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Synthesis and characterization of biological active heterocycle-2-Aminothiazole

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Abstract
A simple synthetic process was used to create substituted amino thiazole. To create the derivatives of the amino thiazole, substituted aromatic ketones and thiourea are first combined in the presence of iodine. By using IR, 1H NMR, 13C NMR, and mass spectroscopic methods, the synthesized derivatives were evaluated for their structural confirmation.

Keywords: 4-Bromo acetophenone, 2-Amino Thiazole, Thiourea, Characterization: IR, 1H NMR, ^{13}C NMR, Mass. and Biological Activity

Introduction
The creation of materials for organic chemistry is greatly attracted to heterocyclic compounds. Rudolf Hantzch created the thiazole ring for the first time in 1887 at the end of the nineteenth century [1].
The term thiazole refers to a large family of derivatives. They are isomeric with the 1, 2-azoles, the nitrogen and sulphur compound being called isothiazole. The numbering system was shown below Fig. 1, for naming derivatives of thiazole [2, 3].

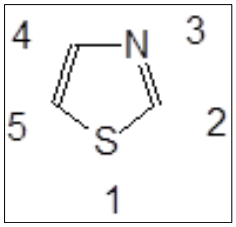


Fig 1: Numbering system of thiazole

Heterocyclic compound containing thiazole and its derivatives are playing a vital role in nature. For example, the thiazolium ring present in vitamin B1 [Thiamine] Serves as an electron sink and its coenzyme form was important for the decarboxylation of α-keto acids. This heterocyclic system has found broad applications in drug development for the treatment allergies, inflammation, hypertension, schizophrenia, bacterial and HIV infections.
The aromatic five-membered ring of the heterocyclic molecule thiazole contains both a nitrogen atom and a sulphur atom. 1,3-azoles are a similar chemical to thiazole (nitrogen and one other hetero atom in a five membered ring). Thiazoles with marine and microbiological origins have antiviral and anticancer properties [4, 5].
In both medicinal and agricultural chemistry, heterocycles with nitrogen and sulphur atoms are a crucial class of chemical. Thiazole is a crucial component of numerous powerful commercial compounds with biological activity, including sulfathiazole and farenizole.
It has been discovered that thiazole and its derivatives have biological importance. A physiologically active molecule with a wide spectrum of biological activities, 2-amino substituted thiazole serves as an intermediary in the synthesis of Schiff base. The class of natural and manmade compounds known as thiazoles is significant. Thiazole compounds exhibit a variety of properties, including antibacterial, antifungal, anti-inflammatory, and anti-cancer properties [10, 11, 12].
Thiazole derivatives have a diverse spectrum of biological and pharmacological properties, making their synthesis significant. The condensation of 4-Bromo acetophenone with thiourea

is a traditional and frequently used technique. Thiourea combined with monohalo aromatic ketone is typically used to insert the thiazole ring into the target molecule [9, 10, 11, 12]. Thiazole derivatives have a diverse spectrum of biological and pharmacological properties, making their synthesis significant. The condensation of 4-Bromo acetophenone with thiourea is a traditional and frequently used technique. Thiourea combined with monohalo aromatic ketone is typically used to insert the thiazole ring into the target molecule.

Materials and Methods

All the chemicals and solvents used in studies were of (AR) grade and were dried and purified before use. The purification of synthesized compound was performed by recrystallization with appropriate solvents [13]. Purity of all the synthesized compound was checked by TLC. Melting points of the synthesized compound were determined by open capillary method and are corrected [14].

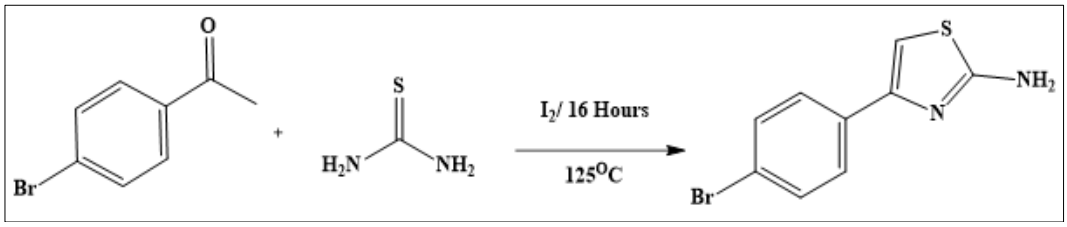
IR spectra were recorded using Nujol with FT-IR Perkin-Elmer model Spectrum One Spectrophotometer, ^{1}H NMR spectra were recorded using $CDCl_3$ with Varian-300 spectrometer NMR instrument using TMS as an internal standard. Mass spectra were recorded in NCMS ES+ spectrometer.

