

### Experimental

The isoxazolines **1c–e** and **2c–e** were synthesised by the cycloaddition of nitrile oxides generated from the corresponding araldoximes and purified by crystallisation while the isoxazolines **1a**, **1b**, **2a** and **2b** were synthesised from the nitrile oxides generated from nitroethane and 1-nitropropane and purified by distillation under reduced pressure. The purity of the isoxazolines were tested by analytical, tlc and m.p. data.

Carbon-13 nmr spectra ( $\text{CDCl}_3$ ) were recorded with TMS as internal standard using a Bruker WH-270 instrument operating at 67.89 MHz. Mass spectra of the isoxazolines showed intense peaks at  $m/z$  values of  $(M)^+$ , the parent ion.

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## Studies and Synthesis of Benzimidazole Derivatives as Potential Antibacterial Agents

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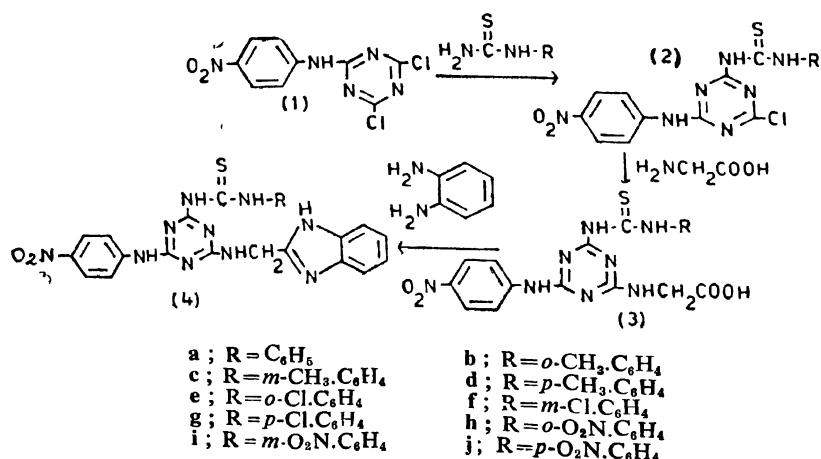
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Benzimidazoles<sup>1</sup>, *s*-triazines<sup>2</sup>, triazinylthioureas<sup>3</sup> and thioureas<sup>4</sup> possess various therapeutic activities. Prompted by the pharmacological importance of those classes of compounds, we have prepared some 2-(4'-nitroanilino)-4-(arylthioureido)-6-(benzimidazol-2'-ylmethylamino)-*s*-triazines (**4a–j**), which comprise all the three moities.

Cyanuric chloride and *p*-nitroaniline in equimolar proportion, were condensed. The intermediate **1** so obtained was reacted with various arylthioureas to get the corresponding intermediates **2**, which were further condensed with aminoacetic acid to give the corresponding intermediates **3**. Compounds **3** were condensed with *o*-phenylenediamine to get the corresponding *s*-triazines (**4a–j**).



## Experimental

Infrared spectra (KBr) were recorded on a Perkin-Elmer 599B spectrophotometer and nmr spectra ( $\text{CDCl}_3$ ) on a Varian EM 390 spectrometer. Melting points were determined in open capillaries and are uncorrected. Purity and homogeneity of the compounds were checked by tlc. Compounds (4a—j) gave satisfactory analytical results for C, H and N.

**2-(4'-Nitroanilino)-4,6-dichloro-s-triazine (1):** It was prepared according to the reported method<sup>5</sup>.

**2-(4'-Nitroanilino)-4-(arylthioureido)-6-chloro-s-triazine (2)<sup>6</sup>:** To a stirred solution of **1** (5.72 g, 0.01 mol) in acetone at 35°, was added a solution of arylthiourea (0.01) in acetone over a period of 0.5 h. The temperature was gradually raised to 45° during 2 h with stirring, maintaining neutral pH. It was then poured onto crushed ice, and the resulting solid was dried and crystallised from ethanol, (75—90%): **2a** m.p. 201°; **b**, 219°; **c**, 260°; **d**, 224°; **e**, 245°; **f**, 207°; **g**, 204°; **h**, 170°; **i**, 177°; **j**, 201°.

**2-(4'-Nitroanilino)-4-(arylthioureido)-6-(acetic acid-2'-ylamino)-s-triazine (3)<sup>6</sup>:** A mixture of **2** (0.015 mol) and aminoacetic acid (1.55 g, 0.0207 mol) in sodium carbonate solution (10.4 ml, 0.414 mol) was refluxed for 3 h on an oil-bath. It was then acidified with HCl and the resulting solid was dried and crystallised from ethanol, (60—70%): **3a**, m.p. 190°; **b**, 177°; **c**, 150°d; **d**, 160°d; **e**, 126°, **f**, 185°; **g**, 200°d, **h**, 101°; **i**, 111°; **j**, 160°d.

**2-(4'-Nitroanilino)-4-(arylthioureido)-6-(benzimidazol-2'-ylmethylamino)-s-triazine (4a—j)<sup>6</sup>.** *General method:* A mixture of **3** (0.01 mol) and *o*-phenylenediamine (0.76 g, 0.007 mol) in 4 *N* HCl (20 ml) was refluxed for 8 h on a water-bath. It was then rendered basic with liquor ammonia and the resulting solid was dried and crystallised from

ethanol, (70—90%): **4a**, m.p. 242°,  $\delta$  ( $\text{CDCl}_3$ ) 7.4—8.3 (ArH), 9.5 (NH imidazole), 4.7 (NH aromatic), 3.0 ( $\text{CH}_2\text{NH}$ ) and 6.55 (NH thiourea); **b**, 239°; **c**, 140°; **d**, 300°; **e**, 298°; **f**, 240°;  $\delta$  ( $\text{CDCl}_3$ ) 7.4—8.3 (ArH), 9.5 (NH imidazole), 4.7 (NH aromatic), 3.0 ( $\text{CH}_2\text{NH}$ ), 6.60 (NH thiourea); **g**, 242°; **h**, 280°; **i**, 284°; **j**, 300°;  $\nu_{\text{max}}$  (for all the compounds) 820—830 ( $\text{C}_5\text{N}_3$  ring), 1 475—1 480 (N—C thiourea), 1 650—1 660 (C—N conjugative cyclic) and 3 390—3 400  $\text{cm}^{-1}$  (NH amine).

Compounds **4a—j** were screened for antibacterial activity against *S. aureus* and *E. coli* at a concentration of 10  $\text{mg ml}^{-1}$  in acetone using agar diffusion method<sup>7</sup>. Compound **4a** showed maximum activity (zone of inhibition 2.5 and 3.0 mm) and compound **4f** showed minimum activity (1.0 and 0.5 mm) against *S. aureus* and *E. coli* respectively.

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