The comparative study of basicities, Li^+ and Na^+ affinities of a series of heterocyclic molecules (Pyrrole, Furan, Thiophene and Pyridine) in the ground state - A DFT Study

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ABSTRACT

A comparative study of the proton affinities (PA), Li^+ affinities and Na^+ affinities of a series of heterocyclic molecules Pyrrole, Furan, Thiophene and pyridine and their protonated, lithium and sodium complexes in the gas phase have been performed theoretically by B3LYP (DFT) method using 6-311G(d,p) basis set with complete geometry optimization both before and after protonation, Li^+ complex formation and Na^+ complex formation. The gas phase protonation, Li^+ complex formation and Na^+ complex formation turns out to be exothermic and the local stereochemical disposition of proton, Li^+, and Na^+ is found almost same in each case. Computed proton, lithium and sodium affinities are sought to be correlated with a number of computed system parameters like the net computed charge on the hetero atom (X) of the free molecules and the net charge on the hetero atom (X) and on proton, Li^+, and Na^+ of the protonated, lithium and sodium complexes. The energetics structural and electronic properties of the complexes indicate that the interaction between proton–free molecule, lithium-free molecule and sodium-free molecule is predominantly an ion-dipole attraction and the ion–

induced dipole interaction as well rather than a covalent interaction. The overall reactivity is explained by distant atom contribution in addition to the contribution from free base.

Key words: B3LYP, DFT, Gaussian, Gas phase, PA, Li-A, Na-A, drug discovery

1. INTRODUCTION

The interactions of acid and base are of great importance in drug discovery & chemistry. Quantitative studies in the gas phase provide the intrinsic acidities and basicities free from interference from solvent molecules and counterions. The most widespread study concerns different gas phase proton transfer equilibria (Hunter et al.,1998), The heterocyclic molecules have lately attracted attention due to their "shifted PKa values" upon compexation to metal ions, because it can rationalize the existence of nucleobases of differing protonation state at physiological P^H (Roitzsah et al., 2004). In an effort to understand the nature and origin of variation in the relative magnitude of the basicities to be expected in a series of above said heterocyclic molecules, the most deadly poisons. Alkali metal ions were the first metal cations to be studied in the gas phase for their coordination properties. This is due to their relatively easy production under vacuum. In contrast with transition metal ions, their reactivity towards ligands is quite simple: in general, they form adducts, or clusters that can be considered as ions "solvated" by one or several ligands (Burk et al., 2000). A comparative study of proton affinity, Li^+ affinity and Na^+ affinity of a series of heterocyclic compounds in the ground state have been calculated theoretically by B3LYP(DFT) method using 6-311G(d,p) basis sets. Recently the ground state basicities of a series of substituted crotonaldehyde and acetophenone in their ground state were reported in the literature (Pandit et al., 2006; Senapati et al., 2008). The ground state Li^+ and Na^+ affinities of a series of substituted crotonaldehyde and acetophenone were also reported in the literature (Pandit et al., 2007; Senapati et al., 2007; Senapati et al., 2010). The purpose of the present work is not only to study the basicities, Li^+ and Na^+ affinities of the above said heterocyclic molecules but also to study on geometrical features of their protonated, lithium, and sodium complexes.

Gas phase methods (Beauchamp et al., 1974; Solomon et al., 1974; Long et al., 1974; Wieting et al., 1974) have the advantage for determining the intrinsic ground state, acid base properties in the absence of complicating effect of solvation. To determine the basicities, geometrical features also in the ground state by B3LYP(DFT) method by using Gaussian O3W program (Lee et al., 1988). Here we analyzed the PA, Li-A and Na-A values (ΔE) to understand whether the pre-complex charge distribution local to the molecules or post-complex relaxation of charge density or both are important for explaining the overall basicity of the molecules in a particular state.