Synthesis of 2-amino-4-(4-bromophenyl) thiazole

The 2-amino-4-(4-bromophenyl) thiazole is prepared by [15] the standard methods scheme-1, 1 mmol of 4-bromoacetophenone was added to a 1 mmol alcoholic solution of thiourea in presence of 2 mmol of iodine and reaction mixture was refluxed on water bath for 16 hours at 125 °C, after the reaction time duration the reaction mixture was cooled for few minutes a solid white precipitated will generate.

After the product was filtered and recrystallized from 70% ethanol.

Yield is 72.91% and melting point is 183 °C-187 °C.



Scheme 1: Synthesis of 2-amino-4-(4-bromophenyl) thiazole

Physical properties of thiazole derivative

Sr. No.	Molecular formula of Compound	M.P. in °C	% Yield in GM	Colour and Solubility	Rf	Molecular Weight.	Elemental analysis in %				
							C	H	N	S	Br
1	$C_9H_7N_2SBr$	183-187	72.91	White $CHCI_3$	0.83	255.13	42.36	2.76	10.97	12.56	31.31

Results and Discussion

The reaction of substituted acetophenone with thiourea and iodine led to the synthesis of a substituted amino thiazole molecule. TLC kept track of this response. The creation of the desired product is confirmed by using spectroscopic methods and their values. The chemical compound amino thiazole is solid-colored and air-stable. Nevertheless, coordinating solvents like DMF and DMSO make it soluble. It is insoluble in water.

Thin layer chromatography [TLC], using various eluents, was used to test the purification of the thiazole chemical first. Hexane and ethyl acetate at a ratio of [7: 3] were used as the eluent and produced the best separation. After that, pure ethanol was used to clean the final product.

Spectroscopic characterization of thiazole derivative

The structure of the prepared thiazole derivative was refined on the basis of their IR spectra. The IR absorption bands were assigned with account taken of the data given in [16].

In IR spectra, the thiazole derivatives show absorption bands in the range 3353 cm^{-1} assigned for N-H group, The absorption bands of the C=N group were observed in the range 1515 cm^{-1} and that for C=C group in the region 1455 cm^{1}. The absorptions for the C-S- C group were observed in between 1091 cm^{1}.

In ^{1}H NMR spectra, the protons of the $–NH_2$ group appeared as singlet in the region of 4.9 ppm. The heteroaromatic (thiazole) protons appeared in the region of 6.7 ppm. Whole aromatic protons appeared in the range 6.39-7.65 ppm respectively.

The ^{13}C NMR spectra provide further support for the structural characterization of the Schiff bases. ^{13}C NMR spectral data of compound have been listed in Table. The number of signals found corresponds with the presence of magnetically nonequivalent carbon atoms, which were assigned by comparison with literature values. The aromatic carbon present in the structures of 2-amino Thiazole derivatives were assigned by comparing the experimental chemical shifts with those calculated from the incremental method. The ^{13}C-NMR spectral data of the 2-amino Thiazole derivatives are in accord with the proposed structures.

In the Mass spectra.

The composition of the resulting amino thiazole derivative was determined by Mass and Elemental analysis. The molecular ion peak for the amino thiazole derivative was observed at 255 m/z.

Table 1: Spectroscopic characterization of thiazole derivative

Sr. No	Mass	IR in cm^{-1}	^{1}H NMR in ppm	^{13}C NMR in ppm
1	255 MW	3353 (N-H), 1515 (C=N), 1455 (C=C), 1091 (C-S-C)	4.9 (s 2H -NH_2), 6.7 (s 1H Hetero aromatic thiazole) 7.49-7.65 (m 4H Aromatic)	168,134, 132,122, 104,77

Biological Activity

Health and welfare of human being are closely associated with microorganism. Microbiology is a very important branch among all the biological sciences and now a day's microbiology has become very important to our society. They play essential role in the ecology of life on the earth, some bacteria are very useful on the other hand some are harmful to mankind or animal. For example, some microorganisms are important commercially through their used in the production of antibiotic i.e., Amphicillin; microorganisms are used in the production of certain foods, like cheese, yoghurt and fermented drinks. Microorganisms are also major tools in the basic research in the biological science; microbial activity is also used to produce the energy such as methane gas for rural consumption. Thus there is no field of human Endeavour, whether it is in the industry, agriculture, food preparation [17-20].

