Synthesis of Some New Biologically Active 5-Phenoxy-4-phenyl-1,3-thiazol-2-amines

J. Chem. Research (S), 1998, 496
J. Chem. Research (M), 1998, 2563–2580

M. M. V. Ramana,* Deepnandan S. Dubhashi and Joseph J. D'Souza

Department of Chemistry, University of Mumbai, Vidyanagari, Santacruz (East), Mumbai 400 098, India

Several new 5-phenoxy-4-phenyl-1,3-thiazole-2-amines have been synthesised *via* Hantzsch's synthesis and some of them have been screened for their *in vitro* antibacterial activity.

Thiazole derivatives have attracted a great deal of interest owing to their antibacterial,[1] antifungal,[2] antiinflammatory[3] and antiviral[4a–c] activities. They are also useful as anti-allergic,[5] anthelmintic[6] agents and as sedative hypnotics.[7] In addition to being used in the pharmaceutical industry, thiazoles also find a wide application in the dye[8] and photographic industry.[8] Owing to these characteristics and our interest in the synthesis of heterocycles containing a thiazole moiety, we were prompted to synthesize some new 2-aminothiazole (1,3-thiazol-2-amino) compounds. Some of these compounds have been screened for their *in vitro* antibacterial activity.

In an approach at achieving our synthetic goal we have selected the widely used Hantzsch's synthesis[9] involving the reaction of α-bromo carbonyl compound with thiourea. For this purpose, 2-phenoxy-1-phenylethanones (**4a**–**n**) obtained by the condensation of phenacyl bromide with various phenols (**3a**–**n**) were brominated to yield the respective 2-bromo-2-phenoxy-1-phenyl ethanones (**5a**–**n**). These were then subsequently condensed with thiourea to afford the corresponding 5-phenoxy-4-phenyl-1,3-thiazol-2-amine hydrobromides (**6a**–**l**) which on basification liberated the 5-phenoxy-4-phenyl-1,3-thiazol-2-amines (**7a**–**n**) (Scheme 1). Some of these 5-phenoxy-4-phenyl-1,3-thiazol-2-amines have been shown to be biologically active in comparison with the standard antibiotic septran as shown in Table 4 (full text). Based on the *in vitro* antibacterial activity results, it can be concluded that the presence of electron withdrawing groups in the *ortho* position of the phenoxy ring increases the *in vitro* antibacterial activity of the compound.

Techniques used: ^{1}H NMR, FTIR, UV, mass spectrometry and elemental analysis.

Schemes: 1

Table 1: Physical data for compounds **5a**–**n**

Table 2: Physical data for compounds **6a**–**l**

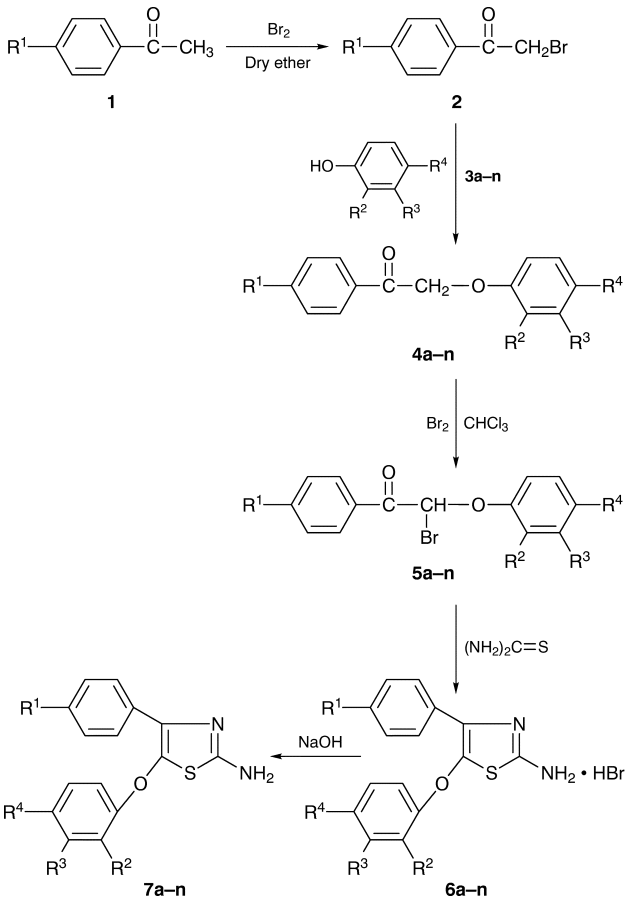
Table 3: Physical data for compounds **7a**–**n**

Table 4: Antimicrobial activity of some derivatives

References: 14

Received, 12th February 1998; Accepted, 15th June 1998
Paper E/8/01237G

*To receive any correspondence.



Scheme 1

References cited in this synopsis

1 F. Russo and M. Santagati, *Farm. Ed. Sci.*, 1976, **31**, 41.
2 Y. Usui, *Ann. Rep. Takeda Res. Leb.* (*Japan*), 1968, **27**, 144 (*Chem. Abstr.*, 1969, **70**, 76696x).
3 S. C. Kuo, L. J. Huang and H. Nakamura, *J. Med. Chem.*, 1984, **27**, 539.
4 (*a*) P. Schauer, M. Lkar, B. Stanovnik and M. Fisler, *Biol. Vestn.*, 1972, **20**, 65; (*b*) P. H. L. Wei and S. C. Bell, *US Pat.* 3 704 239, 1972 (*Chem. Abstr.*, 1973, **78**, 43482 m); (*c*) P. H. L. Wei and S. C. Bell, *US Pat.* 3 775 426, 1973 (*Chem. Abstr.*, 1974, **80**, 70807u).
5 J. H. Musser, R. E. Brown, B. Loev, K. Kaily, H. Jones, R. Kahen, F. Huang, A. Khandwala and M. Leibowetz, *J. Med. Chem.*, 1984, **27**, 121.
6 H. D. Brown, *US Pat.* 3 278 547, 1966 (*Chem. Abstr.*, 1966, **65**, 18593).
7 Y. Sawa and T. Ishida, *J. Pharm. Soc. Japan*, 1956, **76**, 337.
8 J. V. Metzger, *The Chemistry of Heterocyclic Compounds*, Interscience, New York, 1979, vol. 34(II), pp. 162–169.
9 A. Hantzsch and J. H. Weber, *Ber.*, 1887, **20**, 3118.