ISSN 0036-0244, Russian Journal of Physical Chemistry A, 2019, Vol. 93, No. 9, pp. 1703–1707. © Pleiades Publishing, Ltd., 2019.

PHYSICAL CHEMISTRY OF SOLUTIONS

Ultrasonic Investigations on Molecular Interactions of *N*-Phthaloyl Compounds in Protic and Non-Protic Solvents at 303–318 K

Pradip Tekade[a],*, Bhagyashri Tale[a],, and Sonal Bajaj[a]**

[a] *Department of Chemistry, Jankidevi Bajaj College of Science, Jamnalal Bajaj Marg, Civil Lines, Wardha, India*

**e-mail: pradiptekade@gmail.com*

*** e-mail: bhagyashritale@gmail.com*

Received January 27, 2018; revised December 27, 2018; accepted January 15, 2019

Abstract—Ultrasonic studies of (1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)-4-methylpentanoic acid (NPTLU), 2-(2-(2-(4-chlorophenyl)-1H-benzo[d]imidazol-1-yl)-2-oxoethyl)isoindoline-1,3-dione (C-BI-CL-L), 2-(4-methyl-1-(2-(4-nitrophenyl)-1H-benzo [d]imidazol-1-yl) -1-oxopentan-2-yl)isoindoline-1,3-dione (C-BI-NO_2-L), 2-(1-(2-(4-nitrophenyl)-1H-benzo[d]imidazol-1-yl)-1-oxobutan-2-yl)-2,3-dihydroinden-1-one (C-BI-NO_2-G), 2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)-*N*-(4-oxo-2-phenylquinazolin-3(4H)-yl) acetamide (C-QA-GL), and 1-(2-((4-oxo-2-phenylquinqxolin-3(4H)-yl)carbamoyl)benzoyl)pyrrolidine-2-carboxylic acid (C-QA-PR) in solution of polar and non-polar solvent of various concentrations at 303–318 K. Density and ultrasonic velocity measured and with the help of these data, different thermo-acoustical parameters viz. adiabatic compressibility, intermolecular free length, acoustic impedance, surface tension, Rao's constant, molar volume, Wada's constant calculated using standard formulas. The variation of these parameters with concentration and temperature studied using graphical representations of these parameters. Ethyl alcohol and DMSO were chosen as polar and non-polar solvents, respectively. The variation in different properties reveals the presence of specific molecular interactions in solute and solvent used, which will give information regarding drug transmission and absorption.

Keywords: adiabatic compressibility, intermolecular free length, acoustic impedance, surface tension, Rao's constant, molar volume, Wada's constant

DOI: 10.1134/S0036024419090188

INTRODUCTION

Ultrasonic waves are used to study the molecular structures, interactions and molecular energies.We reported ultrasonic studies on molecular interactions in *N*-phenyl-3-(pyridin-4-yl) prop-2-enamide solutions in ethanol at 303, 308, 313 K [1] and ultrasonic study of pyridoxine solutions at different temperatures and concentrations [2]. Ultrasonic study of liquid solutions is also reported by various researchers [3–5]. IR spectroscopy study is also reported to study hydrogen bonding [6–9] and molecular interactions [10].

EXPERIMENTAL

We studied (1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)-4-methylpentanoic acid (NPTLU), 2-(2-(2-(4-chlorophenyl)-1H-benzo[d]imidazol-1-yl)-2-oxoethyl)isoindoline-1,3-dione (C-BI-CL-L), 2-(4-methyl-1-(2-(4-nitrophenyl)-1H-benzo [d]imidazol-1-yl)-1-oxopentan-2-yl)isoindoline-1,3-dione (C-BI-NO_2-L), 2-(1-(2-(4-nitrophenyl)-1H-benzo[d]imidazol-1-yl)-1-oxobutan-2-yl)-2,3-dihydroinden-1-one(C-BI-NO_2-G), 2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)-*N*-(4-oxo-2-phenylquinazolin-3(4H)-yl) acetamide (C-QA-GL), and 1-(2-((4-oxo-2-phenylquinqxolin-3(4H)-yl)carbamoyl) benzoyl) pyrrolidine-2-carboxylic acid (C-QA-PR) (Table 1) in solution of polar and non-polar solvent. AR grade ethanol and DMSO used as a solvent. Density measurements performed by using pyknometer. The ultrasonic velocity (U) of these solutions measured using Digital Ultrasonic Echo Pulse Velocity Meter, Model VCT-70 (Vi Microsystem Pvt. Ltd., Chennai-96) at frequency 2 MHz with an accuracy of 0.1%. The various acoustical parameters like adiabatic compressibility (β_{ad}), intermolecular free length (L_f), acoustic impedance (Z), Wada's constant (W), Rao's constant (R), molar volume (V_m), surface tension (S) are calculated from U and ρ value using standard formulae:

