International Journal of Research in Advent Technology, Vol.6, No.11, November 2018
E-ISSN: 2321-9637
Available online at www.ijrat.org

Dielectric Dispersion Study of Isoxazole Derivatives with Binary Mixtures of DMSO

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Abstract- Isoxazole derivatives namely 3-methyl-4(4-methoxybenzilidine) 4H-isoxazole 5 one, 3-methyl-4(4-hydroxybenzylidene)isoxazol-5(H)one, 3-methyl-4- (4hydroxybenzylidene) isoxazol-5(4H)One, 3-methyl-4 (benzylidene) isoxazol--5(4H)one have been synthesized using aromatic aldehyde, hydroxylamine hydrochloride and β-keto ester in aqueous media. The dielectric permittivity spectra of these isoxazole with binary mixtures of Dimethyl sulfoxide have been measured using Agilent precision LCR meter in the frequency range of 20Hz to 2MHz at different temperatures. The static dielectric permittivities of these binary mixtures were discussed.

Keywords: Isoxazole; DMSO; Dielectric permittivity; LCR meter.

1. INTRODUCTION

Isoxazoles are five membered heterocyclic ring compounds **[1-3]**. Isoxazole nucleus and their derivatives were found to exhibit various biological and pharmaceutical activities including anticancer, antimyacobacterial, antitumor, antioxidant, nematicidal, antituberculosis, antiinflammatory, antifungal, antimicrobial, anticonvalsant, antiviral **[4-7]**. Thus there are ubiquitous medicinal values, isoxazole nucleus containing heterocyclic drug molecule has acquired a leading position in pharma market **[8-10]**, including some of popular drugs of this class are Valedecoxib, Leflunomide, Cycloserine, Zonisamide, drazoxol etc. Dimethyl sulfoxide (DMSO) has the ability to act as a carrier for transferring other drugs through the cell membrane **[11-12]**. Since the isoxzoles are drug molecules and DMSO is incorporated into a number of products for healthcare and drug delivery applications. It is interesting to study the interaction of isoxazole with DMSO molecules. In literature, dielectric study of such synthesized materials is not observed. In the present paper, the synthesis of Isoxazole derivatives namely 3-methyl-4(4-methoxybenzilidine) 4H-isoxazole 5 one (BA) 3-methyl-4 (4-hydroxybenzylidene) isoxazol-5(H)one (PDICH3BA), 3-methyl-4- (4hydroxybenzylidene) isoxazol-5(4H) One(POCH3BA) and 3-methyl-4 (benzylidene) isoxazol--5(4H)one (POHBA) have been carried out using aqueous media. After that the dielectric measurements of these isoxazoles with binary mixtures of DMSO have been carried out using frequency domain technique in the frequency range of 20Hz to 2MHz at temperatures 40°C, 50°C and 60°C.

2. EXPERIMENTAL

2.1 Materials

A reaction mixture (Fig.1) of ethylacetoacetate (1mmol), hydroxylamine hydrochloride(1mmol), aromatic aldehyde (1mmol) and 10 mol% of iodine was added in 10 ml of distilled water and stirrer at room temperature for 5 – 10 min. Further the reaction mixture was subjected to reflux condition for 30 min. The progress of the reaction was monitored by thin layer chromatography after completion of reaction. The precipitate, which is formed, poured on crushed ice or ice-cold water. Further, the precipitate was filtered, washed with cold water and dried on vacuum pump to obtain desired product. Crystallization was carried out using hot ethanol. By using different aromatic aldehydes the synthesized isoxazoles are 3-methyl-4(4-methoxybenzilidine) 4H-isoxazole 5 one (BA) 3-methyl-4 (4-hydroxybenzylidene) isoxazol-

5(H)one (PDICH3BA), 3-methyl-4-(4hydroxybenzylidene) isoxazol-5(4H) One (POCH3BA) and 3-methyl-4 (benzylidene) isoxazol--5(4H)one (POHBA). Characterization was carried out using spectroscopic techniques.

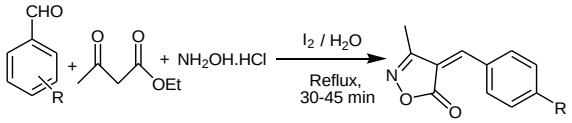


Fig.1 Systematic representation of reaction.