These ion-molecule complexes are involved in molecular recognition process (Ma et al., 1997) and help in removing metal cations from contaminated media. These studied may be used to gain insight into many important biological processes (Karlin et al.,1994; Cervenansky et al., 1995; Novotny et al., 1989), electron transfer process (Lippard et al., 1994; Kallim et al., 1994) and more complicated biological system. We have also looked into the possible origin of the small shift in the Li^+ and Na^+ affinities on the heterocyclic molecules. We have looked that the bond formed by Li^+ and Na^+ is largely ionic, and the alkali metal cation retains 0.8-0.9 units of the positive charge in the complex (Alcami et al., 1989; Alcami et al., 1990; Speers et al., 1994; Alcami et al., 1990; Anvia et al., 1990; Alcami et al., 1996).

2. COMPUTATIONAL DETAILS

Calculations were performed using Gaussian O3W software and B3LYP(DFT) method with 6-311G(d,p) basis sets. In all calculations complete geometry optimization has been carried out on the molecules both before and after protonation, Li^+ complex and Na^+ complex formation. Proton affinities (PA), Li^+ affinities and Na^+ affinities were computed as ($E_{BH}{}^+ - E_B$), ($E_{BLi}{}^+ - E_B - E_{Li}{}^+$), ($E_{BNa}{}^+ - E_B - E_{Na}{}^+$) respectively.

3. RESULT AND DISCUSSION

The molecules studied are listed in table 1 along with their respective abbreviated names and computed total energy (hartree) of the free base(B) and their protonated, Li^+ and Na^+ complexes and also the PA, computed Li^+ affinities and computed Na^+ affinities(ΔE). Table 1 reports the computed total energies (hartree) of the free base $(B)=\{B_1, B_2, B_3, B_4\}$,$BH^+ =(B_1 H^+, B_2 H^+, B_3 H^+, B_4H^+)$, $BLi^+ =(B_1 Li^+, B_2 Li^+, B_3 Li^+, B_4Li^+)$,$BNa^+ =(B_1 Na^+, B_2 Na^+, B_3 Na^+, B_4Na^+)$. It also reports the proton affinities(P.A)=[$E_{BH}{}^+ - E_B$], Li^+ affinities(ΔE)= [$E_{BLi}{}^+ - E_B - E_{Li}{}^+$] and Na^+ affinities(ΔE)= [$E_{BNa}{}^+ - E_B - E_{Na}{}^+$] of the above said molecules at the equilibrium geometry of the G.S. In this method B3 LYP (DFT) with 6-311G (d, p) basis set, it is seen that the P.A values is highest for Pyridine -0.371(hartree) where it is -0.314, -0.2771 and –0.2868 for Pyrrole, Furan and Thiophene respectivly. Here we observed that Li^+affinities of the complex varies in the range -0.0502 to -0.0784(hartree) where as Na^+affinities of the same complex are in the range -0.0389 to -0.0615(hartree). The ΔE values indicating that the gas phase Li^+ and Na^+ complex formation turns out to be exothermic in each case.

Table 2 reports the net charge on X atom (X=N,O,S.N for Pyrrole, Furan, Thiophene and pyridine respectively) at the equilibrium G.S of the free base molecule as well as the computed net charge carried out by proton, lithium, sodium at the equilibrium G.S of protonated, Li^+ substituted and Na^+ substituted complexes. The computed net charge on proton, Li^+ and Na^+ vary within the range 0.18 to 0.38, 0.574 to 0.853 and 0.794 to 0.906 respectively. The magnitude of charges of the complexes indicate that the interaction between proton-free base, Li^+-free base and Na^+-free base is predominantly an ion-dipole attraction and ion-induced dipole interaction as well rather than a covalent interaction. This also showed that both pre and post complex correlation with local charge densities in the immediate neighborhood of the complex formation site are week. It can therefore be anticipated that the Li^+ and Na^+ affinities of these bases cannot be modeled or described by local properties of the hetero atom moiety only. Although it seems that there is a good but non perfect linear correlation between the charge on X atom in the free base (B), and the both Li^+ and Na^+ affinities still it must be shaped strongly by distant atom contribution in addition to the contribution from free base.

