Original Research Paper

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An Efficient Synthesis and Biological Screening of Some New 2-Chloroacetyl Amino-6-Substituted Benzothiazoles

Chemistry

KEYWORDS : 4-substituted anilines, potassium thiocyanate, 2-chloro acetyl amino-6-substitued benzothiazoles, 2-mercaptobenzothiazole, 2-hydrazinobenzothiazole

Anil B. Chidrawar

Assistant Professor, P.G. Department of Chemistry, Degloor College, Degloor, S.R.T.M.U. Nanded, India - 431717

ABSTRACT

A Literature survey indicates that benzothiazole derivatives possess different pharmacological and biological activities; which of most potent activity are anti-inflammatory and anti-bacterial activity. The starting product is 6-substituted-1,3-benzothiazol-2-amine was prepared from 4-substituted anilines and potassium thiocyanate in one step. Substituted Benzothiazolyl-2-amines were reacted with chloroacetyl chloride to yield 2-chloro acetyl amino-6-substitued benzothiazoles, which were reacted with 2-mercaptobenzothiazole and 2-hydrazinobenzothiazole gave 2-(1,3-benzothiazol-2-yl thio)-N-(6-substitued-1,3-benzothiazol-2-yl)acetamides and 2-[2-(1,3-benzothiazol-2-yl)hydrazino]-N-(6-methyl-1,3-benzothiazol-2-yl)acetamides respectively. The synthesized compounds were characterized by elemental analysis and spectral data

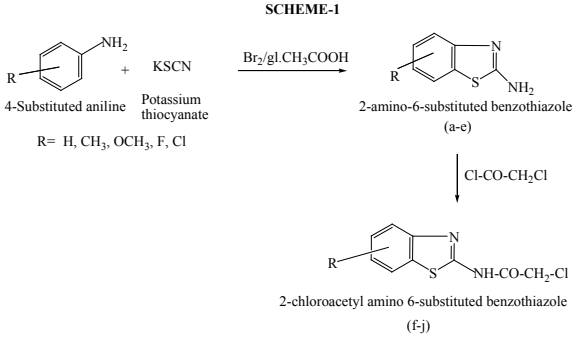
Introduction :

Benzothiazoles are an extremely important class of compounds that occur widely as biologically active natural products, as well as marketed drugs or drug candidates[1]. Accordingly, the development of efficient and general synthetic methodology for Benzothiazole is a meaningful research challenge having great potential for practical applications in the pharmaceutical industry. Benzothiazoles have two hetero atoms attached at the ortho position on the benzene ring.

Substituted benzothiazole is an important class of heterocyclic compounds that exhibits a wide range of biological properties such as inhibitors of stearoyl-coenzyme desaturase[2], antitumor[3-5], antimicrobial[6], LTD_4 receptor antagonist[7], etc. For example, the investigations of benzothiazole as a key pharmacore led to Merck investigational new drugs such as the orexin receptor antagonist[8] and the Gram-positive selective antibacterials[9]. Pyrimido [2,1-*b*] benzothiazole and its 8-substitued derivatives were synthesized by Nair Mohan D.[10] by refluxing diethyl ethoxy methylene malonate with respective 2-amino benzothiazoles. These derivatives were found to have antiviral activity.

Materials and Method :

SCHEME-1



Experimental :

Preparation of 2-amino-6-substituted-1, 3-benzothiazoles (a – e):

To glacial acetic acid (10 ml) pre cooled to 5^0C were added 1 mole of potassium thiocyanate and 1 mole of 4-substituted aniline. The reaction mixture was placed in freezing mixture of ice and salt and mechanically stirred, while 1.1 ml of bromine in 4.0 ml of glacial acetic acid was added from a dropping funnel at such a rate that the temperature does not rise beyond 0^0C. After all the bromine has been added the solution was stirred for an additional two hours at 0 ^{0}C and at room temperature for 10 hours. It was then allowed to stand overnight during which period an organic precipitate is settled at the bottom. Water (4.0 ml) was added quickly and slurry was heated to 85^0C on a steam bath and filtered hot. The orange residue was placed in a reaction flask and treated with 8.0 ml glacial acetic acid, heated again to 85^0C and it was filtered hot. The combined filtrate was cooled and neutralized carefully with ammonia solution to pH 6.0, and then a dark yellow precipitate was separated and was collected. The product was recrystallized twice with benzene by treating with charcoal gave colorless product.

Preparation of 2-chloroacetyl amino-6-substituted benzothiazole (f – j) :

To a solution of 2-amino-6-substituted benzothiazole (10gm) dissolved in 100 ml dry benzene was added a solution of 5 ml chloroacetyl chloride in 30 ml of dry benzene. The reaction mixture was then warmed at 70^0C on a water bath for 90 min. The benzene was distilled off and the residue was filtered, washed with sodium bicarbonate solution followed by water and then it was dried .The product was recrystallized from alcohol.

Result and Discussion :

The objectives of the present work are to synthesize certain benzothiazole derivatives and study their antibacterial and anti-inflammatory activity in particular. Thus an attempt has been made in this direction. As expected substituted benzothiazoles exhibited antimicrobial activity some are equipotent to that of standard employed for comparison. Therefore a detailed study of toxicity is necessary. There is no such a thing as completely safe drug. Drugs are powerful tools which alter physiological processes for the better or for the worse. A society which wishes to benefit from them will not achieve all the benefits are for the biological testing do not always turn out as potential new drugs, but may be intended to serve as models for evaluation of hypothesis.

Antibacterial activity:

All the synthesized compounds were screened for antibacterial activity studies at a concentration of 50 µg /ml & 100 µg /ml using DMSO as a control against *B.substilis*, *B.pumillus*, *Escherchia coli* and *P.aeruginosa* by disc-diffusion method on nutrient agar media, Ampicillin 50 µg /ml & 100 µg /ml used as standard against Gram positive and Gram negative bacteria. It shows that compounds f, g and i was found to possess a broad spectrum activity. While compounds h and j were found to exhibit moderate activities. From the antibacterial screening it was found that the compounds showed significant activity and were found to be good with respect to the standard at the given concentration levels. Hence these compounds appear to be promis-

ing antibacterial, anti-inflammatory agents. Perhaps the substituent at 2nd position of benzothiazole ring and which contains substituted 2-mercapto benzothiazole and 2-hydrazino benzothiazole ring may be largely responsible for the marked bactericidal and anti-inflammatory activity.

Conclusion :

The two moieties, i.e., 2-subtituted benzothiazoles and 2-chloroacetamido -6-substitued benzothiazole moieties independently are showing antibacterial activity. Here when the two moieties are fused and screened for antibacterial studies they showed a broad spectrum of antibacterial activity. They showed good activity against Gram positive and Gram negative bacteria. 2-subtituted benzothiazoles and 2-chloroacetamido -6-substitued benzothiazole are responsible for antibacterial activity, but it is interesting to note that benzothiazole moieties when fused with other moieties showed a broad spectrum antibacterial activity. Hence in search of new generation of antibiotics it may be worthwhile to explore the possibility in this area by fusing different moieties and increase potency.

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