

Internet Electronic Journal of Molecular Design

November 2003, Volume 2, Number 11, Pages 741–756

Editor: Ovidiu Ivanciuc

Special issue dedicated to Professor Nenad Trinajstić on the occasion of the 65th birthday
Part 5

Guest Editor: Douglas J. Klein

Theoretical Study of Alkali Metals Interactions with Thymine Tautomers: Comparison and Analysis

M. Monajjemi,¹ R. Ghiasi,² H. Passdar,³ F. Mollaamin,¹ S. Ketabi,² F. Asaddian,² B. Chahkandi,¹ and M. Karimkhani¹

¹ Science and Research Branch, Islamic Azad University, P.O. Box 14515–775, Tehran, Iran

² Department of Chemistry, Central Tehran Branch, Islamic Azad University, Tehran, Iran

³ Department of Chemistry, North Tehran Branch, Islamic Azad University, Tehran, Iran

Received: July 18, 2003; Revised: September 18, 2003; Accepted: September 21, 2003; Published: November 30, 2003

Citation of the article:

M. Monajjemi, R. Ghiasi, H. Passdar, F. Mollaamin, S. Ketabi, F. Asaddian, B. Chahkandi, and M. Karimkhani, Theoretical Study of Alkali Metals Interactions with Thymine Tautomers: Comparison and Analysis, *Internet Electron. J. Mol. Des.* **2003**, *2*, 741–756, <http://www.biochempress.com>.

Theoretical Study of Alkali Metals Interactions with Thymine Tautomers: Comparison and Analysis[#]

M. Monajjemi,^{1,*} R. Ghiasi,² H. Passdar,³ F. Mollaamin,¹ S. Ketabi,² F. Asaddian,² B. Chahkandi,¹ and M. Karimkhani¹

¹ Science and Research Branch, Islamic Azad University, P.O. Box 14515–775, Tehran, Iran

² Department of Chemistry, Central Tehran Branch, Islamic Azad University, Tehran, Iran

³ Department of Chemistry, North Tehran Branch, Islamic Azad University, Tehran, Iran

Received: July 18, 2003; Revised: September 18, 2003; Accepted: September 21, 2003; Published: November 30, 2003

Internet Electron. J. Mol. Des. 2003, 2 (11), 741–756

Abstract

Motivation. The interaction of alkali metal with thymine is an interesting target of studies in connection with bioinorganic chemistry and biological chemistry of toxicity and carcinogenicity. We studied interactions of one of the oxo groups of thymine and its tautomers with alkali metals (Li, Na, K, Rb and Cs) by *ab initio* calculations. The stability of these species has been studied in gas and solution phases. Characterization of intermolecular (C=O) and intramolecular (C–N) bonds has been studied with the NBO method and, the interactions that cause the strongest stabilization have been studied, as well. The stability of metalated thymine and its tautomers has been studied thermochemically. The present study reports the quantum chemistry analysis of the metal–assisted tautomerization.

Method. *Ab initio* and DFT methods at the HF and B3LYP levels of theory were used.

Results. Interactions of alkali metals with oxo group of thymine and its tautomers stabilize rare tautomers compared to the major form. Investigation of interactions in solution phase shows that with increasing dielectric constants of solvent, the tautomers are stabilizing compared to the major form. Thermochemical analysis shows that the stability of metalated thymine is more for less electropositive metals. These results show that basicity of metalated thymine has been increased. NBO calculations show that in metalated thymine (1, metalated), (5, metalated) the N2 and N4 lone pair is seen to be the lowest occupancy and highest energy Lewis NBO and to be primarily delocalized into antibonds the vicinal π^* C3–O3 and π^* C1–O1 NBO, respectively. In other species lowest occupancy and highest energy Lewis NBO depend on alkali metal.

Conclusions. Metalation of one oxo group of thymine and its tautomers by alkali metals cause to stabilize the rare tautomers. Metalation affects some bonding and structural properties, such as bond distance and atomic charges, are different compared to the nonmetalated form.

Keywords. Metalated thymine; tautomers of thymine; *ab initio* calculation; solvent effect; natural bond orbital (NBO).

Abbreviations and notations

SCRf, Self-consistent reaction field (SCRf) method

NBO, Natural bond orbital

PCM, Polarized continuum model

BSSE, Basis set superposition error

[#] Dedicated to Professor Nenad Trinajstić on the occasion of the 65th birthday.

* Correspondence author; E-mail: m_monajjemi@yahoo.com.

1 INTRODUCTION

The structure and function of DNA depend on metal ions. Metal ions can interact with many sites in DNA [1–3]: phosphate groups, sugar moieties, as well as the DNA bases. The interactions of mono and bivalent metals have been studied [4–7]. The relative stability of each tautomer of the pyrimidine base cytosine is very important in the structure of DNA. The occurrence of rare tautomers has been put forward as a possible mechanism of spontaneous mutation [8]. Metalation can change the probability of formation of rare (minor) tautomers of bases and could affect the ability of nucleobase to be protonated or deprotonated [9]. Formation of rare nucleobase tautomers can occur under the influence of a metal entity. By replacing a hydrogen atom of the N4 amino group of cytosine by a metal entity, the N3 position is protonated to produce a metalated form of the rare iminooxo tautomers of this base [10–12]. Alkali cations, at high concentrations, interact with the nucleic acid bases, destroying the hydrogen bonding of base pair and consequently, compromise the structure integrity of the nucleic acid polymers [13–14]. Furthermore, the presence of these ions in the cell nucleus has an inhibitory effect on the chain initiation process by RNA polymerase [13], so the alkali ions affect syntheses, replication, structure integrity and cleavage of nucleic acid. For these reasons, knowledge of the thermochemical and structure features that govern the interaction between alkali cations and nucleic acid bases can indicate their interactions with more complicated nucleic acids polymers.

Not only monovalent alkaline cations, but also, the divalent alkaline cations (Mg^{2+} , Ca^{2+} , Ba^{2+}), interact with the phosphate groups of the backbone [1–3]. This does not mean that interaction with bases is excluded, for example, a high resolution X-ray study of Z-DNA hexamer shows a barium cation bridging two side-by-side Z-DNA helices in the crystal by simultaneously coordination to the O and N of two guanines. This cation is, at the same time, coordinated to four water molecules [15].

The solvent dependency of tautomeric equilibria has been the subject of many studies [16–18]. The tautomeric equilibria of hydroxyl pyridines have been studied theoretically owing to their relevance to the oxo-amino—hydroxy-amino tautomerism of nucleic acids [19–21]. It has been well established that solvents with large dielectric constants favor the more polar tautomers. The solvent effect is taken into account via the self-consistent reaction field (SCRF) method. This method is based on Onsager reaction field theory of electrostatic solvation. In this model, the solvent is considered as a uniform dielectric with a given dielectric constant ϵ . The solute is placed into a cavity within the solvent. SCRF approaches differ in how they define the cavity and the reaction field. Tomasi's polarized continuum model (PCM) [22,23] defines the cavity as a union of a series of interlocking atomic spheres. The effect of polarization of the solvent continuum is represented numerically. PCM has proved usefulness in describing the effects of the solvent on some characteristics of the molecule in solution [24]. All PCM calculations in this report have been

performed using this formalism as implement in GAUSSIAN 98 [25]. Therefore, in this paper by using the ab initio calculations and quantum chemical approach, we analyzed the energies of formation of metal–assisted tautomers upon metalation the amino groups of the base in gas and solution phases.

