

NOTE

Synthesis and Antifungal Activity of Some 2-Oxothiazolidinopyrazolines

DEVENDRA PANDEY†, AJENDRA KUMAR† and A.K. NAG*
P.G. Department of Chemistry, Gaya College, Gaya-823 001, India.

Pyrazolines are synthesised from reaction of hydrazines with unsaturated aldehydes or ketones. The intermediate hydrazones generally rearrange to pyrazolines on refluxing with acetic acid. Acrolein gives both, a phenylhydrazone and 1-phenyl pyrazoline. Benzal acetone, phenyl propenyl ketone, cinnamaldehyde, etc. give corresponding pyrazolines.

The research work described in this paper is based upon the synthesis of pyrazolines in which a thiazolidine ring is fused. This particular area of study was chosen on account of the wide range of biological activities exhibited by either ring system and it was anticipated that their annealation might give rise to compounds of exceptional interest.

Tetrahydro derivative of thiazole is known as thiazolidine and the oxoderivative of thiazolidine is called thiazolidinone. Thiazolidinones are the important group of compounds of this class. A large number of thiazolidinones are reported in literature for their biological activities such as hypotonic¹, anaesthetic², analgesic³, antibiotic⁴, antifungal⁵, etc., pyrazoline derivatives are also reported to possess antifungal⁶, antidiabetic⁷, herbicidal⁸, anaesthetic⁹, antifertility¹⁰, sedative¹¹ and antimicrobial¹² activities.

Melting points were taken in open capillaries in sulphuric acid bath and are uncorrected. IR spectra in KBr pellets were recorded on a Perkin-Elmer spectrophotometer (ν_{\max} in cm^{-1}) at CDRI Lucknow.

2-Iminothiazolidinone-4 (I)

A mixture of thiourea (0.5 mole), ethanol (250 mL) and chloroacetic acid (0.6 mole) was refluxed for 3 h. It was allowed to cool; the solid was filtered and washed with ethanol. The crude hydrochloride obtained was dissolved in boiled water (75 mL). After 24 h, the crystals were filtered, washed and crystallized from ethanol.

2-Imino-5-Benzylidene-4-Thiazolidinone (II-VI)

Compound (I) (0.05 mole), glacial acetic acid (30 mL), fused sodium acetate (0.05 mole) and aryl aldehyde (0.05 mole) were refluxed for 2 h. After cooling the solid was filtered, washed with alcohol and crystallized from glacial acetic acid.

†Department of Chemistry, K.B.P.G. College, Mirzapur (U.P.), India

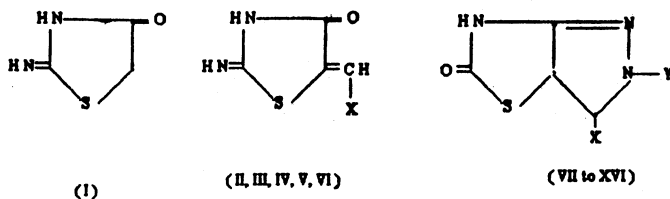
TABLE-1
ANALYTICAL AND SPECTRAL DATA OF 2-OXOTHIAZOLIDINOPYRAZOLINES

Compound number	m.p. (°C)	Yield (%)	m.f.	IR peaks (cm ⁻¹)
(VII)	270	70	C ₁₀ H ₉ N ₃ OS	1590 ν(C=N), 1690 ν(C=O), 3120 ν(NH)
(VIII)	265	7	C ₁₀ H ₉ N ₃ O ₂ S	1600 ν(C=N), 1690 ν(C=O), 3040-ν(NH)
(IX)	325	60	C ₁₁ H ₁₁ N ₃ O ₂ S	1580 ν(C=N), 1680 ν(C=O), 3100 ν(NH)
(X)	311	70	C ₁₁ H ₁₁ N ₃ O ₂ S	1585 ν(C=N), 1680 ν(C=O), 3120 ν(NH)
(XI)	318	60	C ₁₁ H ₁₁ N ₃ O ₃ S	1500 ν(C=N), 1690 ν(C=O), 3280 ν(NH)
(XII)	223	65	C ₁₆ H ₁₃ N ₃ OS	1590 ν(C=N), 1670 ν(C=O), 3120 ν(NH)
(XIII)	240	60	C ₁₆ H ₁₃ N ₃ O ₂ S	1520 ν(C=N), 1680 ν(C=O), 3040 ν(NH)
(XIV)	215	60	C ₁₇ H ₁₅ N ₃ O ₂ S	1590 ν(C=N), 1590 ν(C=O), 3280 ν(NH)
(XV)	276	60	C ₁₇ H ₁₅ N ₃ O ₂ S	1580 ν(C=N), 1680 ν(C=O), 3290 ν(NH)
(XVI)	260	60	C ₁₇ H ₁₅ N ₃ O ₃ S	1540 ν(C=N), 1700 ν(C=O), 3200 ν(NH)

All the compounds gave satisfactory, C, H and N analysis.