2.2 Measurements and data analysis

The dielectric measurement of isoxazoles with DMSO binary mixtures at frequency range from 20 Hz to 2MHz using Agilent precision LCR meter E4980A and Agilent 16452A liquid dielectric test fixture have been done. The static dielectric constants of binary mixtures were determined by using 'capacitive measurement method' with a short compensation at 2 MHz. The detailed measurement techniques have been described elsewhere **[13-14]**.

3. RESULT AND DISCUSSION

3.1 Dielectric permittivity spectra

Figs. 2, 3, 4 & 5 a) show the frequency dependent spectra of the real part of the relative dielectric function ε' for Isoxazole – DMSO binary mixtures respectively. It is observed that the dielectric permittivity for Isoxazole and its binary mixtures with DMSO have very high value at lower frequency and these values lowers with increase in frequency. The higher values of ε' at lower frequencies are due to ionic conduction process and electrode polarization phenomenon. The dielectric permittivity values for pure DMSO and Isoxazole – DMSO binary mixtures becomes independent around 100KHz. In this study the static dielectric permittivity is reported at 2MHz.

3.2 Dielectric loss spectra

Figs 2, 3,4 & 5 b) show the dielectric loss (tan δ) for the Isoxazole –DMSO binary mixtures at 40°C. The dielectric loss peaks exhibit at different frequencies for the same concentrations of Isoxazoles in DMSO. The tan δ spectra has the loss peak value corresponding to the electrode polarization relaxation frequency (f_{EP}), which is used to evaluate the electrode polarization relaxation time, $\tau_{EP}= (2\pi f_{EP})^{-1}$ **[15-16]**.

The dielectric loss behavior of each isoxazole in DMSO is different. DMSO-BA mixtures, the dielectric loss peak value increases and shift towards high frequency from pure DMSO to 2.5% BA in DMSO and further addition of BA (5% and 7.5%) it lowers and shifts towards lower frequency. DMSO-PDICH3BA mixtures, the dielectric loss peak value lowers and shifts towards high frequency for 2.5% of PDICH3BA, on further addition of PDICH3BA (5%) it increases and shifts towards lower frequency. DMSO-POCH3BA mixtures, the dielectric loss peak value increases and shifts towards high frequency systematically, such that τ_{EP} for DMSO> 2.5% POCH3BA > 5% POCH3BA. DMSO-POHBA mixtures, the dielectric loss peak value increases and shifts towards high frequency slowly from 2.5% to 7.5%. The value of static dielectric permittivity of all isoxazoles studied here is goes on increasing with increase in concentration of isoxazole in DMSO.

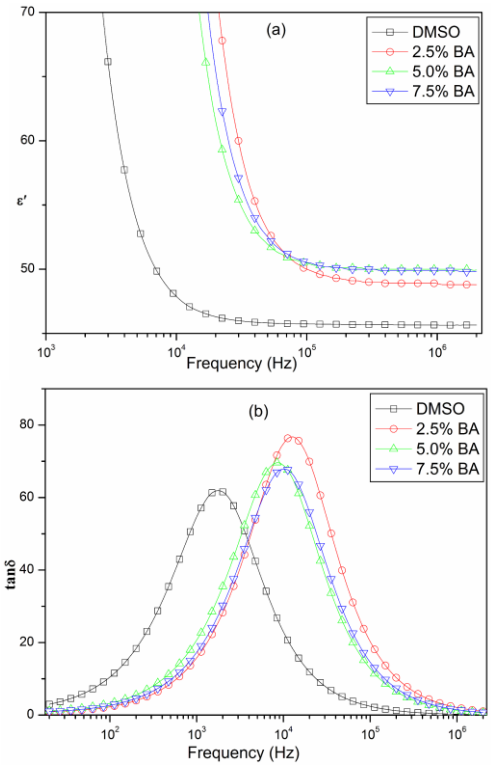


Fig. 2 a) shows the frequency dependent spectra of the real part of the relative dielectric function ε' and b) dielectric loss tangent, tanδ of BA-DMSO binary mixtures.