Table 1

Computed total energies (hartree) of free bases (B)=[B_1,B_2,B_3,B_4] and their Protonated(BH^+), Li^+ complex (BLi^+) and Na^+ complex (BNa^+) and Proton affinities [PA = (E_{BH+} – E_B) hartree], Lithium ion affinities[ΔE= (E_{BLi+} – E_B – E_{Li+}), hartree] and Sodium ion affinities [ΔE = (E_{BNa+} - E_B- E_{Na+}), hartree] at the equilibrium geometry of the ground state

Molecules	Total Energy of B	Total Energy of BH^+	Total Energy of BLi^+	Total Energy of BNa^+	PA = (E_{BH+} – E_B)	Lithium Ion Affinity = (E_{BLi+} – E_B – $E_{Li+)}$	Sodium Ion Affinity = (E_{BNa+} – E_B – $E_{Na+)}$
[B_1]	-210.2260	-210.5408	-217.5807	-372.3588	-0.3148	-0.0698	-0.0514
[B_2]	-230.0834	-230.3605	-237.4185	-392.2037	-0.2771	-0.0502	-0.0389
[B_3]	-553.0696	-553.3564	-560.4137	-715.1938	-0.2868	-0.0592	-0.0428
[B_4]	-248.3468	-248.7178	-255.7101	-410.4897	-0.371	-0.0784	-0.0615

Table 2

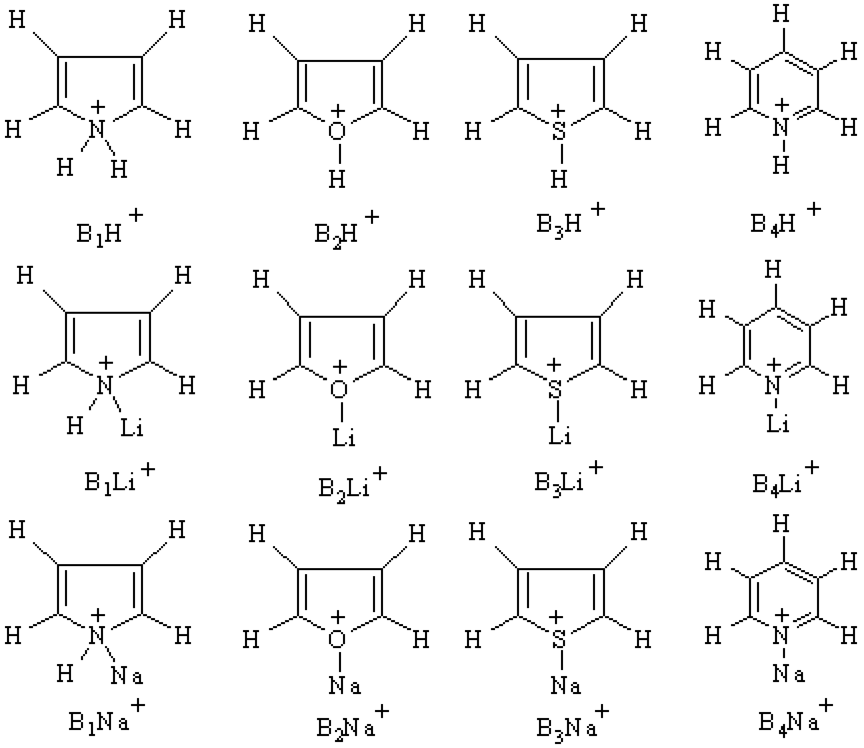
Computed net charge on 'X' atom (q_{X-}) of free bases (B)=[B_1,B_2,B_3,B_4], and their Protonated (BH^+), Li^+ complex (BLi^+) and Na^+ complex (BNa^+) and also the Computed net charge on Proton(q_{H+}), Lithium ion(q_{Li+}), Sodium ion (q_{Na+}) in the equilibrium ground state of free bases and (BH^+) ,(BLi^+) and (BNa^+) complexes

