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Review Paper

Ultrasonic Insight into Substituted Thiazoles and its Biological Activity

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Abstract

The heterocyclic compounds constitute the largest family of organic compounds. The most common heterocyclic compounds especially thiazole are very much interesting in the study of research area. It has been known to possess wide range of biological and pharmacological activities for long time. In recent year substituted thiazole have gained significant interest in the area of drug research and displayed broad range of biological activity such as anti-fungal, anti-bacterial, anti-inflammatory, anti-viral, anti-retroviral, anti-convulsant, anti-cancer, anti-neoplastics activities. So far modifications of substituted thiazole ring have proved highly effectiveness to improve potency and lesser toxicity. The literature survey shows that "The ultrasonic studies of very few thiazoles have been reported so far, hence it was thought to under taken such ultrasonic studies of some substituted thiazoles to obtain ultrasonic velocity data for ternary liquids mixtures. Since, acoustics parameter provides a better insight into molecular environment in liquid molecular interaction which motivates the author to carry out the present review. This review article highlights the recent accelerating rate of investigation in ultrasonic studies of some substituted thiazoles and covers the most active heterocyscles that have considerable important biological activities.

Keywords: Heterocyclic compounds, intermolecular, heterocycles, substituted thiazoles, biological activities, ultrasonic velocity, density, acoustic and thermodynamic.

Introduction

Literature survey revealed that the chemical science was an undivided field before two hundred year ago. Due to vast field, division was necessary into inorganic, organic and Physical chemistry. Organic chemistry has some more disciplines and specialties. Heterocyclic chemistry is most varied classical, fascinating and largest division of organic chemistry and is of immense importance biologically and industrially[1] in this review the main focus has been given on five member heterocycles contain nitrogen and sulphur hetro-atoms. Heterocyclic compounds are cyclic compounds with the ring containing carbon and other element like oxygen, nitrogen and sulphur. They are chemically reactive and flexible and shows better respond to the many biochemical processes. The simplest of the five member's heterocyclic are pyrazole, furan and thiophene. Each member contains a single heteroatom. The five member rings containing more than one or two hetero-atoms are known as azoles viz. pyrrole, thiazole, thiadiazole, oxadiazole[2]. Among the approximately 20 million chemical compounds are identified by the end of the second millennium, out of which more than two-thirds are fully or partially aromatic and near about 50% are heterocyclic's. The presence of heterocyclic in all kinds of organic compounds of interest in electronics biology, optics pharmacology and material science is very well known. Hence most of heterocycles are used in pharmaceuticals, biologically and agrochemical studies. The countless additional modifier heterocycles are used in industrial application, viz. drugs, cosmetics, plastics reprography information storage and so on. For more than a century, heterocycles have constituted one of the largest areas of research in organic chemistry. In heterocyclic compounds, the sulphur and nitrogen containing heterocycles viz. thiazole, thiadiazole have maintained the interest of research through decades of historical development of organic compounds[3]. The ground of this interest were their biological activities and unique structures that lead to several application in different area of agrochemical or recently in material science research. Nitrogen and sulphur organic aromatic heterocycles are formally derived from aromatics carbon cycles with a heteroatom result in significant changes in the cyclic molecular structure due to availability of unshared pair of electrons and the difference in electro negativity between heteroatom and carbon, therefore nitrogen - sulphur heterocyclic viz. thiazole compounds display physico-chemical characteristics and quite different reactivity from the parent hydro carbons[4]. The heterocyclic compounds mainly contain nitrogen, sulphur and oxygen atom constitute a large class of compounds of biological medicinal interest[5]. Thiazole is one of the most intensively investigated classes of aromatic five member heterocyclic. It was first described by Hantzsch and Weber in 1887.

