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Physicochemical properties of some tetrahydropyrimidine derivatives

Shipra Baluja, Ashish Patel

Abstract

Production of tetrahydropyrimidine and their derivatives is of great importance in organic chemistry. Presence of pyrimidine piece in different biological compounds that are used in several medications makes it a crucial component. In this study, some new tetrahydropyrimidine compounds are synthesized and their physicochemical properties such as such as density, refractive index, partition coefficients have been studied in different solvents at 308.15K.

Keywords density, partition coefficients, refractive index, tetrahydropyrimidine compounds

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Introduction

Recently, synthesis of tetrahydropyrimidine and their derivatives has gained high interest in organic chemistry. The pyrimidine fragment is present in various biologically active compounds, many of which have been used in medical practices [1-2]. This class of compounds displays wide range of biological and pharmacological properties. Tetrahydropyrimidines are known to possess calcium antagonistic [3-5], anti-inflammatory [6-8], analgesic [9-10], antitumor [11-12], antidepressant [13], anti-bacterial and antifungal properties [14-16].

Owing to the biological importance of these tetrahydropyrimidine compounds, it is quiet necessary to study their physicochemical properties such as density, refractive index, conductance etc, which would be useful to further study the use of these compounds in biological field.

Properties like refractive index, viscosity and density of binary liquid mixtures over the whole composition range are useful to gain complete understanding of their thermodynamics as well as to utilize them for practical chemical engineering purposes. Further, these properties are useful for the adequate designing of industrial processes [17-19], fermentation [20], dyes [21], canning and preservation of food [22-23] etc. Nowadays, refractive index is used in research related to medical sciences and biotechnology [24-25]. Recent years have seen a rapid increase of research interests in determining the cell physical parameters such as size, shape and refractive index of living cells as demanded by biological studies and cell-based drug screening [2 6-27]. The refractive index method also permits the determination of the concentration distribution of solutes under non-destructive circumstances [28].

Conductivity measurement has been widely used use to determine the dissociation constant and limiting equivalent conductance of weak electrolytes [29], electro-osmotic flow [30], to study conformational changes in poly-electrolytes in aqueous solutions [31], etc. Further, knowledge of conductivity is useful for various biological processes [32-34].

Table 1. Physical parameters and substitutions in synthesized compounds

Code	R	M.F	M.W	Yield (%)	Rf value
ST-1	$C_6H_5^-$	$C_{11}H_{13}N_5$	215.25	78	0.68
ST-2	C_6H_4-CH=CH-	$C_{13}H_{15}N_5$	241.29	60	0.73
ST-3	3-Cl,$C_6H_4^-$	$C_{11}H_{12}ClN_5$	249.70	68	0.44
ST-4	4-Cl,$C_6H_4^-$	$C_{11}H_{12}ClN_5$	249.70	66	0.46
ST-5	4-F,$C_6H_4^-$	$C_{12}H_{15}FN_5$	233.24	62	0.52
ST-6	4-OCH_3,$C_6H_4^-$	$C_{12}H_{15}N_5O$	245.28	84	0.42
ST-7	3-NO_2,$C_6H_4^-$	$C_{11}H_{12}N_6O_2$	260.25	60	0.62
ST-8	3-0CH_3,4-$OHC_6H_4^-$	$C_{12}H_{15}N_5O_2$	261.28	74	0.34
ST-9	4(α-C_4H_3O)$^-$	$C_9H_{11}N_5O$	205.22	82	0.36
ST-10	4-OH-$C_6H_4^-$	$C_{11}H_{13}N_5O$	231.25	56	0.30

Literature survey shows that partition study of compound creates high interest in medicinal or pharmaceutical chemistry research because in pharmacokinetics, the distribution coefficient has a strong influence on ADME properties (Absorption, Distribution, Metabolism, and Excretion) of the drugs [35]. In Pharmacodynamics, the hydrophobic effect is the major driving force for binding drugs to their receptor targets [36-37]. Partition coefficient is the most crucial parameter of QSAR and QSPR study [38-39]. The knowledge of solubility and the octanol-water partition coefficient of drug is important in drug discovery, development, and production [40-45]. Implementation of latest technology makes this research area easy and versatile. Thus, in the present study, physicochemical properties such as density, refractive index, partition coefficients of synthesized tetrahydropyrimidine derivatives have been studied in different solvents at 308.15 K.

Methodology

All the studied synthesized tetrahydropyrimidine derivatives were recrystallized from chloroform. These pure compounds are used for physicochemical studies. The solvents N. N-dimethyl formamide (DMF) and tetrahydrofuran (THF) were of LR grade and were fractionally distilled by the reported method [46]. For each compound, a series of solutions of different concentrations were prepared in DMF and THF solvents.