adiabatic compressibility

$$\kappa = (1/v^2\rho),\ \mathrm{kg}^{-1}\ \mathrm{ms}^2,$$

acoustic impedance

$$Z = v\rho,\ \mathrm{kg\ m}^{-2}\ \mathrm{s}^{-1},$$

Table 1. Structure of studied compounds

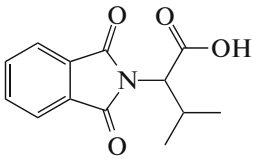
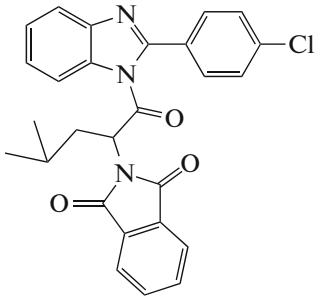
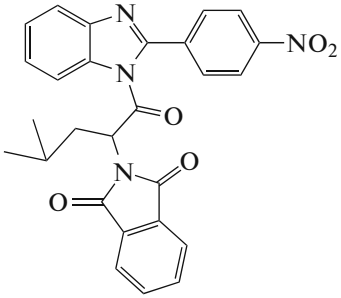
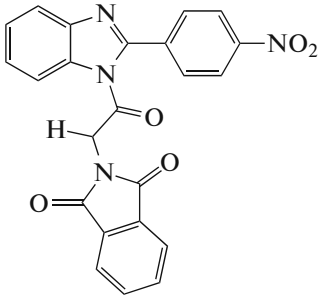
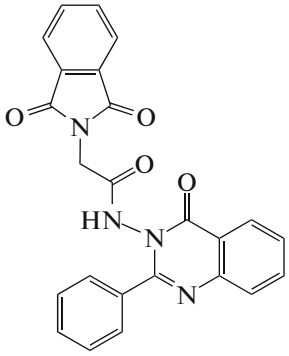
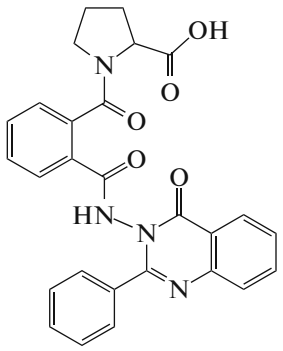
S.N.	Name	Structure
1	2-(1,3-Dioxo-1,3-dihydro-2H-isoindol-2-yl)-4-methyl-pentanoic acid (*N*-phthaloylleucine) (NPT-LU)	
2	2-(2-(2-(4-Chlorophenyl)-1H-benzo[d]imidazol-1-yl)-2-oxoethyl)isoindoline-1,3-dione (C-BI-CL-L)	
3	2-(4-Methyl-1-(2-(4-nitrophenyl)-1H-benzo[d]imidazol-1-yl)-1-oxopentan-2-yl)isoindoline-1,3-dione (C-BI-NO_2-L)	
4	2-(1-(2-(4-Nitrophenyl)-1H-benzo[d]imidazol-1-yl)-1-oxobutan-2-yl)-2,3-dihydroinden-1-one (C-BI-NO_2-G)	
5	2-(1,3-Dioxo-1,3-dihydro-2H-isoindol-2-yl)-*N*-(4-oxo-2-phenylquinazolin-3(4H)-yl)acetamide (C-QA-GL)	

Table 1. (Contd.)

S.N.	Name	Structure
6	1-(2-((4-Oxo-2-phenylquinqxolin-3(4H)-yl)carbamoyl)benzoyl)pyrrolidine-2-carboxylic acid (C-QA-PR)	

free length

$$L_f = (K/v\rho^{1/2}),\ \text{m},$$

Rao's constant

$$R = Vv^{1/3},$$

surface tension

$$v = (S/6.3\times10^{-4}\rho)^{2/3},$$

where ρ is density of the solution, K is Jacobson temperature dependent constant defined as $K = (93.875 + 0.345T) \times 10^{-8}$, M is molecular weight.

FTIR spectrum recorded using Bruker Alpha FTIR spectrometer at Department of Chemistry, Jankidevi Bajaj College of Science, Wardha.

RESULT AND DISCUSSION

Acoustical study. The increase in values of velocity with increasing concentrations indicates the increase in cohesive forces due to solute–solvent interactions, intermolecular attractions and macromolecular motion in solution which is also evidence for the possibility of H-bond formation between solute and solvent. Thus, this increase in ultrasonic velocity may be due to strong dipole–dipole interactions. Increasing value of density with increasing concentration suggests increase in solvent–solvent and solute–solvent interaction due to structure making ability of solute in presence of solvent. Adiabatic compressibility indicates relative change of volume of a liquid with change in pressure or under stress. Higher the values of compressibility, lower will be the intermolecular attractive forces such as dipole–dipole, hydrogen bonding, etc. The distance between the surfaces of the adjacent molecules is called as free length or intermolecular free length. Intermolecular free length (L_f) changes because of intermolecular attraction or repulsion. Decrease in values of intermolecular free length with increasing concentration suggests significant interaction among solute and solvent molecules because as number of ions or particles increases in solution, the gap (intermolecular free length) between two species decreases. Acoustic impedance is the ratio of instantaneous pressure excess at any particle in medium to instantaneous velocity of that particle in medium. The increasing acoustic impedance values also supports effective solute-solvent interactions. The increasing values of apparent molar volume with increase in concentration also confirms the strong solute-solvent and ion-solvent interactions. The values of Rao's constant and Wada's constant variation indicates the changes in molecular interaction. Surface tension is used for the study of surface composition in aqueous solution. A variation of the surface tension supports the effective interactions between the solute and solvent. Graphical representation of various thermo-acoustical parameters shows that there is non-linear variation of these parameters for all the studied binary systems under study over the whole composition and temperature. The deviation from linearity in all the above cases also indicates a strong solute–solvent interaction. On addition of solute in solvents, non-specific physical interactions and unfavorable interactions between unlike component molecules come into play thereby giving the non-linear variation in various thermo-acoustical parameters at different temperature and concentration of binary solvent mixtures.

2-(1,3-Dioxo-1,3-dihydro-2H-isoindol-2-yl)-4-methylpentanoic Acid (N-Phthaloylleucine) (NPT-LU)

The increasing values of ultrasonic velocity, density, acoustic impedance, surface tension with increase in concentration and decreasing values of adiabatic compressibility as well as intermolecular free length suggest strong interaction between solute and solvent.

Table 2. IR absorption frequency, cm^{-1}

S.N.	Compound	Solute	Solute + polar solvent	Solute + nonpolar solvent
1	NPTLU	2953.51	3349.74	3402.38
2	C-BI-NO_2-L	3500	3330.38	3667.79
3	C-BI-NO_2-G	3500	3346	3851.41
4	C-BI-CL-L	3554.30	3741	3741
5	C-QA-PR	3433.02	3334.57	3407.85
6	C-QA-GL	3412.44	3401.60	3328.60

Benzimidazole Derivatives

For all solutions (C-BI-CL-L, C-BI-NO_2-L, C-BI-NO_2-G in Ethanol and DMSO) density, velocity, acoustic impedance, molar volume, surface tension Rao's constant and Wada's constant increases with increase in concentration. Adiabatic compressibility as well as Intermolecular free length decreases with increase in concentration. This indicates strong intermolecular interaction which supports interactions between solute–solute and solvent–solvent molecules. In other words, it is evidence of interactions between molecules in the solution. The non-linear trend for acoustical parameters is may be due to more interactions between solute–solute and solvent–solvent molecules as compared to solute–solvent molecules.

Quinaxaline Derivatives

For solutions of C-QA-GL and C-QA-PR in ethanol. Values of density, velocity, acoustic impedance, Rao's constant, Wada's constant, molar volume, surface tension increases and adiabatic compressibility as well as the intermolecular free length decreases with increase in concentration. This indicates strong intermolecular interaction. For solutions of C-QA-GL in DMSO, density, velocity, acoustic impedance, molar volume, surface tension except Rao's constant and Wada's constant, increases with increase in concentration. Adiabatic compressibility as well as Intermolecular free length decreases with increase in concentration. This supports interactions between solute–solute and solvent– molecules. For solutions of C-QA-PR in DMSO, density, velocity, acoustic impedance, molar volume, surface tension, Rao's constant (except at 303 and 318 K) and Wada's constant (except at 303 and 318 K) increases with increase in concentration. Adiabatic compressibility as well as Intermolecular free length decreases with increase in concentration. This is also evidence of interactions between molecules in the solution. The non-linear trend for acoustical parameters is may be due to more interactions between solute–solute and solvent–solvent molecules as compared to solute–solvent molecules.

FTIR spectral analysis. Results of ultrasonic velocity measurement are further supported by FTIR spectral study (Table 2). The change in values of transmittance and shift in values of frequency of representative peaks –OH and other functional groups present in the compounds in FTIR spectra gives information about molecular interaction which leads to the complex formation among solute and solvent. The variation of ultrasonic velocity and other parameters may be explained on the basis of hydrogen bond formation between solute and solvent. Here all solutes has carbonyl/ hydroxyl/ carboxylic acid functional group and solvent has hydroxyl/carbonyl functional group. So hydrogen bonding between solute and solvent is possible. In these figures, frequency is expressed in terms of wave number. In IR spectra, when solute dissolved in solvent (ethanol/DMF/DMSO) then its IR absorption frequency is found to be different from the value of IR absorption frequency of pure solute. Alteration in frequency in presence of solvents supports hydrogen bonding among solute and solvent. Although, various oxygen and nitrogen atoms are there in the structure of the compound, which are also available for hydrogen bonding with the hydrogen atom in –O–H group of ethanol. It is seen from the FTIR spectrum of binary mixture that, shift in frequency of –OH group is more pronounced as that of other groups. Therefore, it can be concluded that the –OH group form a hydrogen bond. The complex formation can be explained through the molecular structures of compounds and solvent.

CONCLUSION

Ultrasonic studies of NPTLU, C-BI-NO_2-L, C-BI-NO_2-G, C-BI-CL-L, C-QA-PR, and C-QA-GL studied in solution of polar and non-polar solvent of various concentrations at different temperatures viz. 303, 308, 313, and 318 K with a view to understand molecular interactions in these solutions. Ethyl alcohol and DMSO/DMF chosen as polar and non-polar solvents respectively. The interaction between the molecules of liquids takes place because of presence of various types of forces such as dispersion forces, charge transfer, hydrogen bonding, dipole-dipole and dipole-induced dipole interactions. We determined density and ultrasonic velocity of *N*-pthaloyl amino acid analogue at different concentration and temperature. Various acoustical parameters such as adiabatic

compressibility, intermolecular free length, Rao's constant, acoustic impedance, relaxation time, surface tension, molar volume, absorption coefficient, free volume, and free length calculated from the experimental velocity and density measurements. Thus the variation of different parameters with temperature and concentration shows the molecular interaction is taking place between the solute molecules in the liquid mixtures. The acoustical and thermodynamic parameters calculated from measured properties suggest the strong molecular interaction in the solution. All the experimental determinations of adiabatic compressibility (β), molar volume (V), free length (L_f), acoustic impedance (Z), Wada's constant (W), and Rao's constant (R) are strongly correlated with each other. The solute–solute molecular association takes place due to dipole – interaction and the polar nature of different molecular species in the mixture. The solute–solvent association takes place due to slightly polar solute and polar/nonpolar nature of the solvent. The association in this mixture is the result of hydrogen bonding in the binary liquid mixtures. The natures of intermolecular interaction explained on the basis of variation of acoustical parameter and infrared analysis.

For NPTLU, the interaction of solute with DMSO is stronger than ethanol since values of acoustical parameters are more for DMSO since value of density, acoustic impedance, Wadas constant, surface tension are high for DMSO and adiabatic compressibility is low for DMSO.

For benzimidazole derivatives (C-BI-CL-L, C-BI-NO_2-L, and C-BI-NO_2-G) values of acoustical parameters i.e., velocity, Rao's constant (R), Wada's constant (W), molar volume (V_m), except acoustic impedance (Z) and surface tension (S) are higher for DMF than ethanol. On the other hand, values of adiabatic compressibility (β_{ad}) and intermolecular free length (L_f) of all the three solutes are higher in ethanol. This indicates the occurrence of strong interaction between solute (C-BI-CL-L, C-BI-NO_2-L, C-BI-NO_2-G) and DMF. The association in this solution is due to hydrogen bonding between solute and solvent. An analysis of these values suggests strong intermolecular interaction which may be due to hydrogen bond, dipole–dipole interaction, and hyperconjugation Thus, the concept of intermolecular interaction studied on the basis of variation of acoustical parameter.

For quinaxoline derivatives, (C-QA-GL and C-QA-PR), the values of parameters velocity, density, acoustic impedance (Z), Rao's constant (R), Wada's constant (W), molar volume (V_m), surface tension (S), of C-QA-GL are higher for DMSO than ethanol except density, acoustic impedance and surface tension. On the other hand, values of adiabatic compressibility (β_{ad}) and intermolecular free length (L_f) of C-QA-GL are higher in ethanol. All the values of acoustical parameters except molar volume of C-QA-PR are higher for DMSO than ethanol. Conversely, values of adiabatic compressibility (β_{ad}) and intermolecular free length (L_f) of C-QA-PR are higher in ethanol. This indicates the occurrence of strong interaction between solute (C-QA-PR and C-QA-GL) and DMSO.

Moreover, the molecular interaction between solute and solvents confirmed by FTIR study which shows alternation in –OH group frequency (expressed in terms of wave number) when solute dissolves in solvents, which may be due to the presence of hydrogen bonding. It can also be concluded that molecular interactions in the ethanol and DMSO/DMF solution of all solutes are due to complex formation on the basis of hydrogen bonding. This property is directly responsible for the increase in potency of the drug and shows good effectiveness of the drug. So, these compounds possess remarkable and noticeable acoustical property.

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