2-Oxothiazolidine-Δ²-5-Phenyl (substituted) Pyridoxine (VII–XVI)

A mixture of one of the compounds (V–VI) (0.05 mole) hydrazine or phenyl hydrazine (2 mL) and glacial acetic acid (40 mL) were refluxed for 2 h. After cooling the crystals were filtered, washed with ethanol and crystallized from glacial acetic acid. 2-Oxothiazolidinopyrazolines (VII–XI) and (XII–XVI) were obtained by using hydrazine and phenyl hydrazine, respectively with corresponding arylidene derivatives (II–VI).



In order to synthesize 2-oxothiazolidinopyrazolines, 2-iminothiazolidinone-4 (I) was allowed to react with some aromatic aldehyde to give the corresponding arylidene derivatives (II–VI). These arylidines were then concentrated to 2-oxothiazolidinopyrazolines^{13, 14} (VII–XVI) when reacted with hydrazine or phenyl hydrazine. The structures of these compounds are supported by their analytical and spectral results.

All these compounds (VII–XVI) were screened for their antifungal activity against *Aspergillus flavus* and *Ustilago tritici* (Pers) Roster as the test fungi.

- II X = C₆H₅
 III X = 2-OH-C₆H₄
 IV X = 2-MeO-C₆H₄

V	X = 4-MeO-C ₆ H ₄	
VI	X = 3-MeO-4-OH-C ₆ H ₃	
VII	X = C ₆ H ₅	Y = H
VIII	X = 2-OH-C ₆ H ₄	Y = H
IX	X = 2-MeO-C ₆ H ₄	Y = H
X	X = 4-MeO-C ₆ H ₄	Y = H
XI	X = 3-MeO-4-OH-C ₆ H ₃	Y = H
XII	X = C ₆ H ₅	Y = C ₆ H ₅
XIII	X = 2-OH-C ₆ H ₄	Y = C ₆ H ₅
XIV	X = 3-MeO-C ₆ H ₄	Y = C ₆ H ₅
XV	X = 4-MeO-C ₆ H ₄	Y = C ₆ H ₅
XVI	X = 3-MeO-4-OH-C ₆ H ₃	Y = C ₆ H ₅

Compounds (VII–XVI) were screened for their antifungal activity against *Aspergillus flavus* and *Ustilago tritici* (Pers) Roster as the test fungi by Food Poison Technique at concentration levels (0.05, 0.10, 0.15) in Czepak Dox Agar medium (% w/v). The incubation temperature was maintained at 25°C for three days. The spores were sprayed on the medium by sterilized camel hair brush; pure medium was tried as control.

All the ten compounds were found to be active against both the fungi. The concentration, compounds and fungus in which the maximum efficacy was obtained are 0.15% for (XV) and *Aspergillus flavus* respectively.

REFERENCES

1. W.J. Doran and M.A. Shonle, *J. Org. Chem.*, **3**, 193 (1938).
2. F.P. Luduena and J.O. Hoppe, *J. Am. Phar. Ass.* **40**, 122 (1951).
3. Jones, Robinson and Strachan, *J. Am. Chem. Soc.*, **75**, 4845 (1953).
4. H. Peter, Crackett, Chandra, M. Pant and Richard, *Perk Trans.*, **1**, 2785 (1984).
5. P.C. Joshi (Jr.) and P.C. Joshi (Sr.), *J. Indian Chem. Soc.*, **61**, 434 (1984).
6. R.B. Pathak and S.C. Bahal, *J. Indian Chem. Soc.*, **57**, 1108 (1980).
7. Rajeev Jain, N.R.N. Goyal and Sharad Agarawal, *J. Indian Chem. Soc.*, **58**, 203 (1981).
8. James Bick and Robert Peter, *Chem. Abstr.*, **87**, 135405C (1977).
9. I.R. Andrisano, L. Chierice and F. Caraveri, *Chem. Abstr.*, **5249** (1959).
10. Krishna. Joshi, V.N. Pathak and Sharda Sharma, *J. Indian Chem. Soc.*, **61**, 1014 (1954).
11. Andre Passedoueb and H. Rouses, *Chem. Abstr.*, **554**, 465 (1970).
12. Avison and A.C. Morrison, *J. Am. Chem. Soc.*, **72**, 1414 (1950).
13. V.S. Jolly, A.K. Srivastava and K.S. Tiwari, *J. Indian Chem. Soc.*, **57**, 539 (1980).
14. V.N. Mehrotra and R.S. Achari, *J. Indian Chem. Soc.*, **62**, 306 (1985).