In thiazole, sulphur and nitrogen heteroatom's are at 1 and 3 positions. Nitrogen involved in many of the natural vitamin products. The properties of thiazoles are similar to those of oxazole and the nitrogen atom with unshared pair of electron,It

is basic in nature, thiazoles are frequently included in the design or are used as a core structure for the synthesis of chemical libraries. Literature review reveals that thiazoles and its derivatives are very useful compounds in various field of chemistry including medicine and agriculture. Thus the thiazole nuclear has been much studied in the field organic and medicinal chemistry. In recent years an increasing variety of research techniques viz. infrared, Raman effect, dielectric, magnetic resonance are being employed to get an insight in to the molecular behavior of organic liquid mixtures. In present stage of development comparatively ultrasonic technique are yielding fruitful results in the elucidation of molecular behavior in pure liquids and liquid mixtures. This technique determine elastic and thermodynamic, acoustic properties of pure gases, liquids, solids and different types of liquid mixtures, which is applicable in chemical, leather, textile and nuclear industries. As of our knowledge very few works has been reported on the ultrasonic studies of substituted thiazoles in different percentage of dioxane–water, DMSO- water, acetonitrile-water, N, Ndimethylformamide- water and alcohol-water with different composition of substituted thiazole solute. Ultrasonic study will exhibit molecular interaction between two or more solvents with different composition in the presence of thiazole solute. Therefore the present work is undertaken to study the acoustic and thermo dynamical properties of substituted thiazoles in binary or ternary liquid mixtures[6].

History of Heterocyclic chemistry

Heterocyclic chemistry is the branch of chemistry dealing with synthesis, properties and application of heterocyclic compounds. The history of heterocyclic chemistry began in the year1800, in step with the development of organic chemistry. Some noteworthy developments are[7]. 1818: Brugnatelli isolates alloxan from uric acid. 1832: Dobereiner produces furfural (a furan) by treating starch with sulphuric acid, 1834: Runge obtains pyrrole ("fiery oil") by dry distillation of bones, 1906: Friedlander synthesizes indigo dye, allowing synthetic chemistry to displace a large agricultural industry, 1936: Treibs isolates chlorophyll derivatives from crude oil, explaining the biological origin of petroleum. 1951: Chargaff's rules are described, highlighting the role of heterocyclic compounds (purines and pyrimidines) in the genetic code.

General Feature of Heterocyclic compounds

The most common heterocycles are those having five or six member ring and containing nitrogen (N), Oxygen (O) or sulphur (S) as hetero atoms. The best known heterocyclic is pyridine, pyrrole, thiophene, thiazole, isothiazole. In liquid mixtures they have significant following characteristics properties which instigate the researchers.

The structure of heterocyclic can be manipulated to atchive required modifications in functions[8].

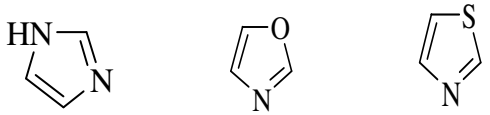
Many heterocycles can be fitted into one of a few broad groups of structure that have overall similarities in properties but significant variations within the group, such variation can include difference in acidity or basicity and different polarity[9].

In heterocycles possible structural variation occurs include the change of one heteroatom for another ring and different positioning of the same hetero atoms within the ring. The important feature of the heterocyclic structure is that it is possible to incorporate functional groups either as substituted or as part of the ring itself[10]. By using intermediate in organic synthesis they can form important and useful ligands[11].

Hetero chemistry studies the synthesis, properties and application of heterocycles. The heterocyclic compounds are very widely distributed in nature and very essential to living organism. They play a vital role in the metabolism of all living cells. Among large number of heterocyclic compounds, Nitrogen heterocycles especially those contain oxygen and sulphur are most abundant[12].

