against six test organisms, namely, *Klebsiella pneumoniae, Escherichia coli, Proteus mirabilis, Staphylococcus aureus, Shigella dysentery and Salmonella typhi*[8]. Further their MIC values against these organisms were determined by 'serial dilution method' using DMF as a solvent. The results are given in Table-2.

TABLE-2
ANTIMICROBIAL ACTIVITY OF THE COMPOUNDS

Sr. No.	Compound	MIC value (in mg/mL) against test organism					
		K. pneumoniae	*E. coli*	P. mirabilis	*S. aureus*	*S. dysentery*	*S. typhi*
1.	1-Carboxamido-3-(2-hydroxy-5-chlorophenyl)-5-(4-dimethyl-aminophenyl)-Δ^2-pyrazoline **(IIa)**	31	62	16	62	125	62
2.	1-Carboxamido-3-(2-hydroxy-5-chlorophenyl)-5-(phenyl)-Δ^2-pyrazoline **(IIb)**	125	500	500	–	250	500
3.	1-Carboxamido-3-(2-hydroxy-5-chlorophenyl)-5-(4-methoxyphenyl-)-Δ^2-pyrazoline **(IIc)**	62	125	125	250	500	125
4.	1-Carboxamido-3-(2-hydroxy-5-chlorophenyl)-5-(2-furyl)-Δ^2-pyrazoline **(IId)**	125	500	125	500	250	250
5.	1-Carboxamido-3-(2-hydroxy-phenyl)-5-(4-dimethyl-aminophenyl)-Δ^2-pyrazoline **(IIe)**	62	–	62	250	–	125
6.	1-Carboxamido-3-(2-hydroxy-5-methylphenyl)-5-(4-dimethyl-aminophenyl)-Δ^2-pyrazoline **(IIf)**	62	–	62	125	250	16
7.	1-Carboxamido-3,5-diphenyl-Δ^2-pyrazoline **(IIg)**	250	125	500	–	500	–
8.	1-Carboxamido-3-phenyl-5-(5-dimethylaminophenyl)-Δ^2-pyrazoline **(IIh)**	62	–	62	125	–	62
9.	1-Carboxamido-3-phenyl-5-(4-methoxyphenyl)-Δ^2-pyrazoline **(IIi)**	125	500	125	–	500	250

RESULTS AND DISCUSSION

These compounds when tested for their antimicrobial activity against *K. pneumoniae, E. coli, P. mirabilis, S. aureus, S. dysentery* and *S. typhi* (at a temperature of 37°C) (±1°C), a large number of them showed positive results.

83% of the total samples tested showed antimicrobial activity. All the compounds have been found to be active against *K. pneumoniae* and *P. mirabilis*. The compound **IIa**, **IIc** and **IId** are found to be active against all the organisms. All these compounds contain —Cl as a common substituent. However, MIC values of **IIa**, which contains $-N(CH_3)_2$ group as another substituent in addition to —Cl, are much more smaller than those of **IIc** and **IId**. It can therefore be concluded that the compounds containing chloro and dimethylamino group as substituents enhance the antimicrobial activity.

REFERENCES

1. N.B. Das and A.S. Mitra, *Indian J. Chem.*, **16B**, 638 (1978).
2. S.G. Roelofan, C. Arnold and Wellmgak, *J. Agric. Food Chem.*, **27**, 406 (1979).
3. H.Z. Katri and S.A. Vunii, *J. Indian Chem. Soc.*, **58**, 168 (1981).
4. M.A. El-Hashash, M. Al-Kady, M.A. Sayed and A.A. Elsawy, *Egypt. J. Chem.*, **27**, 718 (1984).
5. B.D. Saraf, Ph.D. Thesis, Amravati University (1988).
6. V.G. Thakare, Ph.D. Thesis, Amravati University (1988).
7. C.G. Donald and A.R. William, in: Assay Methods of Antibiotics: A Lab. Manual Medical Encyclopedia Ind. (1955).
8. N.S. Egorov, Antibiotics: A Scientific Approach, Mir Publishers, Moscow, pp. 136, 170–71 (1985).

(*Received*: 5 September 2000; *Accepted*: 4 December 2000) AJC-2206