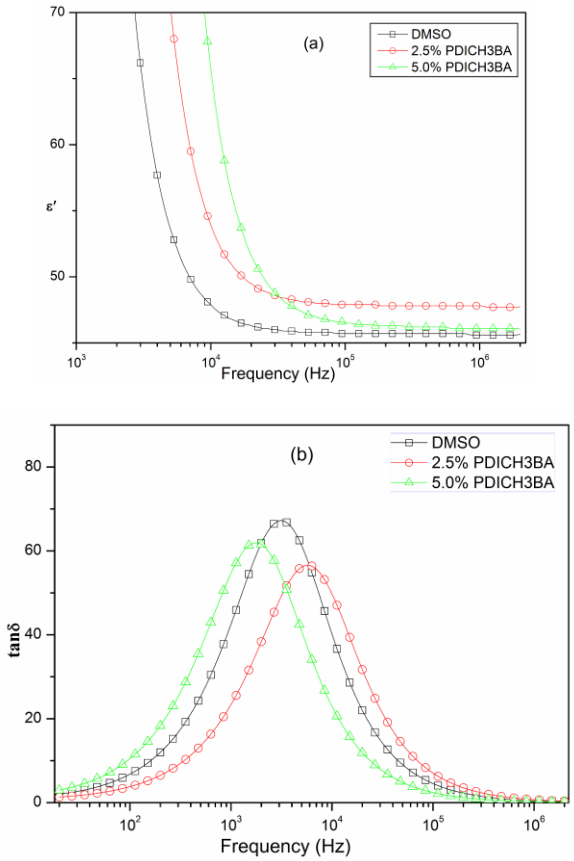
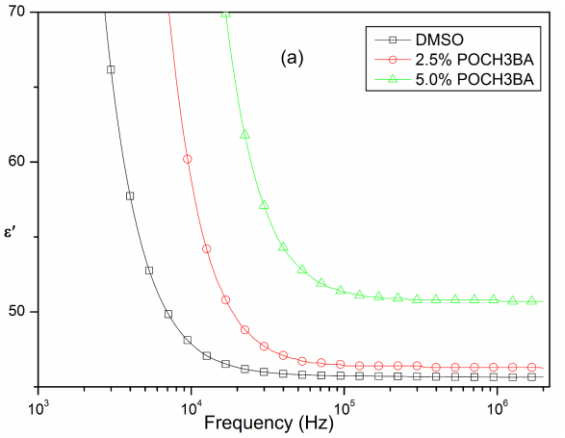


Fig.3 a) shows the frequency dependent spectra of the real part of the relative dielectric function ε' and b) dielectric loss tangent, tanδ of PDICH3BA-DMSO binary mixtures.



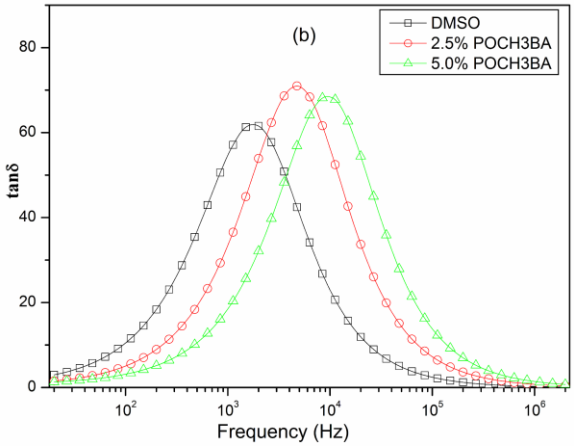


Fig. 4 a) shows the frequency dependent spectra of the real part of the relative dielectric function ε' and b) dielectric loss tangent, tanδ of POCH3BA-DMSO binary mixtures.