Different heterocyclic compounds

The heterocyclic moiety may contain one, two or three hetero atoms in the ring. The heterocycles with one hetero atom are generally stable and those containing three atoms in the ring are less stable and more reactive because of ring strain. Heterocyclic compounds with two hetero atoms are more likely to occur as reactive intermediates. The five member heterocyclic compounds are important in chemistry. The five member N-heterocyclic compounds with an additional hetero atom are termed as azoles. Those azoles containing two nitrogen atoms, one oxygen and one nitrogen atom, one sulfur and one nitrogen atom in the 1, 2- position are named as pyrazole, isoxazole, isothiazole respectively. When both the hetero atoms are present at 1, 3- positions are referred as imidazole, oxazoles and diazole.



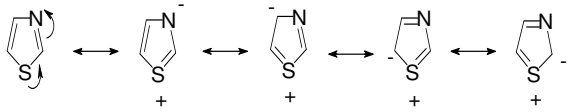
Imidazole Oxazole Thiazole

The condensed ring system of these heterocycles with substituent are also known and they are named as derivatives of parent azole or substituted azoles as Benzopyrazoles, Benzoimidazole, Benzoisoxazoles, Benzooxazoles, Benzoiso-thiozoles, Benzothiazoles[13].

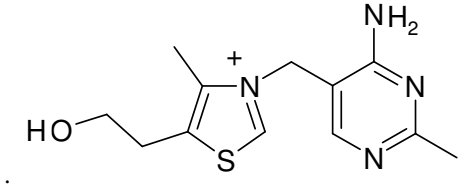
It is recur in literature that nitrogen and sulfur heterocycles results higher efficiency against various diseases[14]. Sulphur is capable of forming both (o and jt) bonds therefore the studies of their binding interaction with receptor moiety is also an interesting field of research during last few years[15]. Out of all the heterocyclic compounds mostly researchers have maintained

their interest in thiazole moiety. As one of the important organic moieties in area of research of pharmacological activity. Thiazole or 1, 3-thiazole is five member heterocyclic compound contain both sulphur and nitrogen atom in the ring and molecular formula is C_3H_3NS. Thiazole is member of azoles heterocycles that include imiadazole and oxazoles. Oxazoles are related compounds with sulfur replaced by oxygen. Thiozole ring are planar and aromatic, it is a pale yellow liquid with boiling point 116-118^{0}C, its specific gravity is 1.2 and it is sparingly soluble in water, it is soluble in alcohol and ether. There is larger pi-electron delocalization in thiozoles as compared to oxazole. This greater aromaticity is evidenced by the chemical shift of the ring proton in NMR spectroscopy (between 7.27 and 8.27) clearly indicating a strong diamagnetic ring current[16].

Resonance structure: Thiozole is aromatic on the basis of delocalization of lone pair of electrons from sulfur atom completing the needed 6 n electron to satisfy Huckel's rule. The resonance forms are:



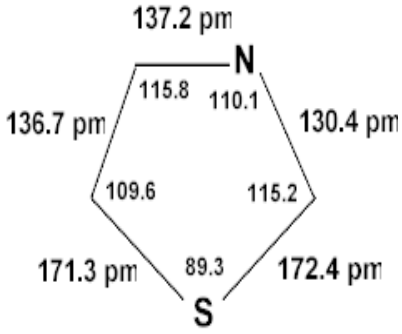
Thiazole is used an intermediate to manufacture synthetic drug, fungicide, dyes. A thiazole ring is found naturally in the essential proteins. In addition to vitamin B_1 (thiamine), the thiazole ring is found in epothioline, it has microbial and marine origins. Its derivatives are found in many potent biologically active molecules such as Sulfathiozole, (antimicrobial drug) Ritonavir, (antiretroviral drug) Abafungin (antifungal drug) with trade name Abasol cream and Bleomycine and Tiazofurin (antineoplastic drug). Many interesting biological activities are associated with some substituted thiazoles[17].



Thiamine

Many thiazoles are flavored compounds. A number of thiazole viz. 2-methylthiazole, 4-methylthiazole, 5-methylthiazole and 5-butlythiazole are all found in roasted peanuts. They are found in foods thiazole contributes to the flavor of brewed coffee. Cooked beef aroma also contains many thiazoles. Many of the heterocyclic compounds having anti-oxidative properties. Microwave spectra reveal the bond length and bond angles in the thiazole molecule and it is noticed that C-S bond (171.3pm) is longer than the other because of the larger sulfur atomic radius.

