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Synthesis of some new thiazolidin-4-ones as possible antimicrobial agents

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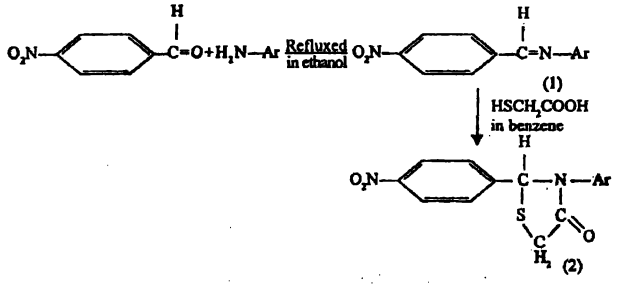
Five new 4-thiazolidinones (2a-e) have been synthesized. All the compounds have been screened *in vitro* for their antimicrobial and antifungal activities.

In continuation of our earlier work[1], five new thiazolidinon-4-ones have been synthesized and evaluated for their biological activities.

Results and Discussion

p-Nitrobenzaldehyde on condensation with primary heterocyclic amines gave heterocyclic Schiff bases (**1a-e**). The latter on reacting with thioglycolic acid in benzene gave five-membered cyclized products, 4-thiazolidinones (**2a-e**).



	Ar
1, 2a	pyridyl
b	thiazolyl
c	benzothiazolyl
d	4-methylpyridyl
e	pyrimidyl

Antimicrobial activity of the compounds was determined by serial dilution method[3]. The results are presented in Table 1. Among the compounds, **2c** was found to be most active against both *S. aureus* and *E. coli*. Antifungal study reveals (Table 1) that **2c** is most active against only two fungi *A. niger* and *A. flavus* and **2b** most active against *C. albicans* which is explained in terms of sulfur content per mole- cules of thiazolidinones. However, all the compounds were less active in comparison to ampicillin which was taken as a standard drug.

Table 1. Antibacterial and antifungal activity data (MIC values) in molar concentration ($\times 10^{-5}$) of **1a-e** and **2a-e***

Compd. no.	*S.a*	*E.c*	*A.n*	*A.f*	*C.a*
1a	22.00	22.00	11.00	11.00	11.00
b	10.72	10.72	10.72	10.72	10.72
c	8.83	8.83	8.83	8.83	8.83
d	20.74	20.74	10.37	10.37	10.37
e	10.96	21.92	10.96	10.96	10.96
2a	8.30	8.30	4.14	4.14	4.14
b	4.07	8.14	2.03	2.03	1.03
c	1.75	1.75	1.75	1.75	3.50
d	7.93	7.93	3.96	7.93	7.93
e	4.13	4.13	2.06	2.06	1.03
Ampicillin	0.68	2.72	1.36	1.36	1.36

**S.a = Staphylococcus aureus, E.c = Escherichia coli, A.n = Aspergillus niger, A.f = Aspergillus flauvs, C.a = Candida albicans.*

Experimental

All the chemicals (A.R. grade) were purified by distillation before use. The purity of the compounds was judged by TLC using benzene and methanol as solvent for Schiff bases and 4-thiazolidinones, respectively, and their C, H and N analyses. Sulfur was estimated by standard procedure[2]. M.ps. were determined in open cappillaries using a Toshniwal apparatus and are uncorrected. IR spectra (KBr) were recorded on a Jascco Report-100 spectrophotometer and PMR spectra ($CDCl_3$/DMSO-d_6) on a Varian EM-390 MHz spectrometer using TMS as internal reference.