2 METHOD AND CALCULATION

The calculations of systems containing C, H, N, O are described by the standard 6–31+G* basis set [26]. For alkali metals (Li, Na, K, Rb and Cs) standard LANL2DZ basis set is used [27] and Na, K, Rb and Cs are described by the effective core potential (ECP) of Wadt and Hay pseudopotential [25,27b] with a doublet– ξ valence using the LANL2DZ. All systems have been optimized at the Hartree–Fock level. In all cases, the steady–state nature (minimum on the potential energy surface) of the optimized complexes has been confirmed by calculating the corresponding frequencies at the same computational level. For the optimized geometries the correlation energies were calculated by Becke3LYP density functional theory (DFT). The calculations have been performed by using the GAUSSIAN 98 suite of program [27].

The natural bond orbital (NBO) [28] analysis has been performed by using NBO as implement in the GAUSSIAN98. NBO calculations have been performed at Hartree–Fock level. The second–order perturbative estimates of donor–acceptor (bond–antibond) interactions have been done in the NBO basis. This is carried out by examining all possible interactions between filled (donor) Lewis type NBOs and empty (acceptor) non Lewis NBOs and estimating their energetic importance by 2nd–order perturbation theory. Since these interactions lead to loss of occupancy form of the localized NBOs of the idealized Lewis structure into the empty non Lewis orbitals (and thus to departures from the idealized Lewis structure description) they are referred as delocalization corrections to the zero order natural Lewis structure. For each donor NBO_{*i*} and acceptor NBO_{*j*} the stabilization energy E(2) associated with delocalization (2e–stabilization) $i \rightarrow j$ is estimated as:

$$E(2) = \Delta E_{ij} = q_i / [F(i, j)^2 (\epsilon_j - \epsilon_i)]$$

where q_i is the donor orbital occupancy, ϵ_j , ϵ_i are diagonal elements (orbital energies) and $F(i, j)$ is the off diagonal NBO Fock matrix element.

PCM reaction field calculation is performed by using the polarizable dielectric model [29–31]. The PCM cavity is defined by using Pauling radius for each solute atom [25]. The model chemistry used for calculations is based on B3LYP method. This corresponds to the approximation method that makes use of Becke–Style parameters density functional theory [32] with the Lee–Yang–Paar correlation functional [33].

The interaction energies (E_I) were determined as the difference between the optimized energy of the base...metals cation [$E(B...M^{n+})$] systems and the sum of the energies of the base [$E(B)$] and

the metal cation [$E(M^{n+})$]:

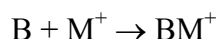
$$E_I = E(B \dots M^{n+}) - [E(B) + E(M^{n+})] \quad (n = 1)$$

The final interaction energies (E_I) have been calculated as the difference between the energy of the complex and the sum of the energies of the monomers, and have been corrected from the inherent basis set superposition error (BSSE) which is calculated, by using the Boys–Bernardi counterpoise technique:

$$E_{I+BSSE}(B \dots M^+) = E(B \dots M^+)_{BM} - [E(B)_B + E(M^+)_M] + [E(B')_B - E(B')_{BM} + E(M')_M - E(M')_{BM}]$$

where $E(B \dots M^+)_{BM}$ represents the energy of the complex, $E(B)_B$ the energy of the isolated monomer B with its basis set, $E(B')_B$ the energy of B in its geometry within the complex calculated with its basis set, and $E(B')_{BM}$ the energy of B in its geometry within the complex with the complete basis set of the complex ($B \dots M^+$) [34].

Metal ion affinity (MIA) was assumed as the negative of the enthalpy variations (ΔH) for the process:



In other words the MIA corresponds to the dissociation energy of the B– M^+ bond.

The variations in zero point energies were considered together thermochemical analysis at 298 K in order to obtain the entropic (ΔS) and free energy (ΔG) variations for the considered process.

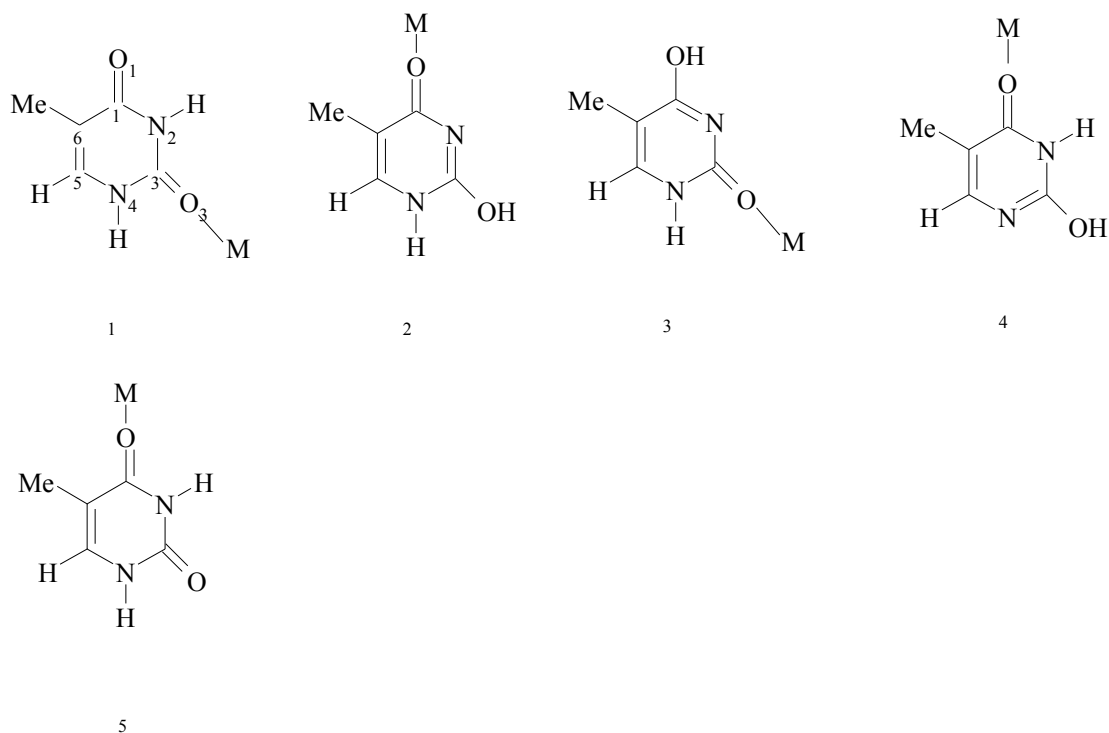


Figure 1. Structures of metalated thymine and its tautomers. Interaction of metal with: (1) Major form up to O3; (2) Rare form (Oxo1–Hydroxy 3, N4–protonated) up to O1; (3) Rare form (Hydroxy 1– Oxo 3, N4–protonated) up to O3; (4) Rare form (Oxo1–Hydroxy 3, N2–protonated) up to O1. (5) Major form up to O1.

Table 1. Energy (Hartree), relative energies (kcal/mol) in Hartree–Fock level for structures (1), (2), (3), (4) and (5) metalated and nonmetalated in gas phase

M		E(Hartree)		$\Delta E(\text{kcal/mol})$	
		HF	B3LYP	HF	B3LYP
–	1	–451.521	0.000	–454.153	0.000
	2	–451.468	33.294	–454.103	31.297
	3	–451.496	16.031	–454.130	14.079
	4	–451.500	13.060	–454.133	12.247
Li	1	–458.834	0.000	–461.507	0.000
	2	–458.118	9.640	–461.494	8.231
	3	–458.831	1.544	–461.506	0.685
	4	–458.821	7.890	–461.496	6.611
	5	–458.837	–1.750	–454.196	0.000
Na	1	–451.575	0.000	–454.178	11.109
	2	–451.55	11.994	–454.192	2.590
	3	–451.569	3.698	–454.184	7.935
	4	–451.560	9.068	–454.200	–2.101
	5	–451.577	–1.370	–461.507	0.000
K	1	–479.263	0.000	–482.153	0.000
	2	–479.239	15.530	–482.131	13.994
	3	–479.255	5.512	–482.146	4.186
	4	–479.248	9.825	–482.139	8.676
	5	–479.265	–1.159	–482.156	–1.805
Rb	1	–474.996	0.000	–477.883	0.000
	2	–474.970	17.979	–477.859	15.169
	3	–474.986	6.155	–477.875	4.744
	4	–474.980	10.088	–477.868	8.994
	5	–474.998	–1.089	–477.885	–1.651
Cs	1	–471.027	0.000	–473.904	0.000
	2	–470.998	17.979	–473.878	16.465
	3	–471.016	6.815	–473.896	5.431
	4	–471.011	10.351	–473.889	9.352
	5	–471.029	–0.996	–473.907	–1.539