The bond angles are also influenced by the presence of hetero atoms, the C-S-C angle is comparable to that of thiophene (90^0)[18]. The calculated pi-electron density marks C_5 as the primary site for electrophilic substitution and C2 as the site for nucleophilic substitution that can react with electrophiles to produce substituted thiazoles.



^{1}H NMR spectral data shows the following chemical shifts; H-2 8.88 ppm, H-47.98 ppm, and H-5 7.41 ppm. The downfield values are typical of aromatic hydrogens. The further downfield shift for H-2 compared to the other hydrogens is due to the deshielding caused by the combined electron-withdrawing effects of nitrogen and sulfur being adjacent to it. ^{13}C NMR spectral data reveals three peaks: C-2 153.4 ppm, C-4 143.7 ppm, and C-5 119.7 ppm, all values typical for aromatic carbons.

Important IR bands include a typical C-H stretching mode at 3084 cm^{-1}, ring stretching modes at 1481 cm^{-1}, 1381 cm^{-1}, and 1319 cm^{-1}, and CH modes at 882 cm^{-1}, 865 cm^{-1}, 803 cm^{-1}, and 728 cm^{-1}.

Heterocycles in Service of Man Kinds

Hetrocycles are inextricably woven in to life of process with respect to biological, pharmacological activity and uses. Heterocyclic compounds especially some thiazoles played a vital role in biological process and are wide spread as natural products, they are widely found in nature particularly in nucleic acid, alkaloids anthocyanins and flavors as well as in harem and chlorophyll. Additionally, some vitamins, proteins, hormones contain aromatic heterocyclics system[19]. Heterocycles are in the service of human kind, it is well known in literature that nitrogen and sulphur compounds are used in medical purpose for the treatment of different kinds of fungal and bacterial infections along with treatment of gastric ulcer cancer etc[20-21]. A brief review of biological activities of substituted thiazoles is presented below. Thiazole dye is used for dying cotton. Benzothiazole derivatives are important in rubber industry. Nucleus imparts an important function in medicinal chemistry and biological activity and serves as a key template for the development of various therapeutic agents. In recent times more than 90% of new drug contain heterocyclic. The application of thiazole were found in drug development for treatment of different diseases viz. allergies[22]. Hypertentions[23], anti-inflamatory activity[24], schizophrenia[25], anti-HIV[26], Hypnotics[27]

and more recently for the treatment of pain[28], as fibrinogen receptor antagonists with anti- thrombic activity[29] and as new inhibitors of bacterial DNA gyrase B[30]. The thiozoles occur in some antibiotics drug like penicillin, micrococcin[31], antibacterial activity and anti-malarial activities. Thiazole containing N=C=S moiety have been used as anti phychotics[32], Number of thiazole derivatives show good biological as well as pharmacological activities like analgesic[33], ant tubercular[34], central nervous system (CNS) stimulate[35], algicidol. Anticonvulsant activity: It is group of drugs used in the treatment of epileptic seizures and also used in the treatment of by polar disorder which as mood stabilizers and anti- malarial[36]. Antifungal activity: It is drug used to treat fungal infections[37]. Anti -microbial activity[38]. Acetyl- co-A- carboxylase inhibitors[39], Diuretic activity[40], Neuroporotective and antioxidant activity[41].