Molecules	q_{X-}				q_{H+}	q_{Li+}	q_{Na+}
	B	BH^+	BLi^+	BNa^+			
B_1(X=N)	-0.327407	-0.331879	-0.335869	-0.313345	0.320275	0.596757	0.801689
B_2(X=O)	-0.229623	-0.251790	-0.434773	-0.404675	0.381043	0.853002	0.906794
B_3(X=S)	0.263189	0.552293	0.429777	.368277	0.183935	0.574659	0.794346
B_4(X=N)	-.288795	-0.316448	-.523101	-.516291	0.294105	0.784705	0.864955

Table 3

Geometrical features of the complexes (BH^+, BLi^+, BNa^+) (length in Å and angle in degree) at the equilibrium geometry of G.S.

Molecules	r (X-H^+)	r (X-Li^+)	r (X-Na^+)	<C-X-H^+	<C-X-Li^+	<C-X-Na^+	<C-C-X-H^+	<C-C-X-Li^+	<C-C-X-Na^+
B_1(X=N)	1.0289	2.1885	2.8535	111.1908	74.7736	73.1617	120.5375	-63.691	-63.1498
B_2(X=O)	0.9767	1.8461	2.2387	119.9221	126.8766	126.904	-146.3458	179.9526	179.9928
B_3(X=S)	1.3622	2.4651	2.9288	99.7029	64.1053	67.7677	105.8556	61.7878	66.8054
B_4(X=N)	1.1016	1.918	2.3000	118.3758	121.1630	121.2712	-180.0163	179.9663	-180.0035



Structure of the proton, Li$^+$ and Na$^+$ Complexes of (Pyrrole, Furan, Thiophene and Pyridine

The local characteristics at or around the molecules are very nearly identical in each case. This is revealed from the data reported in Table 3. Where some of the selected computed geometrical parameters of BH$^+$, BLi$^+$, BNa$^+$ complexes in the G.S are listed. It is seen that X-H$^+$ bond length varies in the range of 0.97A^0-1.36A^0.For Li$^+$ and Na$^+$ complexes X-Li $^+$and X-Na$^+$ bond length varies between 1.8 A^0 to 2.46 A^0 and 2.23 A^0 to 2.92 A^0 respectively for said four heterocyclic molecules. The <C-X-H$^+$, <C-X-Li$^+$ and <C-X-Na$^+$, bond angles are varies in the range 99^0-119^0,64^0-126^0 and 67^0-126^0 respectively. Similarly torsion angle <C-C-X-H$^+$, <C-C-X-Li$^+$ and<C-C-X-Na$^+$ for heterocyclic complexes shows a variation in the range -180.01^0 to 120.53^0,-63.69^0 to 179.96^0 and-180.00^0 to 179.99^0 respectively in the B3LYP (DFT) calculation using 6-311G(d,p) basis set. The torsion angle shows a wide variation. All the molecules in this theoretical study are planer in geometrical structure (from literature). After protonation here we have seen the torsion angle for pyridine is-180.01^0 but for pyrrole, furan and thiophene this values are effected by global density and planarity are destroyed. In case of Li$^+$and Na$^+$ complexes planarity are destroyed for thiophene and for furan, pyridine planarity retained which is established by the value of torsion angle.

4. CONCLUSION

From the present theoretical study it can be well concluded that the gas phase proton affinities, lithium ion affinities and sodium ion affinities of the Pyrrole, Furan, Thiophene and Pyridine are spontaneous. The overall reactivity is fully explained by distant atom contribution in addition to the contribution from the free base.

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Conflict of Interest

The authors declare that there are no conflicts of interests.

Data and materials availability

All data associated with this study are present in the paper.

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