3 RESULTS AND DISCUSSION

3.1 Tautomerization Energies and Tautomeric Equilibria of Metalated Thymine

3.1.1 Gas phase

Computed energies of tautomer (1), (2), (3), (4) and (5) for nonmetalated and metalated thymine and its tautomers are compared by HF and DFT methods (Tables 1, Figure 1). As shown in Tables 1 the order of stabilization of nonmetalated and metalated tautomers is: (1, nonmetalated) > (4, nonmetalated) > (3, nonmetalated) > (2, nonmetalated) and (5, metalated) > (1, metalated) > (3, metalated) > (4, metalated) > (2, metalated), respectively. Their relative stabilities are markedly influenced by the metalation. The interaction of metal with oxo group O1 in (5, metalated), (2, metalated), (4, metalated) and O3 in (3, metalated), (1, metalated) shows that order of destabilization is: (2, metalated) > (4, metalated) > (3, metalated) > (1, metalated) > (5, metalated). The first major difference can be found in the relative stabilities of the tautomers of free and metalated thymine, while the tautomer (1, nonmetalated), (2, nonmetalated), (3, nonmetalated) and

(4, nonmetalated) of nonmetalated thymine is destabilized by only 32.29, 16.03, 13.06 kcal mol⁻¹ with respect to the major form, the destabilization energy in effect of metalation decreases. The differences of energy upon metalation have been shown in Table 1, which increase for different metals (with HF method and B3LYP). See Figure 2. These values show that the results are depending on metals. Stability of tautomers (1, metalated), (2, metalated), (3, metalated), (4, metalated) and (5, metalated) is more for electronegative metals; (Figure 1). Table 1 show that structure (5, metalated) is more stable than (1, metalated).

Table 2. Energy (Hartree), relative energies (kcal/mol) for structures (1), (2), (3) and (4) non-metalated in gas phase and various solvent with DFT (B3LYP) level

Phase	1		2		3		4		
	E (Hartree)	ΔE (kcal/mol)	E (Hartree)	ΔE (kcal/mol)	E (Hartree)	ΔE (kcal/mol)	E (Hartree)	ΔE (kcal/mol)	
Solvent	DMSO	-454.164	0.000	-454.128	22.631	-454.145	12.217	-454.120	27.383
	CH ₂ Cl ₂	-454.166	0.000	-454.128	24.156	-454.147	12.487	-454.146	12.994
	THF	-454.162	0.000	-454.123	24.458	-454.142	12.534	-454.141	12.985
	CHCl ₃	-454.161	0.000	-454.120	25.473	-454.140	12.745	-454.140	12.943
	C ₆ H ₁₂	-454.160	0.000	-454.115	28.349	-454.139	13.281	-454.140	12.543

Table 3. Relative energies (B3LYP) (kcal/mol) for structures (1), (2), (3), (4) and (5) metalated in various solvents

Solvent	Structure	E(Hartree)					ΔE(kcal/mol)				
		M ⁺					M ⁺				
		Li	Na	K	Rb	Cs	Li	Na	K	Rb	Cs
DMSO	1	-461.599	-454.285	-482.208	-477.953	-473.968	0.000	0.000	0.000	0.000	0.000
	2	-461.580	-454.262	-482.187	-477.926	-473.940	11.660	14.714	13.015	17.046	17.735
	3	-461.588	-454.271	-482.194	-477.938	-473.952	7.209	8.962	8.221	9.865	10.398
	4	-461.583	-454.268	-482.190	-477.934	-473.949	9.866	10.931	11.019	11.876	11.978
	5	-461.602	-454.288	-482.208	-477.955	-473.970	-1.860	-1.530	-0.003	-0.772	-0.841
CH ₂ Cl ₂	1	-461.594	-454.281	-482.207	-477.951	-473.967	0.000	0.000	0.000	0.000	0.000
	2	-461.576	-454.258	-482.186	-477.924	-473.939	11.374	14.406	13.275	16.922	17.726
	3	-461.584	-454.268	-482.195	-477.936	-473.951	6.339	5.129	7.637	9.173	9.753
	4	-461.579	-454.264	-482.190	-477.933	-473.948	9.447	10.556	10.661	11.454	11.593
	5	-461.597	-454.283	-482.208	-477.952	-473.968	-1.998	-1.627	-0.364	-0.988	-1.008
THF	1	-461.587	-454.274	-482.200	-477.944	-473.960	0.000	0.000	0.000	0.000	0.000
	2	-461.569	-454.251	-482.179	-477.917	-473.932	11.291	14.294	13.194	16.876	17.667
	3	-461.577	-454.261	-482.188	-477.930	-473.345	6.175	7.963	7.495	9.070	9.613
	4	-461.572	-454.257	-482.183	-477.926	-473.942	9.362	10.478	10.562	11.393	11.518
	5	-461.590	-454.277	-482.201	-477.946	-473.962	-2.028	-1.644	-0.212	-0.992	-1.0265
CH ₃ Cl	1	-461.580	-454.267	-482.197	-477.939	-473.955	0.000	0.000	0.000	0.000	0.000
	2	-461.562	-454.244	-482.175	-477.912	-473.927	11.051	14.028	13.291	16.735	17.608
	3	-461.571	-454.255	-482.185	-477.925	-473.941	5.547	7.356	7.106	8.550	9.128
	4	-461.565	-454.250	-482.180	-477.921	-473.937	9.056	10.190	10.286	11.077	11.232
	5	-461.583	-454.269	-482.197	-477.941	-473.957	-2.132	-1.733	-0.536	-1.144	-1.170
C ₆ H ₁₂	1	-461.553	-454.242	-482.179	-477.917	-473.935	0.000	0.000	0.000	0.000	0.000
	2	-461.538	-454.221	-482.158	-477.892	-473.908	9.779	12.788	13.404	16.075	17.117
	3	-461.548	-454.233	-482.170	-477.906	-473.923	3.383	5.272	5.639	6.850	7.433
	4	-461.541	-454.227	-482.164	-477.901	-473.919	7.923	9.189	9.434	10.116	10.344
	5	-461.557	-454.244	-482.197	-477.919	-473.937	-2.387	-1.856	-0.613	-1.376	-1.303

On the other hand, metalation of thymine markedly enhances its basicity, since charges of N2 in (2, metalated), (3, metalated) and N4 in (4, metalated) have been found more in the metalated complex than in the nonmetalated molecule. See Tables 4 and 5.

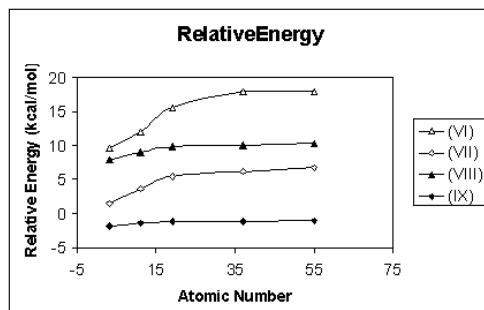


Figure 2. Dependencies of Relative Energies (kcal/mol) of metalated thymine (V) and its metalated tautomers (VI), (VII), (VIII) and (IX) on the atomic number of metal.