Thermodynamic Properties

The chemistry of liquids and mixtures continues fascinate to scientists. Practically liquid is important medium for most chemical reactions, the role of solvent in mediating various chemical reactions is an important and complex question of broad scientific interest. The properties of liquid mixtures have attracted much attention in literature from both theoretical and practical viewpoints. Thus study of liquid mixture properties is necessary for various thermo-acoustics properties and practical applications. From a more fundamental point of view thermodynamic is necessary for understanding properties of complete molecular liquid mixtures and it has been extensively studied using different techniques. In literature survey, reveal that ultrasonic techniques were employed by many workers. Thermodynamic properties viz. density and ultrasonic velocity are temperature dependent which are being measured at the range of different temperatures and atmospheric pressure. Different derived properties can be computed from density and ultrasonic velocity data, since they are important in the study of the thermodynamics trend and theoretical calculation[42]. The different acoustical and thermodynamic parameters like, Adiabatic compressibility (ßs), linear free length(lf), acoustic impedance(Z), relative association(RA), apparent molar volume(Φv) , apparent molar compressibility (Φß), molar sound velocity(R), internal pressure(Πi), Gibbs free energy (ΔG), molar compressibility, free volume (Vf), relaxation time (Γ), absorption coefficient, specific refraction(r) and molar refraction of binary or ternary liquid mixture are computed by many researchers and which are of considerable important in understanding the nature of intermolecular interaction between the polar and non-polar component in liquid mixtures.

Measurement method

On literature review it is reveals that, for the ultrasonic study of pure liquids and liquid mixtures commonly, two methods are being employed by many researchers in liquid medium viz. Interferometric method and pulse - echo method. Interferometric method is traditional and more suitable for absolute measurements over entire frequency range.

Interferometric method: For ultrasonic velocity investigation ultrasonic laser interferometer was developed. In double crystal ultrasonic interferometer the change of the distance between the transmitter and receiver is measured, the transmitter and receiver is measured by a single beam laser feed-back interferometer, it consist of laser and external moving mirror which is our case is piezoreceiver.

Pulse-echo method: This method was developed for the measurements in small volume of medium; the chamber volume of ten must be less than 1 ml. In the first realization, ultrasonic pulses were transmitted into the investigated sample through buffer rod. Two reflection are observed from the interface buffer rod /liquid medium and from the bottom of the measurement chamber, the delay time Δt in an ultrasonic transducer and electronic is eliminated in this differential approach .The ultrasound velocity in the medium is found from the measured delay time difference and earlier found length of the measurement chamber. The acoustic path length is deferring mineral for each channel. The last version of the medium 0.7 ml volume chamber is having with four element linear array[43].

Ultrasonics

It is the science of sound waves above the limits of human audibility. Sound is our experience of the propagation of pressure wave through some physical elastics medium such as air or liquids. The pressure waves are generated from some type of mechanical disturb band, generally human hearing cannot go beyond about 18 KHz. The sound beyond this limit is inaudible and is defined an ultrasound. Ultrasound as sound above 20 KHz and up to 100 KHz can generate greater acoustics energy and affect chemical reactivity. The ultrasound range applied in sono- chemistry has been extended up to 2 MHz .The fig. show frequency range of sound and the applicable frequencies in the field of sonochemistry[44].

Table-1
Sound frequencies range and applications[45]

Application	Frequency
Human hearing	16 Hz – 18 KHz
Power ultrasound	20 KHz-100 KHz
Extended range	20 KHz – 2 MHz
Dignostic Ultrasound	5MHz--10 MHZ

Application of ultrasonic measurements: Acoustic method has shown extended application in the field of solution chemistry, physical chemistry, biochemistry and chemical engineering[46] the physicochemical properties of this compound show the applicability of substances in ultrasonic study. This review is mainly intended to study the application of ultrasound which causes the possible changes in acoustic and thermo dynamical properties of liquid-liquid mixtures and their degree