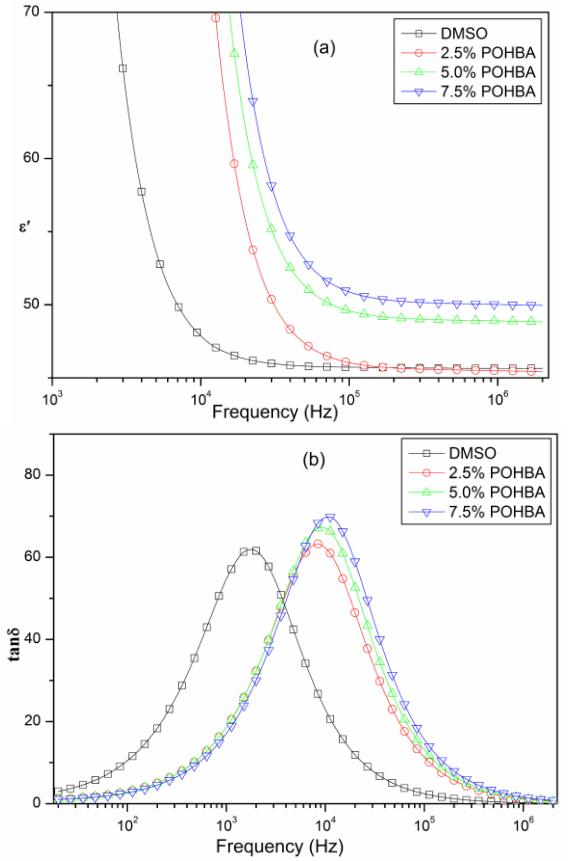


Fig. 5 a) shows the frequency dependent spectra of the real part of the relative dielectric function ε' and b) dielectric loss tangent, tanδ of POHBA-DMSO binary mixtures.

3.3 Static dielectric permittivity

The plots (Fig.6, 7, 8 and 9) of static dielectric permittivity of isoxazoles – DMSO binary mixtures vs. wt. percentage of isoxazoles exhibit non linear nature. This non linearity may be due to certain molecular interactions among the isoxazole–DMSO molecules. The isoxazoles studied here are prepared using water and iodine as catalysis and its donating groups are such that POHBA > POCH3BA > PDICH3BA > BA. If these isoxazoles are compared in context with static dielectric permittivity the ε_0 values for 2.5% of isoxazole (Fig. 10) is such that the ε_0 value of POHBA < POCH3BA < PDICH3BA < BA which is exactly opposite to that of donating groups. The ε_0 value for 5% of isoxazole (Fig. 11) is POCH3BA < BA < POHBA < PDICH3BA. The nature of static dielectric permittivity values is anomalous for all concentrations of isoxazole it may be due to molecular interactions among the isoxazole – DMSO molecules. Due to less solubility of isoxazoles in DMSO, we cannot carry the dielectric measurement over entire concentration range. It limits our further discussion of the hetero molecular interactions among these molecules.

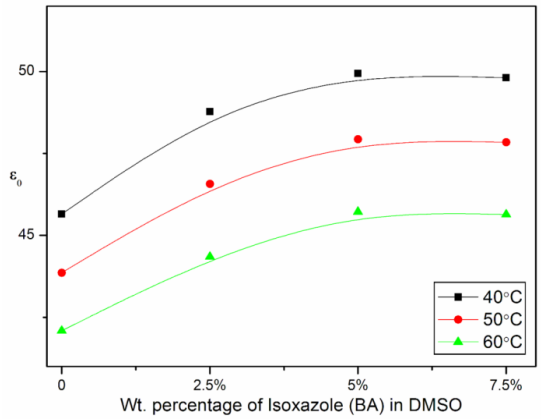


Fig.6 Static dielectric permittivity (ε_0) for BA-DMSO at different temperatures.

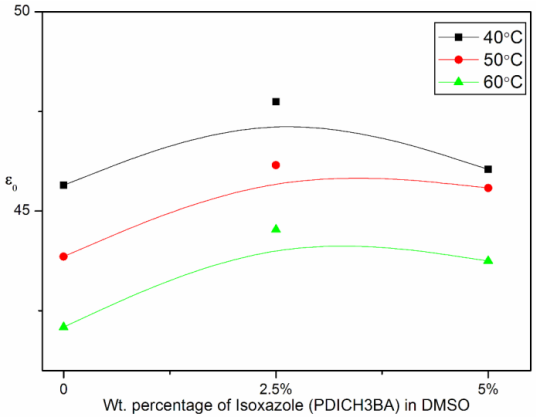


Fig.7 Static dielectric permittivity (ε_0) for PDICH3BA-DMSO at different temperatures.

