Synthesis and Antibacterial Activity of Schiff bases and 4-Thiazolidinones

P. S. KENDEREKAR, R. F. SIDDQUI, P. S. PATIL, S. R. BHUSARE AND R. P. PAWAR*
Organic Chemistry Synthesis Laboratory, Dnyancpasak College, Parbhani-431 401.

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Some new Schiff bases (1a-g), 4-thiazolidinones (2a-g) have been synthesized and tested for their antibacterial activity. The structures of these compounds have been established on the basis of elemental analysis and spectral data (IR and $^1$H NMR).

Schiff bases and 4-thiazolidinones have been claimed to possess higher degree of anticancer and antitubercular activity, the biological activity of schiff bases were due to C=N linkage and the activity of 4-thiazolidinones were due to C-N-S linkage. The schiff bases were synthesized by the condensation of 2-hydroxy naphthaldehyde with different amine, the Schiff bases possess antitubercular, antitumour, fungicidal, medicinal and agrochemical activity. 4-Thiazolidinones have attracted considerable attention as they were also endowed with wide range of pharmaceutical activities. 4-Thiazolidinones from hydrazide, aromatic aldehydes and thioglycolic acid were found to be analgesic, antiseptic. 4-Oxathiazolidinones and 2-amino 4-oxathiazolidinones were reported as anti HIV, anticancer and antitubercular agents. Various 4-thiazolidinones derivatives occupy an important place in medicinal chemistry as they show a variety of pharmacological and microbiological activities, therefore an attempt was made to study the antibacterial activity of some new schiff bases and 4-thiazolidinones prepared in the present investigation.

Schiff bases (1a-g) were synthesized by the condensation of 2-hydroxy-3-iodo-5-bromobenzaldehyde with aromatic amine in ethanol. Compounds (1a-g) on cyclisation with mercapto acetic acid afforded corresponding 4-thiazolidinones (2a-g) as shown in Scheme 1. Melting points were uncorrected. IR spectra were recorded in nujol on Perkin-Elmer-237 spectrophotometer. $^1$H NMR were recorded in CDCl$_3$ on a Perkin-Elmer-R-32 spectrometer using TMS as internal standard (chemical shift are given in $\delta$ ppm).

*For correspondence
E-mail: rppawar@yahoo.com

Scheme 1: Synthetic scheme of Schiff bases prepared in this investigation.
TABLE 1: ANALYTICAL AND ACTIVITY DATA OF COMPOUNDS 1a-g AND 2a-g.

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Molecular formula</th>
<th>m.p. (°)</th>
<th>Yield (%)</th>
<th>Zone of Inhibition in mm*</th>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>E. c</td>
</tr>
<tr>
<td>1a</td>
<td>H</td>
<td>C_{12}H_{2}NOBrI</td>
<td>120</td>
<td>71</td>
<td>05</td>
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<tr>
<td>1b</td>
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<td>115</td>
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<td>68</td>
<td>19</td>
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<tr>
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<td>17</td>
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<tr>
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<td>140</td>
<td>66</td>
<td>06</td>
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<tr>
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<td>C_{13}H_{9}N_2O_3BrI</td>
<td>145</td>
<td>85</td>
<td>05</td>
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<td>189</td>
<td>82</td>
<td>06</td>
</tr>
</tbody>
</table>

Tetracycline | 20 | 20 | 20 | 20


To a mixture of 2-hydroxy-3-iodo-5-bromobenzaldehyde (10 mmol) and p-toluene (10 mmol) dissolved in ethanol, one drop of acetic acid was added. The reaction mixture was refluxed for 2 h. The content were poured on ice cooled water, separated solid was dried and crystallized from ethanol. IR (v max): 1635 (C=O), 1580, 1442 (C=C). 1H NMR (CDCl_3): 2.2 (s, 3H, CH_3), 8.5 (s, 1H, CH=H), 13.1 (s, 1H, OH), 7.0-7.5 (m, 6H, Ar-H). Anal. Cald. For C_{14}H_{10}NO_2SBrI (416.06): C, 40.42; H, 2.66; N, 3.37; Found C, 40.37; H, 2.63, N, 3.35.

To a solution of compound 1d (10 mmol) in dry dioxane (10 ml), a solution of mercapto acetic acid (10 mmol) in dry dioxane (10 ml) was added followed by catalytic amount of ZnCl_2 (15 mg) and the reaction mixture was refluxed for 8 h. The reaction was monitored by TLC. Solvent was evaporated under reduced pressure and separated residue was neutralized by sodium bicarbonate to remove excess of mercapto acetic acid. Solid compound obtained was crystallized from ethanol. IR (v max): 1665 (C=O), 1585, 1470 (C=C). 1H NMR (CDCl_3): 2.3 (s, 3H, CH_3), 4.2 (s, 2H, CH_2), 6.9 (s, 1H, N-CH), 7.5-8.5 (m, 6H, Ar-H), 13.3 (s, 1H, OH). Anal. Cald. For C_{14}H_{11}NO_2SBrI (490.16): C, 39.21; H, 2.67; N, 2.66; Found: C, 39.18; H, 2.66; N, 2.61.

Antibacterial activity was determined using disc diffusion method by measuring zone of inhibition. All the compounds were screened for their antibacterial activity using * Escherichia coli, Bacillus subtilis, Salmonella typhi and Salmonella dysenterae as test organisms. The compounds were tested at 150 ppm concentration using 5 mm filter paper disc. Control experiment was carried out under similar condition by using tetracycline as a standard for comparison. The inhibition zone measured in mm showed that compounds 1b, 1c, 1d, 2b, 2c and 2d were more active than other compounds tested against the above microbes, but none showed better or comparable activity to tetracycline (Table 1).

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REFERENCES

Reverse Phase HPLC Method for Simultaneous Estimation of Tizanidine Hydrochloride and Nimesulide in Tablets

M. S. SHINGARE*, K. R. NAIDU AND U. N. KALE
Department of Chemistry, Dr. B. A. Marathwada University, Aurangabad-431 004.

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A reverse phase high performance liquid chromatography method for the simultaneous estimation of tizanidine hydrochloride and nimesulide in tablets is presented. Cynopropyl column is used to retain tizanidine hydrochloride (k'=1.52) and also have reasonable retention for nimesulide (k'=2.37) with a good resolution and peak symmetry. Effect of change of chromatographic conditions such as pH, %organic modifier (acetonitrile) in mobile phase on retention of drugs were studied and optimized. Both the drugs showed linear response in the concentration range employed (tizanidine hydrochloride, 1.2-2.8 μg/ml and nimesulide, 60-140 μg/ml) and was validated by least squares method at 95% confidence level. The results of analysis have been validated statistically and by recovery studies. The mean recoveries obtained for tizanidine hydrochloride and nimesulide were 99.6% and 100.1%, respectively.

Nimesulide (NIM), 4'-Nitro-2'-phenoxyxemane-sulphonamidil, is widely used as an analgesic, antiinflammatory and antipyretic drug1. It acts as an inhibitor of prostaglandin synthetase and platelet aggregation. Tizanidine hydrochloride (TIZ), 5-chloro-N-(4,5-dihydro-1H-imadazol-2-yl)-2,1,3 benzothiadiazole, is a centrally acting muscle relaxant. A combination of both these drugs, NIM (100 mg) and TIZ (2 mg) in each tablet, is marketed by Unichem Laboratories (Zulu).

Both these drugs are not official with United States Pharmacopoeia, Edn. 24 or European Pharmacopoeia 2000. A literature survey revealed no reported analytical methods for the simultaneous determination of TIZ and NIM either as

*For correspondence