of deviation from ideality. Ultrasonic technique has been found to be excellent qualitative and quantitative tools to obtain information about the molecular structure and intermolecular forces which are exit in sold- liquid and liquid-liquid mixtures which shows considerable effect on the physical and chemical properties of substituted thiazole[47]. i. G.A. Shvekhgeimer et al. analyes the effect of ultrasound on organic reaction involving participation of heterocyclic compounds[48], ii. Rorigo Cella.et al. has explain ultrasound has been utilize to asses a wide synthetically useful organic reaction and also used in therapeutic and diagnostic application viz. medical ultra sonography and teeth cleaning. Use of ultrasound makes it possible to carry out homogeneous and heterogeneous reaction of various types in liquid media and also in solid- liquid system[49]. iii. Javad Safaei Ghomi et.al. gave the advantage of ultrasound in chemical reactions such as shorter times, higher yields and milder condition could be useful for industrial application in the pharmaceutical or fine chemical industry[50]. iv. In recent year the ultrasonic velocity of liquids is fundamentally related to the binding forces between atoms and molecules and has been successfully employed in understanding the nature of molecular interactions in pure liquids, binary and ternary liquids mixtures[51]. v. The use of ultrasonic was proved to be useful probe for generating more information on many areas. The ultrasonic measurements have application in chemical and food processing, material testing under water ranging and cleaning. An ultrasonic vibrations is commonly employed in mechanical machinery material[52]. it is also applicable in preparation of colloids or emulsions in the pregeneration of seeds, for imaging of biological tissues[53]. Activation energy of metabolic process[54]. Formation and destruction of azeotropes in petrochemical industries and in non-destructive testing (NDT) [55]. Ultrasonic study of binary or ternary liquid-liquid mixtures are very important part of thermodynamics, acoustic and transport properties of system containing biologically important substituted thiazoles.

The ultrasound can enhance or promote chemical reaction and mass transfer and offer the potentials for shorter reaction cycles, cheaper reagent and less extreme physical condition, so the application of ultrasound is found in the field of pharmacological activity of thiazole and various areas which have been identified for their great potential for future. Ultrasonic has been applied in studies of chemical synthesis, cleaning in the rinsing process, catalysis, filtration, crystallization, drying, irradiation, extraction, emulsification, material processing, food processing and water treatment[56].

Reported work on substituted thiazoles: Recently, Several researchers has shown interest in study of liquid mixtures containing substituted thiazole as one of the components and they investigated acoustic and thermo dynamic properties of binary and ternary liquid mixtures of some substituted thiazoles and have been reported as: Ku. Deepali P. Gulwade et. al. studied the ultrasonic behavior and molecular interaction of substituted thiazole[57]. Rupali Talegaonkar et. al. have studied some acoustic properties of substituted thiazolyl schiffs bases viz. 2-3(4-methoxy phenyl) -1-(4-phenyl-thiazole-2-ylimino) –ally] 4-methyl phenol 2-3 phenyl-1-(4-phenyl –thiazole-2-ylimino)-ally] -4-methoxy phenol, 2- [3-(4-chlorophenyl)-1(4-phenyl-thiazol-2ylimino)-allyl]-4methyl-phenol. From observation of these properties the molecular interaction in binary solvent mixtures are predicted[58]. Shashikant Ikhe, et.al reported ultrasonic study of substituted isothiazole and pyrazoline in dioxane and dioxane-water mixtures at different temperature viz. 3 (2-hydroxy-3-bromo-5methyl phenyl) 5-phenyl isothiazole[59]. Aly Ashraf A. et.al. Studied molecular interaction of substituted thiazoles in acetone using pulse-echo techniques and result show that acoustics and volumetric parameter gives valuable information about the behavior of thiazolidines in solution of the solute solvent interaction and investigated its antibacterial activity on the basis of adiabatic compressibility[60]. Shipra Baluja et. al. have been studied the acoustical parameter of some benzo(d) thiazole derivatives from ultrasonic velocity and density at different concentration in 1-4 Dioxane and N-N-Dimethyl formamide (DMF) and results are interpreted with significant behavior of benzothiazole in solution[61].