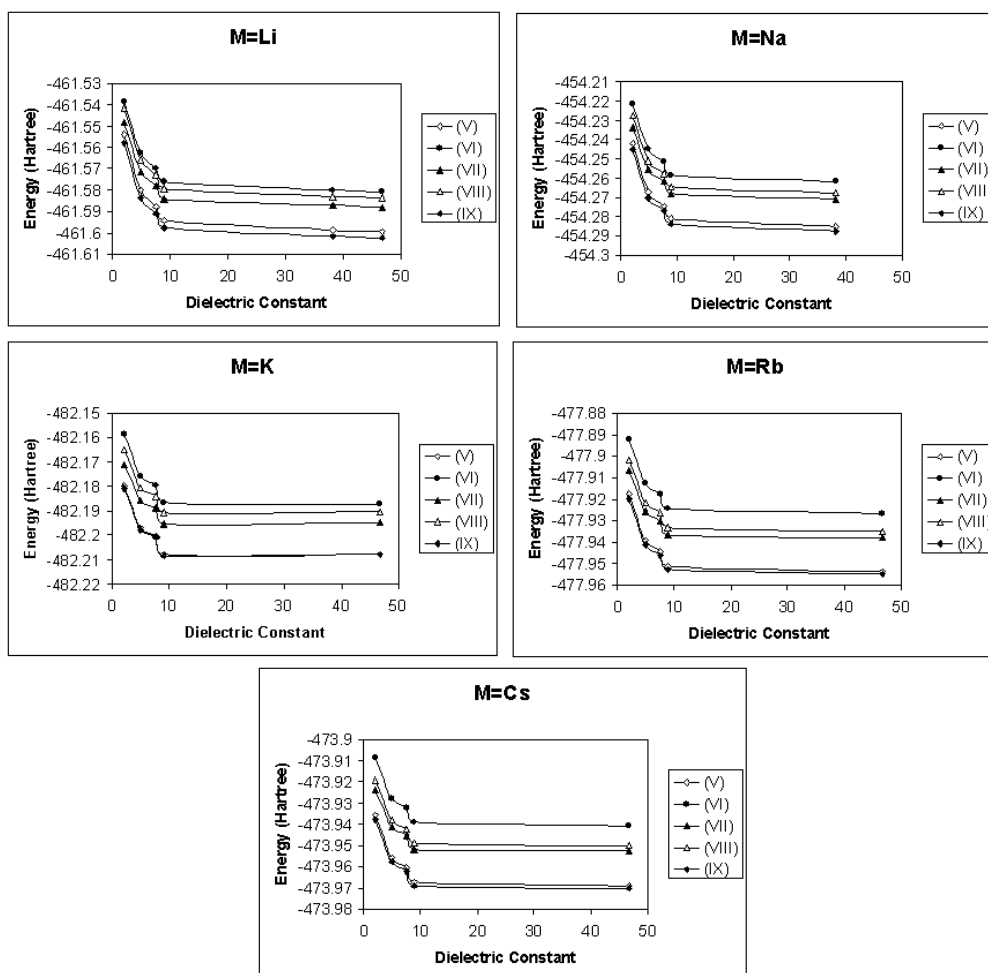


Figure 3. Variation of energy (Hartree) with Dielectric constant for metalated thymine (V) and its metalated tautomers (VI), (VII), (VIII) and (IX) .

Table 4. Natural population of O1, O3, N2 and N4 in gas phase and hybridization coefficient of C3–N3 and C1–O1 bond for (1), (2), (3) and (4) nonmetalated structures calculated by NBO method with Hartree–Fock (HF) level

Structure	Charges				Hybridization Coefficient	
	O1	O3	N2	N4	C1–O1	C3–O3
1	-0.68943	-0.72662	-0.76343	-0.72969	$\sigma:0.5913(sp^{1.98})_C+0.8064(sp^{1.27})_O$ $\pi:0.5175(p)_C+0.8557(p)_O$	$\sigma:0.5963(sp^{1.79})_C+0.8028(sp^{1.36})_O$ $\pi:0.4918(p^{1.00})_C+0.8707(p^{1.00})_O$
2	-0.67469	-0.72854	-0.67451	-0.71880	$\sigma:0.5886(sp^{2.02})_C+0.8084(sp^{1.24})_O$ $\pi:0.5318(p^{1.00})_C+0.8469(p^{1.00})_O$	$\sigma:0.5711(sp^{2.59})_C+0.8209(sp^{1.76})_O$
3	-0.74849	-0.71976	-0.70907	-0.71558	$\sigma:0.5676(sp^{2.83})_C+0.8233(sp^{1.69})_O$ $\pi:0.5031(p^{1.00})_C+0.8642(p^{1.00})_O$	$\sigma:0.5934(sp^{1.82})_C+0.8049(sp^{1.32})_O$ $\pi:0.5031(p^{1.00})_C+0.8642(p^{1.00})_O$
4	-0.70785	-0.75166	-0.72847	-0.69603	$\sigma:0.5928(sp^{1.97})_C+0.8054(sp^{1.29})_O$ $\pi:0.5102(p^{1.00})_C+0.8601(p^{1.00})_O$	$\sigma:0.5721(sp^{2.56})_C+0.8202(sp^{1.80})_O$

Table 5. Charge of M, O1, O3, N2 and N4 of structures (1), (2), (3), (4) and (5) metalated at the HF level

Atom	Structure	NBO Atom					Mulliken Atom				
		M	O1	O3	N2	N4	M	O1	O3	N2	N4
Li	1	0.99064	-0.63333	-0.97360	-0.74171	-0.69719	0.829832	-0.517943	-0.749957	-0.409285	-0.264028
	2	0.96424	-0.81121	-0.71489	-0.82500	-0.68849	0.740690	-0.608956	-0.124074	-0.677684	-0.189188
	3	0.98627	-0.71901	-0.95565	-0.73503	-0.67896	0.820425	-0.101403	-0.740964	-0.674441	-0.198947
	4	0.99022	-0.97119	-0.73814	-0.65668	-0.69032	0.813085	-0.735099	-0.115473	-0.391493	-0.419178
	5	0.99088	-0.95350	-0.67123	-0.73412	-0.71185	0.816202	-0.704052	-0.545738	-0.428404	-0.253899
Na	1	0.99543	-0.64433	-0.91896	-0.74844	-0.70622	0.939272	-0.529364	-0.839241	-0.407853	-0.268539
	2	0.97706	-0.78926	-0.72261	-0.79909	-0.69335	0.986838	-0.675824	-0.145509	-0.756899	-0.242675
	3	0.99146	-0.72393	-0.90207	-0.74361	-0.68845	0.933209	-0.108346	-0.799376	-0.683898	-0.201179
	4	0.99503	-0.91194	-0.74194	-0.66514	-0.70054	0.932713	-0.832074	-0.125479	-0.374946	-0.431929
	5	0.99521	-0.89355	-0.68215	-0.74278	-0.71604	0.934560	-0.798785	-0.560895	-0.413328	-0.264965
K	1	0.99947	-0.65287	-0.88695	-0.75286	-0.71222	0.990466	-0.539132	-0.841006	-0.410698	-0.275517
	2	0.99081	-0.77513	-0.72804	-0.77805	-0.69793	0.899203	-0.641076	-0.137290	-0.713120	-0.215765
	3	0.99719	-0.72804	-0.87223	-0.74450	-0.69468	0.989054	-0.114841	-0.814931	-0.695361	-0.216913
	4	0.99922	-0.87745	-0.74468	-0.67130	-0.70755	0.988203	-0.834153	-0.131706	-0.376848	-0.441557
	5	0.99917	-0.85813	-0.69056	-0.74862	-0.71896	0.988891	-0.798007	-0.571831	-0.411262	-0.273093
Rb	1	0.99978	-0.65618	-0.87251	-0.75443	-0.71436	0.986902	-0.542812	-0.813800	-0.412368	-0.276477
	2	0.99296	-0.76976	-0.72943	-0.76832	-0.69957	0.980671	-0.655255	-0.150285	-0.728401	-0.249631
	3	0.99797	-0.72954	-0.85987	-0.74404	-0.69682	0.986201	-0.117099	-0.786606	-0.695584	-0.216517
	4	0.99970	-0.86231	-0.74567	-0.67363	-0.70997	0.985666	-0.798725	-0.134200	-0.377636	-0.445878
	5	0.99964	-0.84287	-0.69385	-0.75057	-0.71998	0.986710	-0.763149	-0.576469	-0.410860	-0.276994
Cs	1	1.00035	-0.65916	-0.86053	-0.75575	-0.71618	0.974592	-0.546334	-0.774788	-0.417182	-0.281258
	2	0.99559	-0.76582	-0.73058	-0.75912	-0.70113	0.967588	-0.635507	-0.152906	-0.701585	-0.254364
	3	0.99923	-0.73105	-0.85121	-0.74178	-0.69865	0.972178	-0.117856	-0.753545	-0.691222	-0.220152
	4	1.00045	-0.84972	-0.74656	-0.67572	-0.71206	0.972599	-0.758651	-0.136803	-0.382079	-0.449676
	5	1.00037	-0.83012	-0.69676	-0.75223	-0.72090	0.960082	-0.737900	-0.571015	-0.411335	-0.273469