Schiff bases (**1a-e**) : An equimolar (0.2 mol) mixture of *p*-nitrobenzaldehyde and primary heterocyclic amines was refluxed in dry ethanol (40 ml) for 12–18 h. The excess of ethanol was then distilled off under reduced pressure. The resulting solids were washed with ethanol followed by ether, dried and crystallized from benzene (yields 59–72%) : **1a**, m.p. 95°; **b**, 108°; **c**, 118°; **d**, 102°; **e**, 112°; ν_{max} 1615–1610 (C=N azomethine), 1550–1540 (Ar-NO_2); **1a** and **d** 630–620 (in-plane pyridine ring deformation), 420–410 (out-of-plane pyridine ring deformation); **1b** and **c** 690–685 (sym. C–S stretch), 655–650 (asym. C–S stretch), 1490–

1480 (C=N cyclic); **1e** 1570 cm^{-1} (pyrimidine ring bending vibration); **1a** δ 7.43–7.69 (4H, m, ArH), 7.74–7.86 (4H, m, pyridyl-H), 8.24 (1H, s, CH=N); **b** 7.30 (2H, s, thiazolyl-H), 7.39–7.63 (4H, m, ArH), 8.0 (1H, s, CH=N); **c** 7.00–7.30 (4H, m, benzothiazolyl-H), 7.48–7.70 (4H, m, ArH), 8.32 (1H, s, CH=N), **d** δ 2.32 (3H, s, pyridyl-CH_3), 7.46–7.62 (4H, m, ArH), 7.78–7.86 (3H, m, pyridyl-H), 8.22 (1H, s, CH=N), **e**, 7.32–7.41 (3H, m, pyrimidyl-H), 7.52–7.73 (4H, m, ArH), 8.28 (1H, s, CH=N).

4-Thiazolidinones (**2a-e**)[4] : A mixture of thioglycolic acid (0.004 mol) and **1a-e** (0.004 mol) was refluxed for 16–18 h in dry benzene (30 ml). The excess of benzene was then distilled off under reduced pressure and the contents were poured over crushed ice and centrifuged. The resulting solids were washed with ice-cold saturated solution of sodium bicarbonate followed by distilled of water, dried and crystallized from methanol (yields 40–60%) : **2a**, m.p. 185°, **b**, 172°; **c**, 184°; **d**, 205°; **e**, 198°; ν_{max} 1710–1700 (C=O of thiazolidinone ring), 1545–1535 (Ar-NO_2), 1235–1220 (C–S–C of thiazolidinone ring); **2a** and **d**, 635–625 (in-plane pyridine ring deformation), 415–405 (out-of-plane pyridine ring deformation); **2b** and **c**, 690–680 (sym. C–S stretch), 650–640 (asym C–S stretch), 1490–1480 (C=N cyclic), 1565 cm^{-1} (pyrimidine ring bending); **1a**, δ 2.62 (2H, s, S-CH_2), 7.19 (1H, s, CH–N), 7.52–7.76 (4H, m, ArH), 7.83–7.93 (4H, m, pyridyl-H); **b** δ 2.83 (2H, s, S–CH_2), 720 (1H, s, CH–N), 7.36 (2H, s, thiazolyl-H), 7.46–7.68 (4H, m, ArH); **c** δ 2.76 (2H, s, S–CH_2), 7.18 (1H, s, CH–N), 7.23–7.40 (4H, m, benzothiazolyl-H), 7.54–7.89 (4H, m, ArH); **d** δ 1.90 (3H, s, pyridyl-CH_3), 2.89 (2H, s, S–CH_2), 7.28 (s, CH–N), 7.42–7.70 (4H, m, ArH), 7.78–7.96 (3H, m, pyridyl-H); **e** δ 2.85 (2H, s, S–CH_2), 7.25 (1H, s, CH–N), 7.31–7.46 (3H, m, pyrimidyl-H), 7.66–7.86 (4H, m, ArH).

References

1 U Chandra and R C Sharma, *Proc Nat Acad Sci India, Sect A*, 1992, **62**, 739

2 A I Vogel, "Text Book of Quantitative Inorganic Analysis", 4th ed , Longman, London, 1978

3 D F Spooner and G J Sykes, "Methods in Microbiology", Academic, London, 1972

4 A R Surrey, *J Am Chem Soc* , 1947, **69**, 2911