Refractive index and density measurements

The density of solutions were measured by Anton Paar density and sound velocity meter (DSA 5000M) at constant temperature 303.15 K. The Anton Paar automatic refractometer (Abbemat WR) was used for the measurement of refractive index of solutions of synthesized compounds at constant temperature 303.15 K. The uncertainty of temperature was ±0.1° C. The experimental data of density and refractive index of solutions are given in Table 2.

Conductance

For all the synthesized compounds, conductance is measured in DMF and THF at 308.15 K. The conductance of each solution was measured by using Elico Conductivity Meter (Model No.CM 180) having a cell constant 0.89 cm^{-1} at 308.15 K. The measured conductance was corrected by subtracting the conductance of pure solvent.

Partition coefficient

n-Octanol is a compound of analytical grade. The purity of solvent was checked by GC and found to be 99.8%. Milli-Q-water was used throughout for all the experiments. Ten mg sample was dissolved in n-octanol to give 100 ml solution of 100 ppm. This solution was known as standard solution. Suitable dilutions were made from this standard solution (2 µg to 20 µg).

For the solution of each compound in octanol, absorbance (OD) was measured at different wavelengths (λ) using UV spectrophotometer (Shimadzu, UV-1700, Pharmaspec) to determine λ_{max}.

Table 2. The density (ρ_{12}) and refractive index (n) of compounds in DMF and THF at 303.15 K.

Conc. (M)	DMF		THF		DMF		THF	
	ρ_{12} (g.cm^{-3})	n	ρ_{12} (g.cm^{-3})	n	ρ_{12} (g.cm^{-3})	n	ρ_{12} (g.cm^{-3})	n
	ST-1				ST-6			
0.00	0.9304	1.4171	0.8779	1.4032	0.9304	1.4171	0.8779	1.4032
0.01	0.9323	1.4237	0.8776	1.4038	0.9356	1.4260	0.8760	1.4041
0.02	0.9326	1.4246	0.8790	1.4047	0.9372	1.4262	0.8770	1.4058
0.04	0.9331	1.4260	0.8794	1.4056	0.9386	1.4268	0.8788	1.4079
0.06	0.9338	1.4275	0.8800	1.4069	0.9388	1.4272	0.8800	1.4094
0.08	0.9342	1.4289	0.8816	1.4081	0.9391	1.4280	0.8806	1.4100
0.10	0.9353	1.4304	0.8846	1.4093	0.9395	1.4288	0.8825	1.4114
	ST-2				ST-7			
0.01	0.9330	1.4239	0.8790	1.4053	0.9347	1.4259	0.8820	1.4058
0.02	0.9333	1.4248	0.8804	1.4070	0.9348	1.4267	0.8823	1.4062
0.04	0.9338	1.4259	0.8815	1.4082	0.9350	1.4281	0.8829	1.4070
0.06	0.9340	1.4271	0.8820	1.4089	0.9351	1.4291	0.8835	1.4078
0.08	0.9351	1.4291	0.8824	1.4102	0.9354	1.4301	0.8847	1.4091
0.10	0.9370	1.4309	0.8830	1.4109	0.9359	1.4313	0.8860	1.4101
	ST-3				ST-8			
0.01	0.9359	1.4243	0.8797	1.4045	0.9339	1.4268	0.8770	1.4042
0.02	0.9365	1.4248	0.8814	1.4049	0.9350	1.4272	0.8789	1.4062
0.04	0.9370	1.4255	0.8823	1.4052	0.9365	1.4279	0.8792	1.4076
0.06	0.9376	1.4269	0.8832	1.4057	0.9374	1.4287	0.8818	1.4097
0.08	0.9380	1.4281	0.8841	1.4063	0.9383	1.4291	0.8833	1.4112
0.10	0.9384	1.4289	0.8851	1.4077	0.9393	1.4298	0.8850	1.4128
	ST-4				ST-9			
0.01	0.9343	1.4255	0.8769	1.4045	0.9339	1.4257	0.8774	1.4046
0.02	0.9351	1.4258	0.8783	1.4062	0.9349	1.4265	0.8785	1.4052
0.04	0.9354	1.4262	0.8803	1.4071	0.9360	1.4274	0.8792	1.4063
0.06	0.9356	1.4271	0.8822	1.4089	0.9366	1.4279	0.8800	1.4073
0.08	0.9357	1.4288	0.8831	1.4093	0.9378	1.4289	0.8815	1.4086
0.10	0.9376	1.4302	0.8842	1.4099	0.9387	1.4296	0.8828	1.4096
	ST-5				ST-10			
0.01	0.9330	1.4251	0.8770	1.4048	0.9329	1.4259	0.8780	1.4049
0.02	0.9340	1.4249	0.8781	1.4052	0.9333	1.4265	0.8774	1.4059
0.04	0.9341	1.4251	0.8806	1.4062	0.9334	1.4272	0.8794	1.4079
0.06	0.9346	1.4262	0.8823	1.4073	0.9359	1.4292	0.8814	1.4098
0.08	0.9355	1.4279	0.8851	1.4092	0.9363	1.4301	0.8826	1.4108
0.10	0.9356	1.4290	0.8861	1.4094	0.9371	1.4314	0.8850	1.4122

Solutions of different concentrations were prepared in octanol for each compound and absorbance was measured at respective λ_{max} to get calibration curve.