3.1.2 Solution phase

The effect of solvent on stabilization of tautomers shows interesting results. The standard approach of the PCM (without any explicit solvent molecules), as is used here, appears to be a good first step in the theoretical investigation of the effect of solvent. In the first instance, regular variations were observed concerning energy versus dielectric constant (Figure 2). For the nonmetalated and metalated thymine with increasing of dielectric constants of solvent, stability of species increases (Tables 2 and 3, Figure 2).

Table 6. E_i (interaction energies), BSSE (kcal/mol) for structures (1), (2), (3), (4) and (5) metalated at the HF level

Structure	M^+					
	Li	Na	K	Rb	Cs	
Interaction Energy (kcal/mol)	1	-48.078	-35.002	-22.871	-19.597	-16.697
	2	-71.732	-54.932	-40.635	-36.213	-32.012
	3	-62.566	-45.965	-33.390	-29.473	-25.914
	4	-53.248	-37.624	-26.106	-22.569	-19.407
	5	-49.828	-35.002	-24.031	-20.686	-17.694
BSSE (kcal/mol)	1	-48.880	-35.871	-32.653	-20.427	-17.545
	2	-72.501	-55.783	-41.401	-37.048	-32.888
	3	-63.370	-46.902	-34.257	-30.383	-26.855
	4	-54.104	-38.565	-26.964	-23.478	-20.342
	5	-50.581	-35.836	-24.410	-21.490	-18.525

Table 7. Optimized bond distances of M–O3, C3–N3, C1–O1, C1–N2, C2–N3 and C3–N4 (Å) for structures (1), (2), (3), (4) and (5) metalated in gas phase at the HF level

Structure	Bond	M^+					
		–	Li	Na	K	Rb	Cs
1	M–O3	–	1.740	2.117	2.560	2.774	3.0032
	C3–O3	1.197	1.237	1.230	1.223	1.220	1.219
	C1–O1	1.195	1.185	1.188	1.188	1.190	1.190
	C1–N2	1.387	1.411	1.406	1.403	1.401	1.400
	C2–N3	1.370	1.339	1.346	1.350	1.352	1.354
	C3–N4	1.367	1.335	1.341	1.346	1.348	1.349
	M–N2	–	2.027	2.439	2.903	3.128	3.382
	M–O1	–	1.890	2.244	2.661	2.857	3.068
2	C1–O1	1.197	1.223	1.216	1.213	1.211	1.210
	C3–O3	1.328	1.304	1.309	1.315	1.316	1.318
	C1–N2	1.387	1.373	1.377	1.380	1.380	1.380
	C2–N3	1.265	1.289	1.287	1.282	1.281	1.279
	C3–N4	1.356	1.337	1.339	1.341	1.341	1.343
	M–O3	–	1.754	2.132	2.547	2.752	2.967
	C3–O3	1.197	1.239	1.229	1.222	1.220	1.218
	C1–O1	1.321	1.302	1.305	1.308	1.309	1.310
3	C1–N2	1.284	1.304	1.300	1.298	1.296	1.295
	C2–N3	1.370	1.336	1.346	1.352	1.354	1.354
	C3–N4	1.389	1.354	1.359	1.365	1.367	1.369
	M–O1	–	1.730	2.107	2.541	2.753	2.977
	C1–O1	1.200	1.242	1.232	1.226	1.224	1.221
	C3–O3	1.319	1.305	1.307	1.309	1.310	1.311
	C1–N2	1.392	1.363	1.368	1.372	1.374	1.375
	C2–N3	1.346	1.351	1.352	1.350	1.350	1.350
4	C3–N4	1.273	1.278	1.276	1.276	1.275	1.274
	M–O1	–	1.737	2.114	2.553	2.766	2.993
	C1–O1	1.197	1.236	1.227	1.222	1.219	1.218
	C3–O3	1.195	1.184	1.186	1.188	1.189	1.189
	C1–N2	1.387	1.352	1.360	1.364	1.367	1.368
	C2–N3	1.370	1.388	1.386	1.382	1.381	1.380
	C3–N4	1.367	1.370	1.368	1.368	1.367	1.368
	C3–N4	1.367	1.370	1.368	1.368	1.367	1.368

3.2 The Interaction Energies of Metalated Thymine

Table 6 shows the interaction energies of metalated thymine. The interaction energies of the metalated thymine are systematically increased with atomic number of M, which is duo to larger dipole moments. Table 6 shows the value of BSSE for the structures (1, metalated), (2, metalated),

(3, metalated), (4, metalated) and (5, metalated). Clearly for the all complexes, values of BSSE are rather small.

Table 8. Hybridization coefficient of C3–N3 and C1–O1 bonds calculated in (1), (2), (3), (4) and (5) metalated structures by NBO method at the HF level

