Synthesis and antimicrobial activity of \(2-(2'-\text{arylidene-hydrazino-acetyl-amino})-4\)-phenyl-1,3-thiazoles and \(2-[2'-\{4''-\text{substituted-aryl-3''-chloro-2''-oxo-azetidine}\}-\text{acetyl-amino}]\)-4-phenyl-1,3-thiazoles

S K Sonwane, S D Srivastava* & S K Srivastava

Synthetic Organic Chemistry Laboratory,
Department of Chemistry, Dr. H.S. Gour University,
Sagar 470 003, M.P., India

E-mail: drsavstri@rediffmail.com

Received 13 September 2007; accepted (revised) 5 February 2008

As a part of systematic investigation of synthesis and biological activity, several new \(2-(2'-\text{substituted-aryl-hydrazino-acetyl-amino})\)-4-phenyl-1,3-thiazoles, \(3\) and \(2-[2'-\{4''-\text{substituted-aryl-3''-chloro-2''-oxo-azetidine}\}-\text{acetyl-amino}]\)-4-phenyl-1,3-thiazoles, \(4\) have been synthesized from \(2-(2'-\text{hydroxy-hydrazino-acetyl)-amino})\)-4-phenyl-1,3-thiazole, \(2\) using amono-4-phenyl-1,3-thiazole as the starting material. All the synthesized products are evaluated for their antifungal activity against \(A.\) niger, \(A.\) flavus, \(F.\) oxisporium and \(T.\) viride and antibacterial activity against \(B.\) substilis, \(E.\) coli, \(S.\) aureus and \(K.\) pneumoniae respectively. The compounds \(3a\) on treatment with chloroacetyl chloride in the presence of triethyl amine afforded \(2-[2'-\{4''-\text{substituted-aryl}\}-3''-\text{chloro-2''-oxo-azetidine}\}-\text{acetyl-amino}]\)-4-phenyl-1,3-thiazoles, \(4a\) (Scheme 1). Their structures have been elucidated on the basis of their spectral and microanalytical data. All the synthesized compounds have been determined by their spectral and microanalytical data.

Keywords: \(2\)-Amino-4-phenyl-1,3-thiazole, arylidenes, 2-oxo-azetidines, antimicrobial activity.

Thiazole derivatives are known to exhibit analgesic and antinflammatory activity. The \(\beta\)-lactam drugs are still the most prescribed antibiotics used in medicine. Recently 2-azetidines have been assessed for good antidegenerative, antiparkinsonian, anti-inflammatory, antibacterial and antitubercular activity. It also functions as an enzyme inhibitors and are effective on the central nervous system.

Moreover much interest has been focused on biological activity of thiazole derivatives. By considering the above arguments, several new thiazolo-azetidinones products have been synthesized in order to study their biodynamic behaviour. The present paper reports the synthesis of \(2-(2'-\text{arylidene-hydrazino-acetyl-amino})\)-4-phenyl-1,3-thiazoles, \(3a\) and \(2-[2'-\{4''-\text{substituted-aryl-3''-chloro-2''-oxo-azetidine}\}-\text{acetyl-amino}]\)-4-phenyl-1,3-thiazoles, \(4a\) by appropriate methods. All the synthesized compounds have been screened for their antifungal activity against \(A.\) niger, \(A.\) flavus, \(F.\) oxisporium and \(T.\) viride and antibacterial activity against \(B.\) substilis, \(E.\) coli, \(S.\) aureus and \(K.\) pneumoniae respectively.

2-Amino-4-phenyl-1,3-thiazole on reaction with chloroacetyl chloride yielded \(2-(2'-\text{chloroacetyl})\)-amino-4-phenyl-1,3-thiazole, \(1\) which on amination with hydrazine hydrate afforded \(2-(2'-\text{hydroxy-hydrazino-acetyl})\)-amino-4-phenyl-1,3-thiazole \(2\). The compound \(2\) on condensation with various selected aromatic aldehydes yielded \(2-(2'-\text{aryl-dene-hydrazino-acetyl})\)-amino-4-phenyl-1,3-thiazoles \(3a-n\). The compounds \(3a-n\) on treatment with chloroacetyl chloride in the presence of triethyl amine afforded \(2-[2'-\{4''-\text{substituted-aryl}\}-3''-\text{chloro-2''-oxo-azetidine}\}-\text{acetyl-amino}]\)-4-phenyl-1,3-thiazoles, \(4a-n\) (Scheme 1). Their structures have been elucidated on the basis of their spectral and microanalytical data. All the synthesized compounds were evaluated for their antifungal activity against \(A.\) niger, \(A.\) flavus, \(F.\) oxisporium and \(T.\) viride and antibacterial activity against \(B.\) substilis, \(E.\) coli, \(K.\) pneumoniae and \(S.\) aureus respectively.