A known amount of the compound under investigation was dissolved in n-octanol at a concentration not higher than 20 µg. Equal volumes of this solution and water is mixed in oven dried stoppered flask and the mixture was stirred at room temperature for 24 hrs.. After 24 hrs, the solution was transferred into 60 ml of separating funnel and allowed to stand in order to separate the aqueous and organic layers. The organic layer will be the upper one while lower one will be aqueous. The organic layer was then analyzed by UV spectrophotometer. Using calibration curve, the concentration of compounds in organic layer was then evaluated.

The partition coefficient is highly influenced by pH. Hence, in the present study, a wide range of pH (0.84 to 8.0) is selected. For 0.84 pH, 0.1 N HCl was taken whereas for 6.0, 7.4 and 8.0, phosphate buffer was used. These values of pH were selected due to their existence in human body. As HCl is present in gastric juice in stomach, 0.1 N HCl was taken for the reaction. Blood [45] has 7.4 pH, so the study was done at pH 7.4. Further, the middle and upper range of body pH is 6.0 and 8.0 respectively, so study was also done at all of these pH values.

Table 3. Experimental and calculated densities of compounds in DMF and THF solutions at 303.15 K

Compound Code	Density ($g.cm^{-3}$) calculated from experimental data using eq. (1)		Density ($g.cm^{-3}$) calculated from eq. (2)
	DMF	THF	
ST-1	1.1405	1.2143	1.3048
ST-2	1.1756	1.0845	1.2404
ST-3	1.1962	1.1716	1.3865
ST-4	1.1545	1.2259	1.3865
ST-5	1.1339	1.4478	1.3648
ST-6	1.2918	1.1217	1.2840
ST-7	1.0711	1.1360	1.5496
ST-8	1.3046	1.2261	1.3191
ST-9	1.3891	1.1574	1.5199
ST-10	1.2563	1.2663	1.3444

Results and Discussion

The physical parameters and substitutions in synthesized compounds are given in Table 1.

Spectral data

2,4-diamino-6-phnyl-1,4,5,6-tetrahydropyrimidine-5-carbonitrile (ST-1)
mp 141-143°C; IR (KBr): 3151(N-H str), 3093(Ar, C-H str), 2943(C-H str), 2867(C-H str), 2245(C≡N str), 1610(Ar, C=C str), 1519(Ar, C=C str), 1512(Ar, C=C str), 1490(C-H ben), 1427(C-H ben), 1377(C-H ben), 1265(C-C str) cm-1; MS: m/z = 215 $[M]^+$.

2,4-diamino-6-styryl-1,4,5,6-tetrahydropyrimidine-5-carbonitrile (ST-2)
mp 112-114 °C; IR (KBr): 3161(N-H str), 3021(CH=CH str), 3091(Ar, C-H str), 2952(C-H str), 2879(C-H str), 2267(C≡N str), 1609(Ar, C=C str), 1515(Ar, C=C str), 1508(Ar, C=C str), 1481(C-H ben), 1425(C-H ben), 1379(C-H ben), 1252(C-C str) cm-1; MS: m/z = 241 $[M]^+$.

2,4-diamino-6-(3-chlorophenyl)- 1,4,5,6-tetrahydropyrimidine-5-carbonitrile (ST-3)
mp 153-155 °C; IR (KBr): 3163(N-H str), 3097(Ar, C-H str), 2933(C-H str), 2877(C-H str), 2265(C≡N str), 1608(Ar, C=C str), 1514(Ar, C=C str), 1502(Ar, C=C str), 1489(C-H ben), 1421(C-H ben), 1371(C-H ben), 1255(C-C str), 744(C-Cl str) cm-1; MS: m/z = 249 $[M]^+$.

2,4-diamino-6-(4-chlorophenyl)- 1,4,5,6-tetrahydropyrimidine-5-carbonitrile (ST-4)
mp 162-164°C; IR (KBr): 3167(N-H str), 3092(Ar, C-H str), 2942(C-H str), 2876(C-H str), 2260(C≡N str), 1609(Ar, C=C str), 1508(Ar, C=C str), 1518(Ar, C=C str), 1481(C-H ben), 1422(C-H ben), 1376(C-H ben), 1250(C-C str), 742(C-Cl str) cm-1; MS: m/z = 249 $[M]^+$.

2,4-diamino-6-(4-fluorophenyl)- 1,4,5,6-tetrahydropyrimidine-5-carbonitrile (ST-5)
mp 128-130°C; IR (KBr): 3170(N-H str), 3094(Ar, C-H str), 2949(C-H str), 2875(C-H str), 2250(C≡N str), 1622(Ar, C=C str), 1510(Ar, C=C str), 1520(Ar, C=C str), 1486(C-H ben), 1422(C-H ben), 1371(C-H ben), 1259(C-C str), 1065(C-F str) cm-1; MS: m/z = 233 $[M]^+$.