Anti-Bacterial Activity

The newly synthesized thiazoles were screened for their antibacterial activity against bacterial strains by disc diffusion method. The discs measuring 6.25mm in diameter were punched from Whatman No. 1 filter paper. Batches of 100 discs were dispensed to each screw capped bottles and sterilized by dry heat at 140 °C for an hour. The test compounds were prepared with different concentrations using dimethyl formamide. One millilitre containing 100 times the amount of chemical required in each disc was added to each bottle which contains 100 discs. The discs of each concentration were placed in triplicate in nutrient agar medium seeded with fresh bacteria separately. The incubation was carried out at 37.8 °C for 24 h. Nitrofurazone was used as a standard drug. Solvent and growth controls were kept. The zone of inhibition and minimum inhibitory concentrations [MIC] was noted.

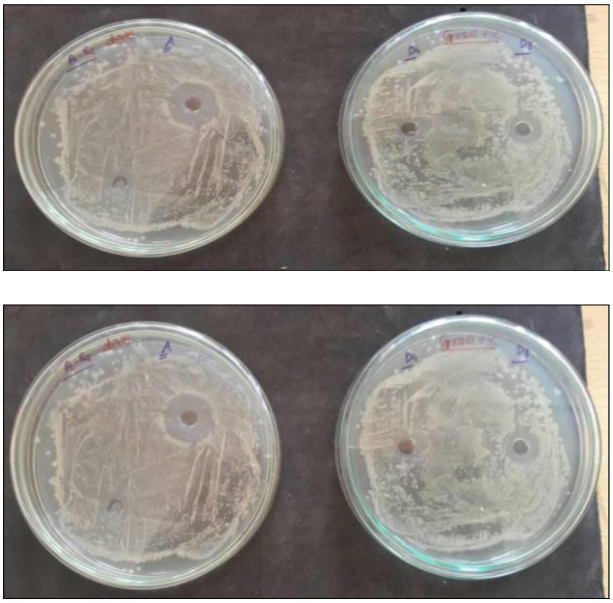


Fig 1: Antibacterial Activity of Thiazole Compound.

Anti-Fungal Activity

Antifungal activity for newly prepared compound was screened by serial plate dilution method. Sabourands agar media was prepared by dissolving peptone (1 g), D-glucose (4 g) and agar (2 g) in distilled water (100 ml) and adjusting the pH to 5.7. Normal saline was used to make a suspension of spores of fungal strain for lawning. A loopful of particular fungal strain was transferred to 3ml saline toget a suspension of corresponding species. A 20ml of agar media was poured in to each of the petridishes. Excess of suspension was decanted and the plates were dried by placing in an incubator at 37 °C for 1 h. Using an agar punch well were made on these seeded agar plates and 10 mg/ml of the test compounds in DMSO were added into each well labeled. A control was also prepared for the plates in the same way using solvent DMSO. The petridishes were prepared in triplicate and maintained at 37 °C for 3e4 days. Antifungal activity was determined by measuring the diameter of the inhibition zone. Activity of each compound was compared with Amphotericin B as standard. The minimum inhibitory concentration (MIC) for the Amphotericin B in DMSO was more than 1 mg/ml against the tested species.

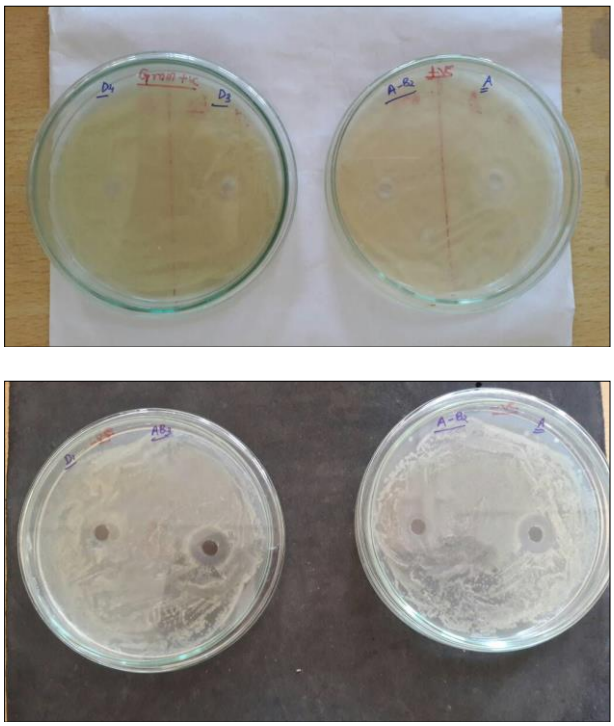


Fig 2: Antifungal Activity of Thiazole Compound.