The studies of some substituted thiazole which have been taken under ultrasonic investigation are as follows: Aminothiazole 2-Aminothiazole): It is pale yellow crystalline heterocyclic compound, its molecular formula is $C_3H_4N_2S$ and mol. Wt. is 100.14g/mole, it is soluble in water, alcohol and ether. It is used in sulfur drugs, biocides. It is an intermediate of dyestuffs, photographic chemicals and pharmaceuticals.

2-amino, 5-methyl thiozole (2-Amino 5 methyl thiazole, 5-methyl 1, 3-thiazole 2-amine). Its molecular formula $C_4H_6N_2S$, Molecular weight: 114.17 g/mole An 2-aminothizole derivatives used in characterization and DNA-interaction studies via formation of metal complexes that binds competitively to DNA. 2-amino-5methylthiazole can be used in solar cells to influence the interaction with the TIO_2 photo electrode, which in turn alter the dye-sensitized solar cell performance. It is active pharmaceutical ingredients, advanced intermediates for synthesis of molecules used in preparation of drug.

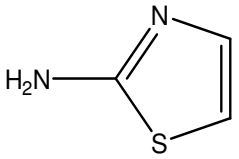
2-chlorobenzothiazole (2Chlorobnenzo [D] thiazole, Benzothiazole, 2-chloro, 2-Benzothiazolyl chloride): It is yellow brownish liquid, insoluble in water, molecular formula is C_7H_4ClNS, molecular weight: 169.63 g/mole, MP. 294-296 K (lit), BP: 414 K (Lit) Density 1.303g/cm^3 at 298 K (lit).

2-bromo thiazole (2-Bromo-1-3 thiazole): It is colourless, irritating, flammable liquid. Molecular formula C_3H_2BrNS, Molecular weight: 164.02 g/mole, MP. 117^{0}c BP: (Lit) Density 1.82g/cm^3 (lit), Insoluble in water.

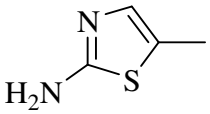
Mercaptobenzothiazole (MBT) or (Benzothiazolethiol): It is yellow powdered compound. It is very toxic. Molecular formula is $C_6H_5NS_2$, Molecular weight: 167.24, MP. 444 K , BP. 533 K,

Density 1.24 (lit),Insoluble in water, soluble in alkalis', alcohol, Acetone, Benzene, and Chloroform.

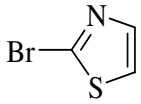
It is used as anti-infective, anti-fungal, fungicide, Bactericide, Wood preservative, rubber industry as vulcanizing accelerant. It is also used in latex foam curing systems.



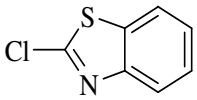
2-aminothiazole



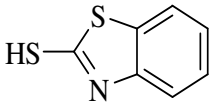
2 amino 5- methyl thiazole



2-bromo thiazole



2-chloro benzothiazole



2-mercapto benzothiazole

The above characteristic properties of substituted thiazole had motivated the author to measure the ultrasonic velocity of some substituted thiazoles which give better insight in studding various inter-molecular interaction and thermo acoustic properties in binary or ternary liquid mixture with acetonitrile 1-4dioxane, N N-Di-mehylformamide(DMF), methanol, ethanol, 1-propanol,1-butanol[62-63] solvents in water at different temperatures.

Conclusion

After the review of literature survey, the detail study of some five member substituted thiazoles under identical set of experimental condition is still lacking, thus, it is intend to study the acoustic and thermodynamic properties of some substituted thiazoles in the light of ultrasonic technique by interferometer method. The present article is an attempt to review the reported scientific investigation in the field of ultrasonic velocity and density measurement for heterocycles and the detailed research associated with substituted thiazoles moiety indicates a broad spectrum of biological activities, thermo acoustical properties of different substituted thiazoles. The review will be fruit full base for further modification on substituted thiazoles moiety and this modification can be utilized as potent therapeutic agent in future and also display valuable acoustic properties and ultrasonic application agent for researchers.

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