		C3–O3				
		Li	Na	K	Rb	Cs
1	σ	0.5838 (sp ^{2.01}) _C +0.8119(sp ^{1.27}) _O	0.5891(sp ^{1.95}) _C +0.80819(sp ^{1.34}) _O	0.5900(sp ^{1.91}) _C +0.8074(sp ^{1.35}) _O	0.5907(sp ^{1.90}) _C +0.8069(sp ^{1.35}) _O	0.5912(sp ^{1.88}) _C +0.8065(sp ^{1.35}) _O
	π	0.3936 (p ^{1.00}) _C + 0.9193(p ^{1.00}) _O	0.4162 (p ^{1.00}) _C +0.9093(p ^{1.00}) _O	0.4316(p ^{1.00}) _C +0.9021(p ^{1.00}) _O	0.4375(p ^{1.00}) _C +0.8992(p ^{1.00}) _O	0.4426 (p ^{1.00}) _C +0.8967 (p ^{1.00}) _O
2	σ	0.5748 (sp ^{2.48}) _C +0.8183(sp ^{1.69}) _O	0.5734(sp ^{2.51}) _C +0.8193 (sp ^{1.70}) _O	0.5724(sp ^{2.55}) _C + 0.8199 (sp ^{1.71}) _O	0.5721(sp ^{2.55}) _C +0.8202(sp ^{1.71}) _O	0.5719(sp ^{2.56}) _C +0.8203 (sp ^{1.72}) _O
	π	–	–	–	–	–
3	σ	0.5848 (sp ^{2.07}) _C +0.8112 (sp ^{1.33}) _O	–	–	0.5891(sp ^{1.95}) _C +0.8081(sp ^{1.33}) _O	0.5893 (sp ^{1.94}) _C + 0.8079(sp ^{1.33}) _O
	π	–	0.4314(p ^{1.00}) _C + 0.9022 (p ^{1.00}) _O	0.4462 (p ^{1.00}) _C + 0.8949(p ^{1.00}) _O	0.4514(p ^{1.00}) _C +0.8923(p ^{1.00}) _O	0.4553 (p ^{1.00}) _C +0.8903 (p ^{1.00}) _O
4	σ	0.5751 (sp ^{2.46}) _C + 0.8181(sp ^{1.75}) _O	0.5744(sp ^{2.48}) _C + 0.8186 (sp ^{1.70}) _O	0.5738 (sp ²) _C + 0.8190 (sp) _O	0.5736(sp ^{2.5}) _C +0.8192(sp ^{1.75}) _O	0.5734(sp ^{2.51}) _C + 0.8193 (sp ^{1.76}) _O
	π	–	–	–	–	–
5	σ	0.5939 (sp ^{1.75}) _C + 0.8046(sp ^{1.30}) _O	0.5939(sp ^{1.75}) _C + 0.8045(sp ^{1.30}) _O	0.5939(sp ^{2.50}) _C + 0.8045 (sp ^{1.75}) _O	0.5939(sp ^{1.76}) _C +0.8045(sp ^{1.31}) _O	0.5940(sp ^{1.77}) _C + 0.8045 (sp ^{1.31}) _O
	π	0.5157 (p ^{1.00}) _C +0.8567 (p ^{1.00}) _O	0.5117(p ^{1.00}) _C + 0.8592 (p ^{1.00}) _O	0.5086(p ^{1.00}) _C + 0.8610 (p ^{1.00}) _O	0.5073(p ^{1.00}) _C +0.8618(p ^{1.00}) _O	0.5062(p ^{1.00}) _C + 0.8624 (p ^{1.00}) _O

		C1–O1				
		Li	Na	K	Rb	Cs
σ		0.5890(sp ^{1.95}) +0.8081(sp ^{1.22}) _O	0.5892(sp ^{1.96}) _C +0.8080(sp ^{1.22}) _O	0.5892 (sp ^{1.96}) _C +0.8080 (sp ^{1.23}) _O	0.5893(sp ^{1.96}) _C +0.8079(sp ^{1.23}) _O	0.5893 (sp ^{1.97}) _C +0.8079 (sp ^{1.23}) _O
	π	0.5396(p ^{1.00}) _C +0.8419(p ^{1.00}) _O	0.5358(p ^{1.00}) _C +0.8443(p ^{1.00}) _O	0.5328(p ^{1.00}) _C + 0.8462 (p ^{1.00}) _O	0.5316(p ^{1.00}) _C +0.8470 (p ^{1.00}) _O	0.5306 (p ^{1.00}) _C + 0.8476(p ^{1.00}) _O
σ		0.6372(sp ^{1.71}) _C + 0.7707(sp ^{1.57}) _O	0.5860(sp ^{2.16}) _C +0.8103(sp ^{1.28}) _O	0.5857(sp ^{2.13}) _C +0.8106 (sp ^{1.75}) _O	0.5857(sp ^{2.12}) _C +0.8106(sp ^{1.25}) _O	0.5856(sp ^{2.12}) _C +0.8106 (sp ^{1.24}) _O
	π	0.4768(p ^{1.00}) _C + 0.8790(p ^{1.00}) _O	0.4883(p ^{1.00}) _C + 0.8727(p ^{1.00}) _O	0.4961(p ^{1.00}) _C +0.8683 (p ^{1.00}) _O	0.4986(p ^{1.00}) _C +0.8668 (p ^{1.00}) _O	0.5006 (p ^{1.00}) _C +0.8657 (p ^{1.00}) _O
σ		0.5694(sp ^{2.75}) _C +0.8221(sp ^{1.61}) _O	0.5687(sp ^{2.27}) _C +0.8225(sp ^{1.62}) _O	0.5683(sp ^{2.79}) _C +0.8228 (sp ^{1.63}) _O	0.5681(sp ^{2.80}) _C + 0.823(sp ^{1.63}) _O	0.5680(sp ^{2.80}) _C + 0.8231 (sp ^{1.63}) _O
	π	–	–	–	–	–
σ		0.5815(sp ^{2.23}) _C + 0.8136 (sp ^{1.21}) _O	0.5863 (sp ^{2.16}) _C +0.8101 (sp ^{1.27}) _O	0.5870(sp ^{2.11}) _C + 0.8096 (sp ^{1.27}) _O	0.5877(sp ^{2.09}) _C +0.809(sp ^{1.28}) _O	0.588(sp ^{2.08}) _C + 0.8088 (sp ^{1.28}) _O
	π	–	0.4318(p ^{1.00}) _C + 0.9020 (p ^{1.00}) _O	0.4480(p ^{1.00}) _C + 0.8941(p ^{1.00}) _O	0.4541(p ^{1.00}) _C +0.8910(p ^{1.00}) _O	0.4593(p ^{1.00}) _C + 0.8883 (p ^{1.00}) _O
σ		0.5791(sp ^{2.23}) _C +0.8153 (sp ^{1.18}) _O	0.5841(sp ^{2.16}) _C + 0.8117 (sp ^{1.24}) _O	0.5850(sp ^{2.11}) _C + 0.8110 (sp ^{1.25}) _O	0.5857(sp ^{2.10}) _C +0.8105(sp ^{1.25}) _O	0.5862 (sp ^{2.08}) _C +0.8102(sp ^{1.26}) _O
	π	0.4162(p ^{1.00}) _C +0.9093(p ^{1.00}) _O	0.4404(p ^{1.00}) _C + 0.8978 (p ^{1.00}) _O	0.4565(p ^{1.00}) _C + 0.8897 (p ^{1.00}) _O	0.462 (p ^{1.00}) _C + 0.8866 (p ^{1.00}) _O	0.4677 (p ^{1.00}) _C + 0.8839 (p ^{1.00}) _O

3.3 Geometry Parameters

3.3.1 Intermolecular parameters

All the intermolecular distances M–N and M–O for metalated thymine have been shown in Table 7. The intermolecular M–N2 distance in (2, metalated) monotonically increases with the atomic number for the alkaline metals (Table 7, Figure 3). The increasing is more pronounced where this difference is more than 1.3 Å. The intermolecular M–O1 distance in (2, metalated), (4, metalated), (5, metalated) and M–O3 distance in (1, metalated), (3, metalated) monotonically increases with the atomic number for the alkali metals (Table 9, Figure 3). This is more pronounced where the difference is more than 1.2 Å and 1.3 Å, respectively. The bond characterization of C1–O1 and C3–

O3 bonds in all compounds is compatible with the results of NBO calculations. Hybridization coefficients for these bonds have been shown in Tables 4 and 8. NBO calculations show the σ and π -bonding contribution in C3–O3 bond of (1, metalated), (3, metalated) and C1–O1 bond of (2, metalated), (4, metalated) and (5, metalated).