The compound was tested for antimicrobial activity against some pathogens. The compound was found to be active against the bacteria *E. coli*, *B. Subtilis* and fungus *A. niger*, *C. Albicans*, *staphylococcus aureus*, *pseudomonas aeroginosa*, *klebsiella pneumoniae*. The synthesized compound showed significant activity and showed enhanced antimicrobial activity than those of another compound from which they are synthesized. Spectral data was recorded at IICT Hyderabad, The biological data was recorded at school of life science S.R.T.M. University Nanded, and synthesis was carried out at research laboratory department of chemistry shivaji Mahavidyalaya, Udgir.

Conclusion

Due to the presence of electron donating or electron withdrawing groups on the structures of the acetophenone compounds, the synthesis of substituted amino thiazole compounds produced very variable yields. While the electron withdrawing groups reduced the electron density at the carbon atom of the carbonyl group, increasing the yield of product and shortening the reaction time, the electron-donating groups increased the electron density at the carbon atom of the carbonyl group, improving their electrophilic properties.

In the current investigation, an attempt has been made to create a thiazole derivative by reacting an aromatic ketone with thiourea when iodine is present. The synthesis of the intended products was validated by evidence for their structures obtained using IR, 1H, 13C NMR, and mass spectrometry. The results lead us to the conclusion that the synthesis is superior in terms of yield and purity, as well as saving solvent and time.

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References

1. Hantzch R, Weber HJ. Brachiate. 1887;20:3118.
2. Eicher T, Hauptmann S. The chemistry of heterocyclic, reactions, syntheses, and application. Welly, New York; c2003.
3. Zeki A Naser Al-Shamkhani, Hanan A Al-Hazam. Research Journal of Pharmaceutical, Biological and Chemical Sciences.
4. Pandeya SN, Sriram D, Nath G, De Clercq E. Eur. J. Pharma. Soc. 1999;9:25.
5. More PG, Bhalvankar RB, Patter SC. J Ind. Chem. Soc. 2001;78:474.
6. Siddiqui IR, Pravin K Singh, Jaya Singh, Jagdamba Singh. Synthesis and fungicidal activity of 4, 4'-bis [2"-(5"'-substituted rhodanin-3"'-yl) thiazole-4"-yl] bibenzyls. Indian J of chem. 2005;44B:2102-06.
7. Gindher T, Reddy RB, Prasanna B, Chandra Mouli GVP. Synthesis and Pharmacological Evaluation of thiazoles. Ind J Chem. 2001;40B:1279.
8. Chandrasekhar S, Narsimulu Ch, Sultana SS, Reddy NRK. Synthesis of thiazoles under solvent free condition. Org Lett. 2002;4:4399.
9. Furniss BS, Hannaford AJ, Smith PWG, Tatchell AR. Vogel's practical organic chem. 5th Ed. (Logman Scientific Technical, John Wiley and Sons; c1989.
10. AI Vogel. A Text book of quantitative inorganic chemistry 3rd Ed., (ELBS, London); c1961.
11. Maurya MR, Gopinathan C. Indian J Chem. 1996;35A:701.
12. Jayaramadu M, Reddy KH. Indian J Chem., 1999;38A:1173.
13. Sharma RP, Kothari AK, Sharma NK. Indian J Derm. Vener. Lepr. 1995;61:26.
14. Ballchausen CJ, Gray HB. Inorg. Chem. 1962;1:11.
15. Furniss BS, Hannaford AJ, Smith PWG, Tatchell AR, Vogel's practical organic chem. 5th Ed. (Logman Scientific Technical, John Wiley and Sons); c1989.
16. Cross AD. An Introduction to Practical Infra-red Spectroscopy, London: Butterworths, 1960. Translated under the Title Vvedenie v prakticheskuyu infrakrasnuyu spektroskopiyu, Moscow: Inostrannaya Literatura. 1961. p. 110.
17. Pelezar MJ, Jr. Chan ECS, Noelkrieg R. Microbiology, McGraw Hill, International Edition, 5th Ed. 1986;19-30:66, 101.
18. Satpathy KC, Mlshra HP, Patel BN. J Ind. Chem. Soc. 1982;59:49.
19. Cavallito CJ. Ann. Rev. Pharmacol, 1968;8:39.
20. Bloom BM, Laubach GD. Ann. Rev. Pharmacol, 1962. p. 67.