2,4-diamino-6-(4-methoxyphenyl)- 1,4,5,6-tetrahydropyrimidine-5-carbonitrile (ST-6)
mp 116-118 °C; IR (KBr): 3170(N-H str), 3094(Ar, C-H str), 2949(C-H str), 2875(C-H str), 2250(C≡N str), 1619(Ar, C=C str), 1508(Ar, C=C str), 1518(Ar, C=C str), 1478(C-H ben), 1426(C-H ben), 1368 (C-H ben), 1254(C-C str), 1157(C-O-C str) cm-1; MS: m/z = 245 $[M]^+$.

Table 4. Calculated molar refraction and refractive index of 0.1 M solution of compounds in DMF and THF at 303.15 K

Compounds	Solvents			
	DMF		THF	
	$(MRD)_2$	n	$(MRD)_2$	n
ST-1	114.6601	2.3786	73.0112	1.7662
ST-2	119.6821	2.2822	92.6678	1.7736
ST-3	107.8992	2.0531	73.1031	1.6026
ST-4	116.7910	2.1278	86.8397	1.7980
ST-5	115.3017	2.2076	74.4360	1.8980
ST-6	103.1046	2.1386	97.7948	1.8526
ST-7	129.9348	2.1108	86.1133	1.6762
ST-8	113.3016	2.2177	102.7612	1.9493
ST-9	98.7597	2.6587	76.6407	1.8134
ST-10	119.3591	2.5593	91.2837	2.0012

2,4-diamino-6-(3-nitrophenyl)-1,4,5,6-tetrahydropyrimidine-5-carbonitrile (ST-7)
mp 141 -143°C; IR (KBr): 3107(N-H str), 3086 (Ar, C-H str), 3047 (C-H str), 1597 (Ar, C=C str), 1527 (Ar, C=C str), 1512(Ar, C=C str), 1479(C-H ben), 1427(C-H ben), 1315(C-H ben), 1217(C-C str) cm-1; MS: m/z = 260 $[M]^+$.

2,4-diamino-6-(4-hydroxy-3-methoxyphenyl)-1,4,5,6-tetrahydropyrimidine-5carbo nitrile (ST-8)
mp 132-134°C; IR (KBr): 3480(OH str), 3164(N-H str), 3023 (Ar, C-H str), 2947(C-H str), 2822(C-H str), 2241(C≡N str), 1606(Ar, C=C str), 1523(Ar, C=C str), 1538(Ar, C=C str), 1482(C-H ben), 1357(C-H ben), 1330(C-H ben), 1230(C-C str), 1078(C-O-C str), cm-1; MS: m/z = 261 $[M]^+$.

2,4-diamino-6-(furan -2-yl)- 1,4,5,6-tetrahydropyrimidine-5-carbonitrile (ST-9)
mp 72-74°C; IR (KBr): 3124(N-H str), 3043(Ar, C-H str), 2922(C-H str), 2847(C-H str), 2245(C≡N str), 1606(Ar, C=C str), 1552(Ar, C=C str), 1529(Ar, C=C str), 1456(C-H ben), 1394(C-H ben), 1330(C-H ben), 1230(C-C str), 1070(C-O-C str), 1022(C-O-C str) cm-1; MS: m/z = 205 $[M]^+$.

2,4-diamino-6-(4-hydroxyphenyl)-1,4,5,6-tetrahydropyrimidine-5-carbonitrile(ST-10)
mp 176-178°C; IR (KBr): 3635(O-H str), 3165(N-H str), 3088(Ar, C-H str), 2942(C-H str), 2865(C-H str), 2250(C≡N str), 1619(Ar, C=C str), 1510(Ar, C=C str), 1528(Ar, C=C str), 1482(C-H ben), 1426(C-H ben), 1371(C-H ben), 1259(C-C str), 1210 (C-O str) cm^{-1}; MS: m/z = 231 $[M]^+$.

Physicochemical Studies
Table 2 shows the experimental values of densities and refractive index of solutions of all the ten synthesized compounds in DMF and THF at 308.15 K.

The density of solution (ρ_{12}) is related to densities of the solvent, solute and their weight fractions g1 and g2 according to the equation:

$$\frac{1}{\rho_{12}} = \frac{g_1}{\rho_1} + \frac{g_2}{\rho_2} \qquad \ldots (1)$$

where ρ_{12} is the density of solution and ρ_1 and ρ_2 are the densities of solvent and solute respectively.