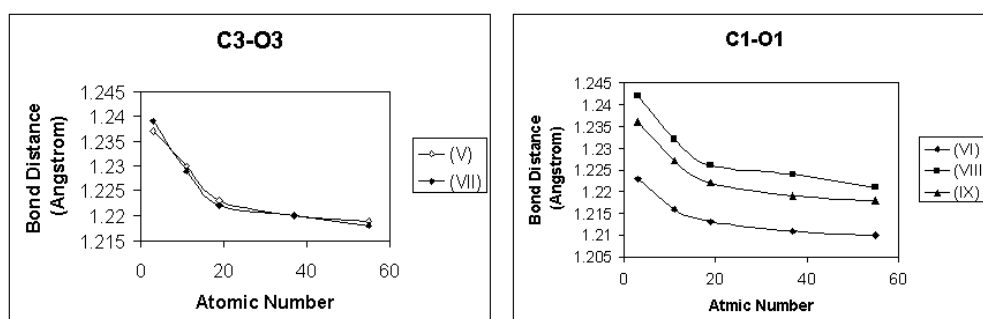


Figure 4. Dependencies of C1–O1 (in VI, VIII, IX), C3–O3 (in V, VII) intermolecular distances on the atomic number of metal.

The intermolecular distance C1–O1 in for metalated thymine (1, metalated) is smaller than nonmetalated, in (2, metalated), (4, metalated) and (5, metalated) is larger than nonmetalated. The intermolecular C1–O1 in (1, metalated) distance increases with atomic number of the alkali metal, while in (3, metalated), (4, metalated) and (5, metalated) it decreases with atomic number of the alkali metal (Table 7, Figure 3). The increasing is not pronounced, where this difference is more than 0.0015 Å (for Li^+ to Cs^+). On the other hand, the intermolecular distance C3–O3 in (1, metalated), (3, metalated) for metalated thymine is smaller than nonmetalated, but in (4, metalated), (5, metalated) is larger than nonmetalated. The intermolecular C3–O3 distance in (1, metalated) decreases with atomic number of the alkali metal (Table 7, Figure 4), but increases with atomic number of the alkali metal in (3, metalated), (4, metalated), (5, metalated). The decreasing is not pronounced, where this difference is more than 0.018 Å (for Li^+ to Cs^+).

3.3.2 Intramolecular parameters

Distances of C1–N2, N2–C3 and C3–N4 are shown in Table 7. The C1–N2 distance in (1, metalated), (3, metalated) decreases and in (2, metalated), (4, metalated) and (5, metalated) increases with increasing of atomic number of alkali metal. The double bond characterization of C1–N2 is the following order: (3, metalated) > (5, metalated) > (4, metalated) > (2, metalated) > (1, metalated). The N2–C3 distance in (2, metalated), (2, metalated) and (5, metalated) decreases and in (1, metalated), (3, metalated), and (5, metalated) increases with increasing of atomic number of alkali metal. So, the double bond characterization of N2–C3 bond increases in the following order: (2, metalated) > (3, metalated) > (1, metalated) > (4, metalated) > (5, metalated). The C3–N4 distance in (4, metalated) and (5, metalated) decreases and in (1, metalated), (2, metalated) and (3, metalated) increases with increasing of atomic number of metal. Therefore, we conclude that the double bond characterization of C3–N4 bond increases in the following order: (4, metalated) > (2,

metalated) > (1, metalated) > (3, metalated) > (5, metalated). See Figure 5.

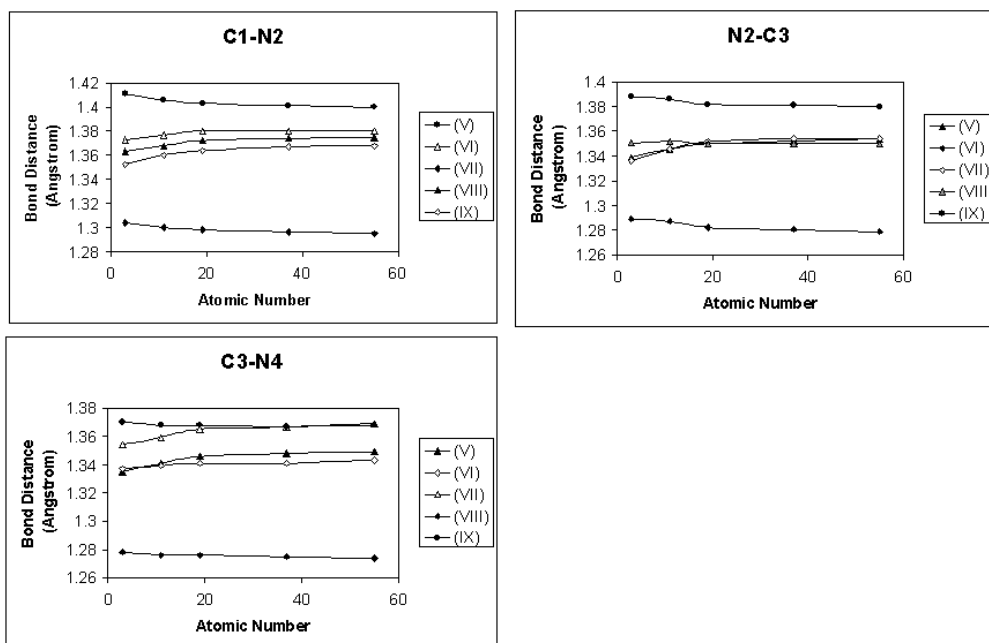


Figure 5. Dependencies of C1–N2, N2–C3, and C3–N4 intramolecular distances on the atomic number of metal for metalated thymine (V) and its tautomers (VI), (VII), (VIII) and (IX).

Table 9. Enthalpy ($\Delta H = MIA$), Entropy (TS) and Free Energy (ΔG) variations for the formation process (1), (2), (3), (4) and (5) metalated complexes, at 298 K, computed at HF level of theory ^{a,b}

	Structure	HF				
		Li	Na	K	Rb	Cs
$\Delta H(\text{kcal/mol})$	1	-47.191	-33.057	-22.400	-19.155	-16.276
	2	-69.880	-53.436	-39.292	-34.918	-30.749
	3	-61.539	-45.292	-32.833	-28.954	-25.421
	4	-52.457	-37.140	-25.705	-22.189	-19.046
	5	-48.896	-34.388	-23.517	-20.201	-17.232
T $\Delta S(\text{kcal/mol})$	1	-7.215	-6.996	-6.572	-6.379	-6.173
	2	-7.851	-7.536	-6.905	-6.684	-6.409
	3	-7.165	-6.678	-6.175	-6.413	-5.99
	4	-7.234	-7.015	-6.054	-6.444	-6.237
	5	-7.300	-7.357	-6.651	-6.463	-6.247
$\Delta G(\text{kcal/mol})$	1	-39.976	-26.061	-15.828	-12.776	-10.103
	2	-62.029	-45.900	-32.387	-28.234	-24.340
	3	-54.374	-38.614	-26.658	-22.541	-19.431
	4	-45.223	-30.125	-19.651	-15.745	-12.809
	5	-41.596	-27.031	-16.866	-13.738	-10.985
K	1	0.28	0.18	0.11	0.09	0.07
	2	0.43	0.32	0.22	0.19	0.17
	3	0.38	0.27	0.18	0.15	0.13
	4	0.31	0.21	0.13	0.11	0.09
	5	0.29	0.19	0.12	0.10	0.07

^a All values are in kcal/mol

^b The basis set for M = Li, Na, K, Rb and Cs is LANL2DZ and for other atoms is 6–31+G*. Also, electron core potential for M = Li, Na, K, Rb and Cs has been considered

3.4 Thermochemical Analysis

Thermochemical analysis is studied for metalated and nonmetalated thymine and its tautomers. The values of ΔH , ΔS and ΔG are reported in 298 K in Table 9. ΔS values are almost the same for all complexes. The equilibrium constants of all complexes are given in Table 9. Which is less for more electropositive metals (compatible with symbiosis effect [35]). The absolute value of ΔG decreases with increasing of metal ion radius which shows that the stability of the complex decline. See Table 9. It sounds right, because as we have indicated previously, with metal ion radius increment bond length increases, as a result the bonding strength decreases. The reaction can be considered as:

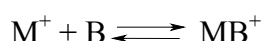


Table 10. %Total Lewis, highest energy lewis NBO lowest and lowest occupancy of N1, N3 (1), (2), (3), (4) and (5) metalated, respectively.