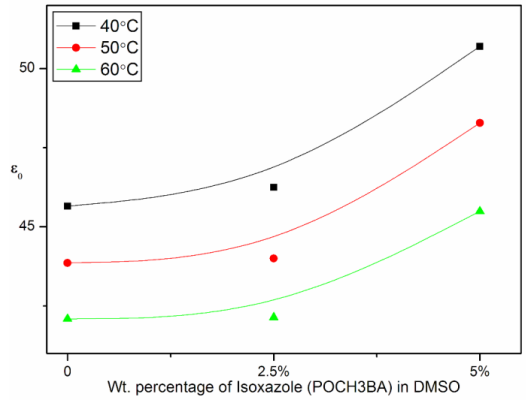


Fig.8 Static dielectric permittivity (ε_0) for POCH3BA-DMSO at different temperatures.

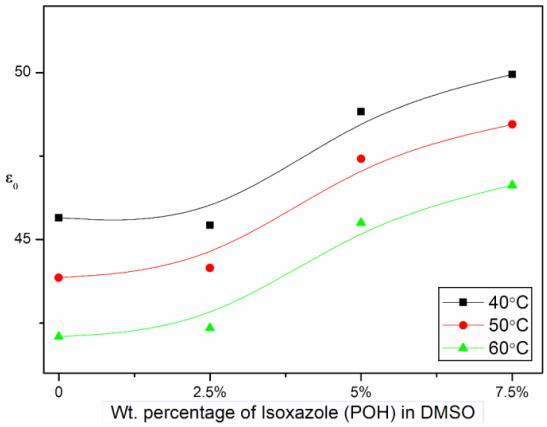


Fig.9 Static dielectric permittivity (ε_0) for POHBA-DMSO at different temperatures.

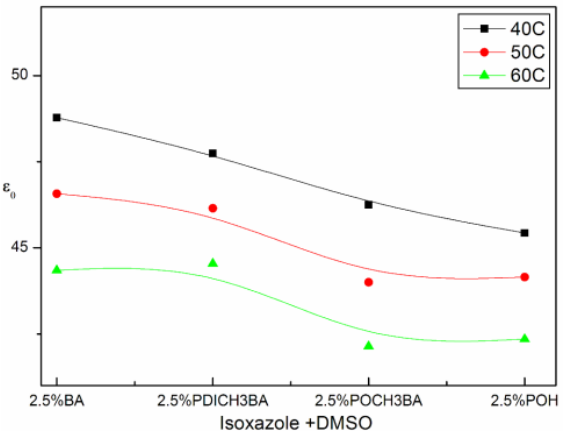


Fig.10 Static dielectric permittivity (ε_0) for 2.5% Isoxazoles in DMSO.

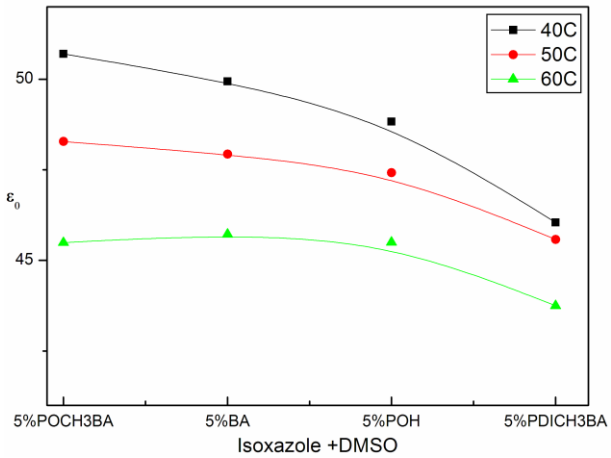


Fig.11 Static dielectric permittivity (ε_0) for 5% Isoxazoles in DMSO.

4. CONCLUSION

Isoxazole derivatives namely 3-methyl-4(4-methoxybenzilidine) 4H-isoxazole 5 one, 3-methyl-4(4-hydroxybenzylidene)isoxazol-5(H)one, 3-methyl-4- (4hydroxybenzylidene) isoxazol-5(4H)One, 3-methyl-4 (benzylidene) isoxazol--5(4H)one have been synthesized using aromatic aldehyde, hydroxylamine hydrochloride and β-keto ester in aqueous media. The dielectric characterization of these isoxazole with binary mixtures of Dimethyl sulfoxide have been carried out using frequency domain technique in the frequency range of 20Hz to 2MHz. The dielectric spectra and static dielectric permittivity have been reported for the isoxazole- DMSO binary mixtures at different temperatures.

Acknowledgements

Financial support provided by SERB, DST, New Delhi (SR/FTP/PS-203/2012) is gratefully acknowledged.

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