The densities of all the synthesized compounds were evaluated from the slope of plots of $1/g_1\rho_{12}$ verses g_2/g_1. The inverse of slope gives density of compound (ρ_2). Table 3 shows these calculated densities for all the compounds. Further, the density of compounds was calculated by using the following equation:

$$\rho = KM/N_A \sum \Delta V_i \qquad \ldots (2)$$

Table 5. The equivalent conductance (λ_C) of compounds in DMF at 303.15 K

Conc. (gm/lit)	λC (cm2/mho.equiv.)				
	DMF				
	ST-1	ST-2	ST-3	ST-4	ST-5
0.000	-	-	-	-	-
0.001	4.6000	5.5200	4.4160	6.3480	3.1556
0.002	3.9560	4.6000	4.0940	5.4740	2.3920
0.004	3.1740	3.2200	3.2430	3.5650	2.2310
0.006	2.9440	3.0667	3.0207	3.1587	2.0547
0.008	2.7485	2.8750	2.9440	2.9785	2.1160
0.010	2.6496	2.7600	2.5944	2.9624	1.9596
0.020	2.3092	2.3460	2.3000	2.6772	1.6468
0.040	2.1022	2.1160	2.0700	2.3230	1.7940
0.060	1.8093	1.9167	1.8707	2.3460	1.4475
0.080	1.7595	1.8400	1.8745	2.0815	1.3455
0.100	1.5456	1.6928	1.6836	1.8216	1.2512
	ST-6	ST-7	ST-8	ST-9	ST-10
0.001	3.8364	4.2136	4.2412	4.4712	2.6312
0.002	3.2154	3.7260	4.0940	4.1860	2.2402
0.004	2.8405	3.2200	3.6800	3.8870	2.0470
0.006	2.6603	2.8673	3.3580	3.5113	2.0087
0.008	2.4898	2.6565	3.2085	3.1050	1.9493
0.010	2.4610	2.4748	2.9256	3.1188	1.9044
0.020	2.2149	2.1758	2.8474	2.7784	1.7020
0.040	2.1448	2.0953	2.7140	2.7370	1.4536
0.060	2.1198	2.0853	2.4073	2.4840	1.3800
0.080	1.9027	1.9550	2.0930	2.1850	1.4490
0.100	1.8515	1.8188	1.8685	1.9228	1.4628
	THF				
	ST-1	ST-2	ST-3	ST-4	ST-5
0.000	-	-	-	-	-
0.001	0.1780	0.1780	0.0623	0.1869	0.1246
0.002	0.1691	0.1602	0.0623	0.1856	0.1233
0.004	0.1647	0.1535	0.0556	0.1769	0.1217
0.006	0.1617	0.1498	0.0490	0.1577	0.0979
0.008	0.1569	0.1457	0.0523	0.1491	0.0854
0.010	0.1469	0.1442	0.0561	0.1329	0.0768
0.020	0.1264	0.1255	0.0725	0.1100	0.0598
0.040	0.0850	0.0975	0.0581	0.0837	0.0561
0.060	0.0599	0.0786	0.0479	0.0605	0.0481
0.080	0.0468	0.0728	0.0448	0.0533	0.0457
0.100	0.0400	0.0659	0.0467	0.0478	0.0435
	ST-6	**ST-7**	**ST-8**	**ST-9**	**ST-10**
0.001	0.0623	0.1246	0.0534	0.0445	0.0623
0.002	0.0579	0.1215	0.0579	0.0579	0.0579
0.004	0.0556	0.1128	0.0378	0.0779	0.0556
0.006	0.0490	0.1003	0.0341	0.0935	0.0490
0.008	0.0478	0.0884	0.0289	0.1079	0.0501
0.010	0.0418	0.0828	0.0294	0.1095	0.0472
0.020	0.0414	0.0641	0.0245	0.1304	0.0378
0.040	0.0323	0.0455	0.0207	0.1052	0.0345
0.060	0.0286	0.0398	0.0197	0.0939	0.0316
0.080	0.0253	0.0363	0.0175	0.0792	0.0284
0.100	0.0234	0.0299	0.0165	0.0732	0.0254

ρ indicates the density of the compound, K is packing fraction which is equal to 0.599 for organic compounds, M is for molecular weight of the compound, N_A is the Avogadro's number and ΔV_i is the

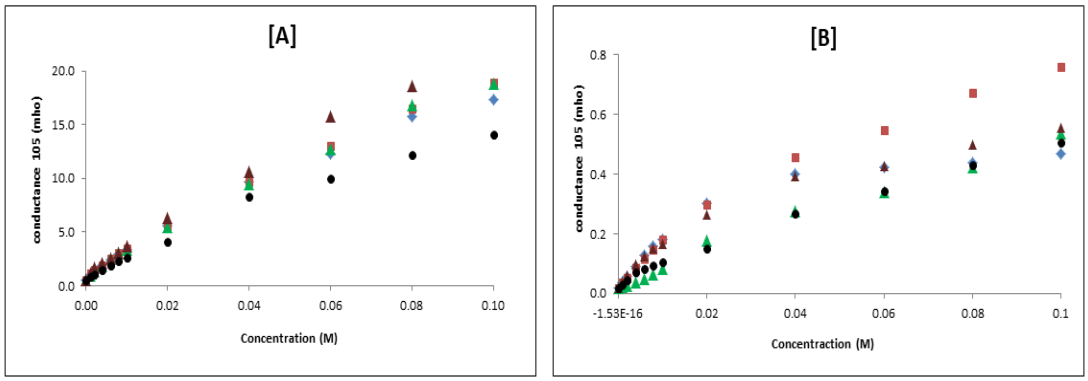


Figure 1. The variation of conductance with concentration for compounds (ST-1-ST-5) in [A] DMF and [B] THF at 303.15 K.

♦: ST-1, ■: ST-2, ▲: ST-3, ▲: ST-4, ●: ST-5

volume increment of the atoms and atomic groups present in the compound. The density of all the studied compounds have been evaluated and reported in Table 3.

Comparison of densities evaluated from graphs and those calculated from eq. (2) showed that calculated values were different from those evaluated graphically. For the same compound, density in the two different solvents was different. This suggests that one has to consider the role of solvent in the measurement of the physical parameters of any solutions. It is because of the fact that, in every solution molecular interactions exists which differ in different solvents. Generally, intermolecular interactions do not affect the density but due to the presence of different substituted groups in solutes, interactions differ in different solvents which may cause change in volume; thereby, affecting the density of solute in a particular solvent.

Further, the molar refraction of a pure liquid (MRD) 1 can be calculated using the Lorentz-Lorenz equation :

$$(MRD)_1 = \left[\frac{n^2-1}{n^2+1}\right]\frac{M}{\rho} \qquad \ldots (3)$$

where n, M and ρ are refractive index, molecular weight and density of pure liquid respectively.

For solutions, the following eq. (4) was used to determine molar refraction.

$$(MRD)_{12} = \left[\frac{n_{12}^2-1}{n_{12}^2+1}\right]\left[\frac{X_1M_1+X_2M_2}{\rho_{12}}\right] \qquad .(4)$$

where n_{12} and ρ_{12} are refractive index and density of solution respectively. X_1 and X_2 are the mole fractions and M_1 and M_2 are the molecular weight of the solvent and solute respectively.

From the values of the molar refraction of solution and pure solvent, molar refraction of solid compounds were determined by following equation:

$$(MRD)_{12} = X_1(MRD)_1 + X_2(MRD)_2 \qquad (5)$$

From the density and molar refraction data, the refractive indexes of all the compounds were calculated from eq. (3). The molar refraction $(MRD)_2$ and refractive index of all the compounds are reported in Table 4 for 0.1 M solution.

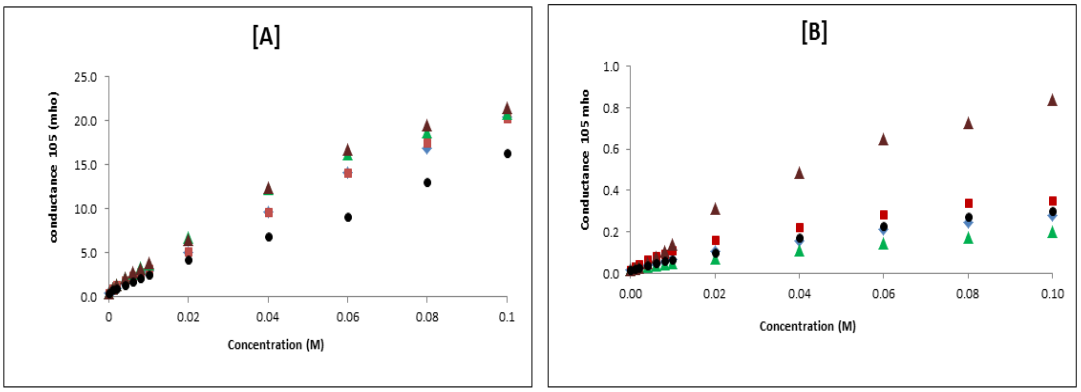


Figure 2. The variation of conductance with concentration for compounds (ST-6-ST-10) in [A] DMF and [B] THF at 303.15 K.

♦: ST-6, ■: ST-7, ▲: ST-8, ▲: ST-9, ●: ST-10

In obtained results, refractive index and $(MRD)_2$ of compounds were distinct in each solvent due to different interaction of every solvent with various functional groups (Table 4). Some of these solvents had formation of hydrogen bonding, while in some there was breakage of bonds. The refractive index and molar refraction are not only dependent on the atomic refraction but also upon single, double or triple bonds. However, it is outlined that bond refraction is more effectual than atomic refraction.

The refractive index and molar refraction depends not only upon. Further, bond polarity also causes change in molar refraction. Thus, type of solvent affects the refractive index and molar refraction of a solute.

The measured conductance (k) of each solution was used to determine the specific conductance (κ), which was then used for the calculation of equivalent conductance (λc). The equations used for calculating the specific conductance (κ) and equivalent conductance (λc) are:

$$\kappa = k\theta \qquad \ldots (6)$$

$$\lambda_c = 1000\frac{\kappa}{C} \qquad \ldots (7)$$

where θ is the cell constant and c is the concentration (g.equi./lit.) of solution. The cell constant θ was 0.89 cm^{-1}.

Figures 1 and 2 shows the variation of measured conductance with concentration. It was observed that for all the compounds, conductance increased nonlinearly with the concentration. However, at lower concentrations, variation was linear. Further, conductance was lower in THF solutions than that in DMF solutions. The lower conductivities of THF solutions may be due to the greater electro relaxation effect owing to the higher permittivity of THF, which contributes large interionic repulsions. The equivalent conductance values of all the compounds in both DMF and THF solutions are reported in Table 5. In DMF solutions, equivalent conductance (λc) is found to increase with dilution. Thus, most of the compounds exhibit weak electrolytic behavior in DMF solutions.

In THF solutions, for some compounds, there is regular increase in equivalent conductance with dilution; thereby, indicating their weak electrolytic behavior. For some compounds (ST-3 and ST-9), equivalent conductance increased with dilution in the beginning, but after √C =0.15, it starteddecreasing. Similar behavior was observed by other workers in DMSO solutions; however, its reason was not clear.

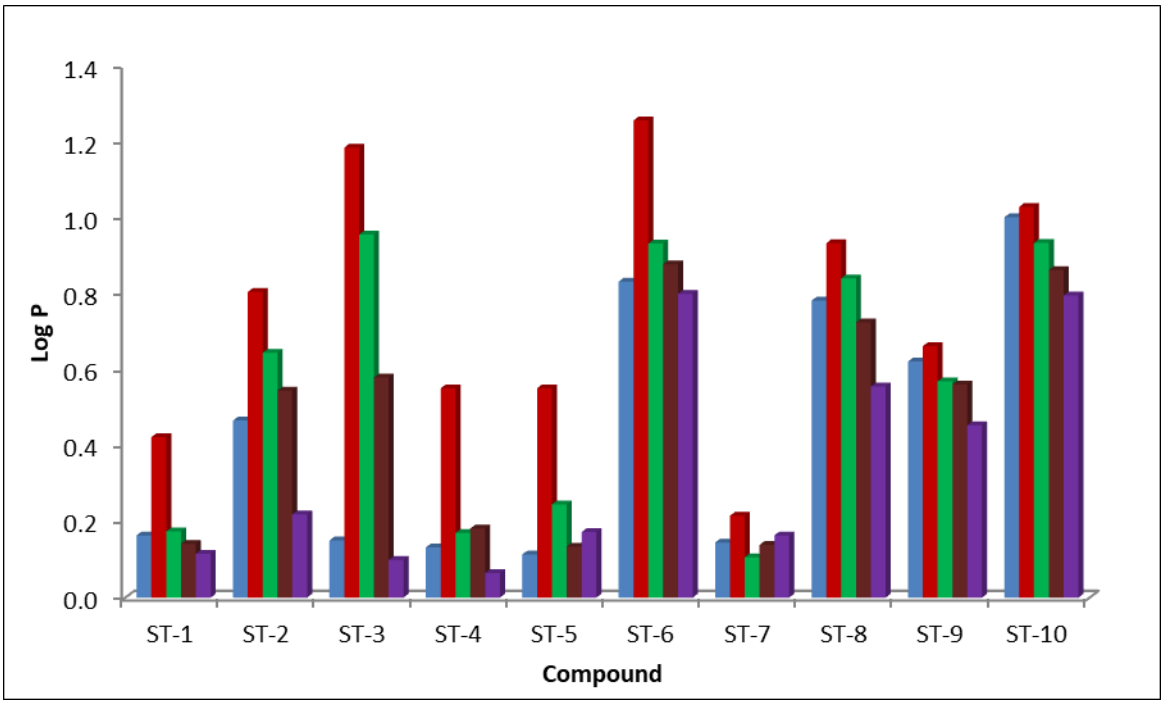


Figure 3. log P values for compounds
■: water, ■: 0.1 N HCl, ■: 6.0 Ph, ■: 7.4 pH, ■: 8.0 pH

For some compounds, λ0 value can be evaluated by extrapolation of plot of λc versus √C. However, for weak electrolytes, it is difficult to determine λ0. Singh and Prasad [47] gave following equation to evaluate λ0 value.

$$k = k_0 + \lambda_0 c + c\phi_{(c)} \qquad \ldots (8)$$

where k and k_0 are the electrolytic conductivity of the solutions and solvent respectively. c is the equivalent concentration and the function $\Phi_{(c)}$ denotes the effect of interionic interactions.

The limiting conductivity can be evaluated accurately from the limiting slope of smaller linear portions of the curve of k verses c, provided other derivatives (dk_0/dc) and $d[c\Phi_{(c)}]/dc$ in differential form of equation (8) are neglected as compared to λ0, which can be determined from differential form of equation (8) is:

$$\frac{dk}{dc} = \frac{dk_0}{dc} + \lambda_0 + \frac{d\left[c\phi_{(c)}\right]}{dc} \qquad \ldots (9)$$

These λ_0 values are reported in Table 6 along with those determined by extrapolation.

From Table 6, it can be observed that in both the solvents, calculated values of limiting equivalent conductance (λ_0) were in fair agreement with those evaluated graphically suggesting thereby that equation (8) can be used for the studied systems. The log P values for the studied compounds at different pH are given in Table 7. The log P value depends upon the hydrophilic and hydrophobic character of compounds and had inverse relation with hydrophilicity of compounds. Table 7 shows that log P varies with pH.

Table 6. The limiting equivalent conductance (λ_0) of compounds in DMF and THF at 303.15 K

Compound Code	λ_0 mho.cm2.equi.$^{-1}$ from graph	$\lambda_0 10^3$ mho.cm2.equi.$^{-1}$ from eq. (4)	λ_0 mho.cm2.equi.$^{-1}$ from graph	$\lambda_0 10^3$ mho.cm2.equi.$^{-1}$ from eq. (4)
	DMF		THF	
ST-1	-	4.874	0.205	0.197
ST-2	-	5.811	0.200	0.190
ST-3	5.950	4.904	-	0.050
ST-4	-	6.648	0.184	0.220
ST-5	4.250	3.081	-	0.198
ST-6	5.550	3.918	0.049	0.072
ST-7	5.650	4.575	0.158	0.161
ST-8	4.950	4.520	-	0.063
ST-9	5.550	4.789	-	0.075
ST-10	3.250	2.792	0.070	0.069

However, no regular pattern was observed. The variation of log P with pH for all the studied compounds is also shown in Figure 3. It is clear from Figure 3 that ST-10 shows maximum hydrophobicity almost in all pH. It was followed by ST-6. ST-7 was found to have minimum log P for almost all pH range in comparison to other compounds suggesting thereby its highly hydrophilic character. Further, for all the compounds, log P values are higher for 0.1 N HCl i.e., at minimum pH.

All the studied compounds had the same central moiety, but different side chains i.e, substituents, as shown in Table 1. Thus, the hydrophobic or hydrophilic character of a compound depends not only on pH, but also on substituent. As reported in Table 1, ST-10 had hydroxy group at para position, whereas ST-8 had methoxy group at para position. Thus, the presence of hydroxy group increased the hydrophobicity (as in ST-10) in comparison to methoxy (as in ST-6). However, when both methoxy and hydroxyl groups were present (as in the case of ST-8), hydrophobic character was in between ST-6 and ST-10. It means lower hydrophobicity. From this observation, one can assume that if -OCH_3 and –OH both are present in the same compound, it increases the polar (hydrophilic) character in the solution due to the presence of two electronegative oxygen atoms. Thus, the substitution in compound plays a major role in the nature of solution.

Further, the position of functional group is also important in the hydrophobic-hydrophilic character of the compound. In ST-4, chloro group was present at the para position which gave least log P, while for ST-3, log P values were quite high in comparison to ST-4 although it also had chloro group, but at meta position.

Table 7. log P values for the synthesized compounds

Compounds Code	Max. absorption Wavelength (nm)	log P				
		Water	0.1N HCl	6.0 pH	7.4 pH	8.0 pH
ST-1	308	0.1636	0.4223	0.1741	0.1415	0.1153
ST-2	350	0.4658	0.8044	0.6443	0.5445	0.2190
ST-3	230	0.1504	1.1841	0.9550	0.5790	0.0989
ST-4	318	0.1320	0.5506	0.1699	0.1818	0.0647
ST-5	314	0.1135	0.5509	0.2452	0.1341	0.1722
ST-6	350	0.8314	1.2556	0.9315	0.8771	0.7994
ST-7	292	0.1449	0.2152	0.1063	0.1388	0.1637
ST-8	382	0.7814	0.9327	0.8402	0.7244	0.5553
ST-9	342	0.6210	0.6617	0.5689	0.5607	0.4537
ST-10	360	1.0009	1.0283	0.9333	0.8618	0.7948

Other noticeable matter in this study was that ST-4 and ST-5 showed almost same behavior. ST-4 contained chloro group at para position, whereas ST-5 contained fluoro group at para position. This suggests that the effect due to the presence of difference halogens is negligible at the same position. Overall observation shows that all compounds exhibited higher hydrophobic character in acidic pH. In some compounds, higher hydrophobic character was also observed in water. In higher basic solutions, almost all compounds showed higher hydrophilic character.

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