Experimental Section

Melting points were taken in open capillaries and are uncorrected. Purity of compounds was monitored on silica gel G coated TLC plates. IR spectra were recorded on a Schimadzu 8201 PC spectrophotometer in KBr, \(^1H\) NMR spectra on a Bruker DRX 300 spectrometer in CDCl\(_3\) at 300 MHz using TMS as an internal standard and mass spectra on a Jeol SX-102 (FAB) instrument. Elemental analyses were performed on a Carlo Erba-1108 instrument. The analytical data of all the compounds were highly satisfactory. The reagent grade chemicals were purchased from the commercial sources and purified by either distillation or recrystallization before use.
was separated out which was filtered, washed with water, purified over the column chromatography and recrystallised from methanol to give compound 1. Yield 79%, m.p. 171-73°C; IR: 3356 (-NH), 1665 (>C=O), 2963 (-CH2), 2847 (-CH of thiazole), 1409 (-C=N), 1188, 1072, 686 (C-S-C), 3023, 1597, 742 cm\(^{-1}\) (aromatic ring); \(^1\)H NMR: \(\delta\ 6.89-7.78\ (m, 5H, Ar-H), 6.58\ (s, 1H, C-5 of thiazole), 8.15 \(\text{s, 1H, -NH}\), 4.35 \(\text{s, 2H, -CH}_2\); m/z: 252 (M\(^+\)), 216, 203, 175, 133, 77, 57, 56, 45, 42, 41, 40, 32, 31, 16.

2-(2'-Hydrazinoacetyl)-amino-4-phenyl-1,3-thiazole 2: The compound 1 (0.10 mole, 25.26 g) and hydrazine hydrate (0.10 mole, 4.90 g) in methanol (100 mL) was refluxed on a water-bath for about 10 hr. It was filtered, cooled, purified over the column chromatography and recrystallised from methanol to give compound 2. Yield 82%, m.p. 149-51°C; IR: 3356 (-NH), 1665 (>C=O), 2964 (-CH2), 2848 cm\(^{-1}\) (-CH of thiazole), 1186, 1073, 688 (C-S-C), 1413 (-C=N), 3028, 1599, 738 cm\(^{-1}\) (aromatic ring); \(^1\)H NMR: \(\delta\ 6.90-7.76\ (m, 5H, Ar-H), 6.55\ (s, 1H, C-5 of thiazole), 8.15 \(\text{s, 1H, -NHCO}\), 4.79 \(\text{s, 2H, -NH}_2\), 7.88 \(\text{s, 1H, -NH}\), 4.34 \(\text{s, 2H, -CH}_2\); m/z: 248 (M\(^+\)), 232, 217, 203, 175, 133, 77, 57, 56, 45, 42, 41, 40, 32, 31, 16.

Other compounds 3b-n were synthesized in the similar manner using compound 2 and various selected aromatic aldehydes. Characterization data are presented in Table I.
Ar-H), 6.58 (s, 1H, C-5 of thiazole), 8.16 (s, 1H, -NHCO), 7.79 (s, 1H, -NHN), 4.17 (d, J = 5.00, Hz, 1H, N-CH-Ar), 5.14 (d, J = 5.00, Hz, 1H, -CHCl), 4.34 (s, 2H, -CH 2); m/z: 412 (M +), 384, 232, 217, 209, 208, 203, 195, 181, 180, 175, 167, 152, 134, 133, 41 (Chart 2).

Other compounds 4b-n were synthesized in the similar manner using compounds 3b-n. Characterization data are presented in Table I.

**Antimicrobial activity**

All the synthesized compounds 1, 2, 3 a-n and 4 a-n have been screened in vitro for their antifungal activity against A. niger (An), A. flavus (Af), F. oxysporium (Fo) and T. viride (Tv) at two concentrations (50 and 100 ppm) and antibacterial activity against B. substilis (Bs), E. coli (Ec), S. aureus (Sa) and K. pneumoneae (Kp) at two concentrations (50 and 100 ppm) by filter paper disc method. Standard fungicide griseofulvin and antibacterial streptomycin were also screened under the similar conditions for comparison. The following compounds were found active against the tested fungi: 4c (An), 4d (An, Tv), 4e (An, Af), 4f...
(An, Af, Fo, Tv), 4g (An, Af, Tv) and bacteria : 4b (Bs), 4c (Bs), 4d (Ec), 4e (Bs, Kp, Sa), 4f (Bs, Kp), 4g (Bs, Sa) respectively.

Acknowledgement
The authors are thankful to SAIF, CDRI, Lucknow for providing spectral and analytical data of the compounds. We are also grateful to Dr. Mrs. Archana Tiwari, Department of Biotechnology, Dr. H. S. Gour University for providing help in carrying out the antimicrobial screening. We are also grateful to Head, Department of Chemistry, for giving the facilities to carryout the work.

References: