Acoustical studies of some derivatives of 1,5-benzodiazepines at 298.15 K

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ABSTRACT

Some new derivatives of 1,5-Benzodiazepines have been synthesized and their structural characterizations are done by IR, NMR and Mass Spectral data. The ultrasonic velocity, density and viscosity of these synthesized compounds have been measured in dimethyl formamide and tetrahydrofuran at 298.15 K. From these experimental data, some acoustical parameters such as isentropic compressibility, intermolecular free path length, Rao’s molar sound function, relaxation strength, solvation number etc., have been calculated which helps in understanding the molecular interactions occurring in these solutions.

*Keywords: Benzodiazepine derivatives; ultrasonic Study; acoustical parameters; DMF; THF

1. INTRODUCTION

In recent years, much effort has been made to study ultrasonic properties of liquid mixtures. However, scanty work has been done for solutions of organic compounds. Over the last few years, our research group is actively engaged in studying different types of organic compounds in various solvents. In continuation of these investigations, the present paper reports acoustical properties of some Benzodiazepine derivatives in DMF and THF over entire concentration range at 298.15 K. The results are interpreted in terms of molecular interaction occurring in the solution.

2. EXPERIMENTAL

Five new Benzodiazepine derivatives have been synthesized. The reaction scheme is given in Figure 1. The compounds were recrystalized before use. The physical properties of synthesized compounds are given in Table 1 along with different substitutions. The DMF and THF used in the present work were of AR grade and were purified according to the standard procedure. For all the compounds, solutions were prepared in DMF and THF over a wide range of concentrations and were stored in air tight bottles.

The computation of ultrasonic and thermodynamic properties requires the measurements of ultrasonic velocity viscosity and density. The densities (ρ) of pure solvents and their solutions were measured by using a single capillary pycnometer, made of borosil glass having a bulb capacity of 10 ml.
The ultrasonic velocity \((U)\) of pure solvents and their solutions were measured by using single crystal variable path ultrasonic interferometer operating at 2 MHz. The accuracy of density and velocity are \(\pm 0.0001 \text{ g/cm}^3\) and \(\pm 0.1 \% \text{ cm/sec}\) respectively.

The viscosity \((\eta)\) of pure solvents and solutions were measured by an Ubbelohde viscometer with an accuracy of 0.05 %. All the measurements were carried out at 298.15 K. The uncertainty of temperature is \(\pm 0.1 \text{ K}\) and that of concentration is 0.0001 moles /dm\(^3\).

3. RESULTS AND DISCUSSION

Table 2 shows the experimental data of density \((\rho)\), viscosity \((\eta)\) and ultrasonic velocity \((U)\) of solutions of benzodiazepine derivatives at 298.15 K. The variation of ultrasound velocity \((U)\) with concentration is shown in Figure 2. It is observed that in DMF and THF solutions, density, ultrasonic velocity and viscosity values increases with concentration for all the compounds.

From these experimental data of density, viscosity and ultrasound velocity of pure solvent and solutions, various acoustical parameters were calculated using the reported standard equations\(^8\). Figure 3 shows the variation of isentropic compressibility \((\kappa_s)\) with concentration, which is reverse in nature than that of velocity \((U)\). Further, Table 3 shows that intermolecular free length \((L_f)\) and relaxation strength \((r)\) also decreases with increase in concentration for all the compounds.

The increase of \(U\) and decrease of \(\kappa_s\), \(L_f\) and \(r\) suggest aggregation of solvent molecules around solute molecules indicating thereby the presence of solute-solvent interactions.

Properties like molar sound function \((R_m)\), molar compressibility \((W)\) and Vander Waals constant \((b)\) are observed to increase linearly with concentration for all the systems in both solvents. The linear variation of these acoustical properties indicates the absence of complex formation in these systems, as shown in Table 3 and Figure 4.

Figure 5 shows the variation of solvation number \((S_n)\) with concentration. The solvation number \((S_n)\) is a measure of structure forming or structure breaking tendency of a solute in solutions. In all the systems, \(S_n\) values are positive and increases with increase in concentration in both the solvents. The positive solvation number is due to structure forming tendency of these compounds in both the solvents.

Further, the apparent molar compressibilities \((\phi_k)\) of the solutions are fitted to Gucker’s relation\(^10\)

\[
\phi_k = \phi^0_k + S_k \sqrt{C}
\]

From the plot of \(\phi_k\) verses \(\sqrt{C}\), \(\phi^0_k\) and \(S_k\) values are evaluated from the intercept and slope. The isentropic compressibility of all the solutions were also fitted to the following Bachem’s relation\(^11\):

\[
\kappa_s = \kappa^0_s + AC + BC^{3/2}
\]

and values of \(A\) and \(B\) were evaluated from the intercept and slope respectively. All these values of intercept and slopes are given in Table 4.

It is evident from Table 4 that in both DMF and THF solutions, \(A\) and \(\phi^0_k\) values are negative whereas \(B\) and \(S_k\) values are positive for all the compounds. The negative \(A\) and \(\phi^0_k\)
and higher B values indicates solute-solvent interactions. The higher $S_k$ values are also the indication of predominance of solute-solvent interactions.

Table 1. Physical constants of 1,5-benzodiazepines.

| Sr. No. | Code | R    | M.F.       | M. Wt. (g/mol) | $R_f$ Value | M.P. °C | Yield % |
|---------|------|------|------------|----------------|-------------|---------|---------|
| 1       | NKG-A| 4-OH | C$_{24}$H$_{15}$ClF$_3$N$_3$O | 415.8         | 0.74        | 248     | 61      |
| 2       | NKG-B| 4-CH$_3$ | C$_{25}$H$_{15}$ClF$_3$N$_3$ | 413.9         | 0.82        | 186     | 55      |
| 3       | NKG-C| 4-Cl  | C$_{24}$H$_{14}$ClF$_3$N$_3$ | 434.4         | 0.59        | 232     | 52      |
| 4       | NKG-D| 2-OH  | C$_{24}$H$_{15}$ClF$_3$N$_3$ | 415.8         | 0.63        | 177     | 58      |
| 5       | NKG-E| H    | C$_{24}$H$_{15}$ClF$_3$N$_3$ | 399.8         | 0.70        | 182     | 62      |

Table 2. The density (ρ), ultrasonic velocity (U) and viscosity (η) of 1,5-benzodiazepine derivatives in DMF and THF at 298.15 K.

| Conc. (M) | Density g·cm$^{-3}$ | Velocity x 10$^5$ cm·s$^{-1}$ | Viscosity x 10$^3$ poise | Density g·cm$^{-3}$ | Velocity x 10$^5$ cm·s$^{-1}$ | Viscosity x 10$^3$ poise |
|-----------|---------------------|--------------------------------|--------------------------|---------------------|--------------------------------|--------------------------|
| NKG-A     |                     |                                |                          |                     |                                |                          |
| 0.00      | 0.9449              | 1.4616                         | 8.1418                   | 0.8815              | 1.2780                         | 4.6005                   |
| 0.01      | 0.9472              | 1.4628                         | 8.4259                   | 0.8822              | 1.2796                         | 4.7869                   |
| 0.02      | 0.9503              | 1.4636                         | 8.5980                   | 0.8845              | 1.2804                         | 4.9152                   |
| 0.04      | 0.9546              | 1.4648                         | 8.7095                   | 0.8866              | 1.2812                         | 5.1107                   |
| 0.06      | 0.9559              | 1.4664                         | 8.8547                   | 0.8922              | 1.2820                         | 5.2144                   |
| 0.08      | 0.9576              | 1.4672                         | 8.9514                   | 0.8947              | 1.2828                         | 5.3538                   |
| 0.10      | 0.9587              | 1.4680                         | 9.1318                   | 0.8998              | 1.2844                         | 5.4794                   |
| NKG-B     |                     |                                |                          |                     |                                |                          |
| 0.01      | 0.9463              | 1.4640                         | 8.3899                   | 0.8828              | 1.2792                         | 4.7752                   |
| 0.02      | 0.9490              | 1.4648                         | 8.5501                   | 0.8845              | 1.2792                         | 4.8816                   |
| 0.04      | 0.9510              | 1.4664                         | 8.6646                   | 0.8863              | 1.2792                         | 5.0001                   |
| 0.06      | 0.9545              | 1.4668                         | 8.7772                   | 0.8884              | 1.2796                         | 5.0983                   |
| 0.08      | 0.9581              | 1.4676                         | 8.8872                   | 0.8915              | 1.2800                         | 5.2442                   |
| 0.10      | 0.9622              | 1.4700                         | 9.0676                   | 0.8957              | 1.2808                         | 5.4317                   |
| NKG-C     |                     |                                |                          |                     |                                |                          |
| 0.01      | 0.9508              | 1.4636                         | 8.2449                   | 0.8845              | 1.2796                         | 4.7470                   |
| 0.02      | 0.9520              | 1.4648                         | 8.3881                   | 0.8882              | 1.2804                         | 4.8344                   |
| 0.04      | 0.9551              | 1.4664                         | 8.5244                   | 0.8897              | 1.2828                         | 4.9366                   |
| 0.06      | 0.9575              | 1.4676                         | 8.7484                   | 0.8917              | 1.2844                         | 5.0344                   |
| 0.08      | 0.9604              | 1.4684                         | 8.8680                   | 0.8929              | 1.2860                         | 5.1506                   |
| 0.10      | 0.9660              | 1.4700                         | 9.1156                   | 0.8956              | 1.2888                         | 5.2494                   |
| Conc. (M) | L_f (Å³) | R | R_m 10^{-3} cm^{-3} s^{-1/3} | b cm^{-3} mol^{-1} | L_f (Å³) | r | R_m 10^{-3} cm^{-3} s^{-1/3} | b cm^{-3} mol^{-1} |
|----------|----------|---|-----------------------------|-------------------|----------|---|-----------------------------|-------------------|
| NKG-D    |          |    |                             |                   |          |   |                             |                   |
| 0.01     | 0.9482   | 1.4632 | 8.2665                      | 0.8837            | 1.2784   | 4.7502 |
| 0.02     | 0.9529   | 1.4648 | 8.4121                      | 0.8864            | 1.2792   | 4.8996 |
| 0.04     | 0.9546   | 1.4664 | 8.5320                      | 0.8892            | 1.2796   | 5.0353 |
| 0.06     | 0.9578   | 1.4676 | 8.7306                      | 0.8930            | 1.2812   | 5.1285 |
| 0.08     | 0.9603   | 1.4696 | 8.8589                      | 0.8946            | 1.2828   | 5.2095 |
| 0.10     | 0.9642   | 1.4712 | 9.0131                      | 0.8973            | 1.2836   | 5.3314 |
| NKG-E    |          |    |                             |                   |          |   |                             |                   |
| 0.01     | 0.9464   | 1.4628 | 8.3267                      | 0.8829            | 1.2780   | 4.6825 |
| 0.02     | 0.9489   | 1.4636 | 8.4690                      | 0.8832            | 1.2792   | 4.7550 |
| 0.04     | 0.9523   | 1.4656 | 8.6362                      | 0.8858            | 1.2800   | 4.8364 |
| 0.06     | 0.9563   | 1.4676 | 8.7614                      | 0.8882            | 1.2816   | 4.9320 |
| 0.08     | 0.9591   | 1.4688 | 8.8478                      | 0.8905            | 1.2836   | 5.0163 |
| 0.10     | 0.9612   | 1.4700 | 8.9972                      | 0.8942            | 1.2852   | 5.1089 |

**Table 3.** Variation of some acoustical parameters with concentration of 1,5-benzodiazepine derivatives in DMF and THF at 298.15 K.

| Conc. (M) | L_f (Å³) | R | R_m 10^{-3} cm^{-3} s^{-1/3} | b cm^{-3} mol^{-1} | L_f (Å³) | r | R_m 10^{-3} cm^{-3} s^{-1/3} | b cm^{-3} mol^{-1} |
|----------|----------|---|-----------------------------|-------------------|----------|---|-----------------------------|-------------------|
| NKG-A    |          |    |                             |                   |          |   |                             |                   |
| 0.00     | 0.1476   | 0.1655 | 4.0746                      | 77.3503           | 0.1747   | 0.3620 | 4.1205                      | 81.8016           |
| 0.01     | 0.1473   | 0.1641 | 4.1496                      | 78.7525           | 0.1754   | 0.3676 | 4.2097                      | 83.6946           |
| 0.02     | 0.1469   | 0.1632 | 4.2198                      | 80.0700           | 0.1762   | 0.3743 | 4.2943                      | 85.5290           |
| 0.04     | 0.1465   | 0.1619 | 4.3662                      | 82.8259           | 0.1759   | 0.3731 | 4.4853                      | 89.3044           |
| 0.06     | 0.1462   | 0.1600 | 4.5260                      | 85.8271           | 0.1742   | 0.3616 | 4.6896                      | 93.0893           |
| 0.08     | 0.1460   | 0.1591 | 4.6820                      | 88.7694           | 0.1733   | 0.3572 | 4.8771                      | 96.7016           |
| 0.10     | 0.1459   | 0.1582 | 4.8405                      | 91.7573           | 0.1723   | 0.3528 | 5.0482                      | 99.9793           |
| NKG-B    |          |    |                             |                   |          |   |                             |                   |
| 0.01     | 0.1472   | 0.1628 | 4.1538                      | 78.8120           | 0.1743   | 0.3600 | 4.2067                      | 83.4684           |
| 0.02     | 0.1469   | 0.1619 | 4.2251                      | 80.1504           | 0.1739   | 0.3588 | 4.2908                      | 85.1117           |
| 0.04     | 0.1466   | 0.1600 | 4.3820                      | 83.0963           | 0.1737   | 0.3576 | 4.4721                      | 88.6803           |
| 0.06     | 0.1463   | 0.1596 | 4.5286                      | 85.8671           | 0.1731   | 0.3556 | 4.6394                      | 91.9492           |
| 0.08     | 0.1459   | 0.1587 | 4.6727                      | 88.5846           | 0.1726   | 0.3540 | 4.7989                      | 95.0724           |
| 0.10     | 0.1454   | 0.1559 | 4.8135                      | 91.2038           | 0.1718   | 0.3508 | 4.9624                      | 98.2285           |
| NKG-C    |          |    |                             |                   |          |   |                             |                   |
| 0.01     | 0.1469   | 0.1632 | 4.1424                      | 78.6030           | 0.1746   | 0.3616 | 4.2448                      | 84.2606           |
| 0.02     | 0.1467   | 0.1619 | 4.2293                      | 80.2300           | 0.1744   | 0.3608 | 4.3672                      | 86.6724           |
| 0.04     | 0.1463   | 0.1600 | 4.3977                      | 83.3925           | 0.1742   | 0.3600 | 4.6120                      | 91.5119           |
| 0.06     | 0.1460   | 0.1587 | 4.5672                      | 86.5832           | 0.1737   | 0.3588 | 4.8420                      | 96.0450           |
| 0.08     | 0.1457   | 0.1577 | 4.7317                      | 89.6873           | 0.1734   | 0.3576 | 5.0860                      | 100.8535          |
| 0.10     | 0.1451   | 0.1559 | 4.8791                      | 92.4461           | 0.1727   | 0.3568 | 5.2882                      | 104.8410          |
Table 4. Bachem’s constants $A$, $B$, $\phi_v$, $S_v$, $\phi_k$ and $S_k$ of 1,5-benzodiazepine derivatives in DMF and THF at 298.15 K.

| COMPOUNDS | A · $10^{11}$ dyn$^{-1}$·cm$^3$·mol$^{-1}$ | B · $10^{11}$ dyn$^{-1}$·cm$^{-1/2}$·mol$^{-3/2}$ | $\phi_k$ · $10^8$ dyn$^{-1}$·mol$^{-1}$ | $S_k$ · $10^8$ dyn$^{-1}$·cm$^{-3/2}$·mol$^{-3/2}$ |
|-----------|--------------------------------------------|-----------------------------------------------|---------------------------------|-----------------------------------|
|           | DMF                                        | THF                                           |                                 |                                   |
| NKG-A     | -2.82                                      | 5.33                                          | -1.57                          | 5.28                              |
| NKG-B     | -2.90                                      | 5.36                                          | -0.70                          | 2.40                              |
| NKG-C     | -4.20                                      | 12.05                                         | -3.50                          | 11.33                             |
| NKG-D     | -2.33                                      | 2.00                                          | -3.40                          | 10.27                             |
| NKG-E     | -1.97                                      | 1.85                                          | -1.07                          | 3.00                              |
|           | THF                                        |                                               |                                 |                                   |
| NKG-A     | -2.79                                      | 2.30                                          | -0.49                          | 0.83                              |
| NKG-B     | -3.16                                      | 5.46                                          | -0.94                          | 8.80                              |
| NKG-C     | -2.83                                      | 1.97                                          | -2.15                          | 0.75                              |
| NKG-D     | -0.72                                      | 3.33                                          | -1.00                          | 3.90                              |
| NKG-E     | -2.91                                      | 3.50                                          | -1.68                          | 3.75                              |
Figure 1. Reaction Scheme.

\[
\text{F} \quad \text{NH}_2
\]

\[(\text{CH}_3\text{CO})_2\text{O} \quad + \quad \text{H}_2\text{SO}_4
\]

\[\text{F} \quad \text{NH} \quad \text{O}
\]

\[\text{Vilsmeier - Haack Formylation}\]

\[\text{POCl}_3 + \text{DMF}
\]

\[\text{F} \quad \text{Cl} \quad \text{R} \quad \text{O} \quad \text{H}_2\text{SO}_4
\]

\[\text{NH}_2 \quad \text{NH}_2 \quad + \quad \text{Cl}
\]

\[\text{R} \quad \text{COCl}_3 \quad 40\% \text{NaOH}
\]

\[\text{F} \quad \text{Cl} \quad \text{R} \quad \text{O}
\]

\[\text{H}^+ \quad \text{NH}_2 \quad \text{NH}_2
\]

\[\text{F} \quad \text{R} \quad \text{N} \quad \text{H} \quad \text{N} \quad \text{H} \quad \text{R} = \text{Aryl}
\]
**Figure 2.** Variation of Ultrasonic velocity (U) with concentration of 1,5-benzodiazepine in (A) DMF and (B) THF at 298.15 K.
Figure 3. Variation of Isentropic compressibility ($\kappa_s$) with concentration of 1,5-benzodiazepine in (A) DMF and (B) THF at 298.15 K.
Figure 4. Variation of molar compressibility (W) with concentration of 1,5-benzodiazepine in (A) DMF and (B) THF at 298.15 K.
Figure 5. Variation of Solvation Number ($S_n$) with concentration of 1,5-benzodiazepine in (A) DMF and (B) THF at 298.15 K.

4. CONCLUSION

All the studied compounds exhibited solute-solvent interactions in DMF and THF solutions.

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