Studies and Synthesis of Benzimidazole Derivatives as Potential Antibacterial Agents

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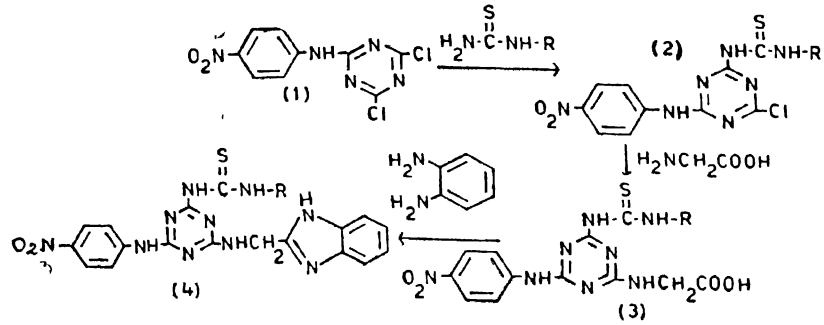
Benzimidazoles[1], *s*-triazines[2], triazinylthioureas[3] and thioureas[4] possess various therapeutic activities. Prompted by the pharmacological importance of those classes of compounds, we have prepared some 2-(4′-nitroanilino)-4-(arylthioureido)-6-(benzimidazol-2′-ylmethylamino)-*s*-triazines (**4a—j**), 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**).



a ; R = C_6H_5
b ; R = *o*-$CH_3.C_6H_4$
c ; R = *m*-$CH_3.C_6H_4$
d ; R = *p*-$CH_3.C_6H_4$
e ; R = *o*-$Cl.C_6H_4$
f ; R = *m*-$Cl.C_6H_4$
g ; R = *p*-$Cl.C_6H_4$
h ; R = *o*-$O_2N.C_6H_4$
i ; R = *m*-$O_2N.C_6H_4$
j ; R = *p*-$O_2N.C_6H_4$

Experimental

Infrared spectra (KBr) were recorded on a Perkin-Elmer 599B spectrophotometer and nmr spectra ($CDCl_3$) on a Varian EM 390 spectrometer. Melting points were determined in open capillaries and are uncorrected. Purity and homogenecity 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[5].

*2-(4'-Nitroanilino)-4-(arylthioureido)-6-chloro-*s*-triazine* (**2**)[6]: 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**)[6]: 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**)[6]. *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°, δ ($CDCl_3$) 7.4—8.3 (ArH), 9.5 (NH imidazole), 4.7 (NH aromatic), 3.0 (CH_2NH) and 6 55 (NH thiourea) ; **b**, 239° ; **c**, 140° ; **d** 300° ; **e**, 298° ; **f**, 240° ; δ ($CDCl_3$) 7.4—8.3 (ArH), 9.5 (NH imidazole), 4.7 (NH aromatic), 3 0 (CH_2NH), 6,60 (NH thiourea) ; **g**, 242° ; **h**, 280° ; **i**, 284 ; **j**, 300° ; ν_{max} (for all the compounds) 820—830 (C_3N_3 ring),) 1 475—1 480 (N—C thiourea), 1 650—1 660 (C—N conjugative cyclic) and 3 390—3 400 cm^{-1} (NH amine).

Compounds **4a—j** were screend for antibacterial activity against *S. aureus* and *E. coli* at a concentration of 10 mg ml^{-1} in acetone using agar diffusion method[7]. 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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