M	%Total Lewis	NBO	Lowest occupancy	Highest energy Lewis NBO (a.u)	
Li	1	99.4904	LP(1)N2	1.69240	-0.54135
	2	98.2178	LP(1)N4	1.68767	-0.57063
	3	99.2886	LP(1)N4	1.73310	-0.55846
	4	99.4665	LP(1)O3	1.73240	-0.57526
	5	99.4993	LP (1)N2	1.68790	-0.54256
Na	1	99.9543	LP(1)N2	1.70170	-0.52845
	2	99.7711	LP(1)N4	1.87005	-0.68008
	3	99.9147	LP(1)N4	1.66770	-0.52013
	4	99.9503	LP(1)N2	1.66252	-0.53073
	5	99.9521	LP(1)N2	1.69827	-0.52965
K	1	99.9907	LP(1)N2	1.70782	-0.51734
	2	99.9428	LP(1)N4	1.70162	-0.54418
	3	99.9786	LP(1)N4	1.67450	-0.50919
	4	99.9886	LP(1)N2	1.66974	-0.51982
	5	99.9887	LP(1)N2	1.70518	-0.51858
Rb	1	99.9960	LP(1)N2	1.70995	-0.51297
	2	99.9770	LP(1)N4	1.70404	-0.53944
	3	99.9907	LP(1)N4	1.67678	-0.50498
	4	99.9953	LP(1)N2	1.67221	-0.51541
	5	99.9954	LP(1)N2	1.70752	-0.51420
Cs	1	99.9978	LP(1)N2	1.71168	-0.50881
	2	99.9886	LP(1)N4	1.70632	-0.53475
	3	99.9951	LP(1)N4	1.67883	-0.50085
	4	99.9976	LP(1)N2	1.67427	-0.51129
	5	99.9977	LP(1)N2	1.70944	-0.51002

3.5 Population Analysis

Mulliken population analysis, like all atomic charge assignment schemes, is an arbitrary method for assigning atomic charges. Generally, changes in Mulliken population provide a reasonable estimation of changes in electron density within closely related molecules. Mulliken population analysis assigns atomic charges by dividing molecular orbital overlap evenly between each pair of atoms involved in a chemical bond. To identify any artifacts in the Mulliken population analysis, a

natural bond orbital was also performed. The Mulliken charges for M, O1, O3, N2 and N4 on metalated thymine (1, metalated), (2, metalated), (3, metalated), (4, metalated) and (5, metalated) are given in Table 5. The analysis of the atomic charges is studied by the natural bonding orbital (NBO) method, as well. Atomic charges of selected atoms of metalated thymine that participate in hydrogen bondings between DNA bases and N2 have been shown in Tables 4 and 5.

Table 11. The stabilization energy E (2) associated with delocalization for interactions that to give the strongest stabilization in (1), (2), (3), (4) and (5) metalated structures

Structure		Li	Na	K	Rb	Cs
1	Donor NBO	LP (1) N2	LP (1) N2	LP (1) N2	LP (1) N2	LP (1) N2
	Acceptor NBO	BD*(1) C 3–O3	BD*(1) C 3–O3	BD*(1) C 3–O3	BD*(1) C 6–O11	BD*(1) C 3–O3
	E(2)(kcal/mol)	117.02	108.58	102.60	100.45	98.62
2	Donor NBO	LP (1) N 2	LP (1) N 2	BD*(2) C 1–O1	BD*(2) C 1–O1	BD*(2) C 1–O1
	Acceptor NBO	BD*(2) C 3–N4	BD*(2) C 3–N2	BD*(2) C 5–C 6	BD*(2) C 5–C 6	BD*(2) C 5–C 6
	E(2)(kcal/mol)	105.89	102.53	120.35	137.10	157.06
3	Donor NBO	LP (3) O3	BD*(2) C 6–O3	LP (1) N 4	LP (1) N 4	BD*(2) C 1–N2
	Acceptor NBO	BD*(2) N 4–C 6	BD*(2) C 1–N2	BD*(2) C 3–O3	BD*(2) C 3–O3	BD*(2) C 5–C 6
	E(2)(kcal/mol)	143.33	325.23	92.68	90.83	92.19
4	Donor NBO	LP (3) O1	LP (1) N 2	LP (1) N 2	LP (1) N 2	LP (1) N 2
	Acceptor NBO	BD*(2) C 1–N 2	BD*(2) N 4–C 3	BD*(2) C 1–O1	BD*(2) C 1–O1	BD*(2) N 4–C 3
	E(2)(kcal/mol)	139.47	84.43	88.24	86.63	85.88
5	Donor NBO	LP (1) N 2	LP (1) N 2	LP (1) N 2	LP (1) N2	LP (1) N 2
	Acceptor NBO	BD*(2) C 1–O1	BD*(2) C 1–O1	BD*(2) C 1–O1	BD*(2) C 1–O1	BD*(2) C 1–O1
	E(2)(kcal/mol)	106.93	99.00	93.26	91.06	88.90

It was found that charge of N2 in metalated thymine is more than nonmetalated (Tables 4 and 5). Increment of dipole moment of metalated thymine shows that N2 in (3, metalated) and N4 in (4, metalated) are more basic in metalated thymine. As shown above, metalation of the major form strongly influences the electronic structure, and this leads to energetic stabilization of the structure. Therefore, the increasing basicity of the N2 in (3, metalated) and N4 in (4, metalated) can be attributed to the relative stabilization of the major form.

Identify principle delocalizing acceptor orbitals associate with each donor NBO and their topological relationship to this NBO, *i.e.*, whether attached to the same atom (geminal), to an adjacent bonded atom (vicinal) or to a more remote site, is possible. These acceptor NBOs will generally correspond to the principle delocalization tails of the non Lewis molecular orbital (NLMO) associated with the parent donor NBO.

The Lewis NBO s in Table 10 describes percentage of the total density, with the remaining non Lewis density found primarily in the valence–shell antibonding. In metalated thymine (1, metalated) the N2 lone pair is seen to be the lowest occupancy and highest energy Lewis NBO and to be primarily delocalized into antibonding the vicinal π^* C3–O3 NBO. In metalated thymine (5, metalated) the N2 lone pair is seen to be the lowest occupancy and highest energy Lewis NBO and to be primarily delocalized into antibonding the vicinal π^* C1–O1 NBO. See Table 11. In other tautomers the lowest occupancy and highest energy Lewis NBO have been shown in Table 11.

Table 11 shows that in other species lowest occupancy and highest energy Lewis NBO depend on alkali metal.

3.6 Donor Acceptor Interaction Perturbation Theory Energy Analysis

The localized orbitals can interact strongly in the best calculated lewis structure. A filled bonding or lone pair orbital can act as a donor. An empty or filled bonding, antibonding or lone pair orbital can act as an acceptor. These interactions can strengthen and weaken bonds. For example, a lone pair donor → antibonding acceptor orbital interaction will weaken the bond which is involved with the antibonding orbitals. Conversely, an interaction with a bonding pair as the acceptor will strengthen the bond. Strong electron delocalization in the best lewis structure will also show up as donor–acceptor interactions. Table 11 shows the interactions that give the strongest stabilization.

4 CONCLUSIONS

Therefore in this paper we have shown:

1. *Ab initio* calculations indicate that metalation of one oxo group of thymine and its tautomers by the elements of group IA (Li, Na, K, Rb and Cs) stabilize them respect to the major form.
2. Stability of tautomers decreases with increasing atomic number of alkali metal.
3. Metalation increases basicity of the nitrogen atom N2 of the ring.
4. Stability of tautomers increases with increasing dielectric constant of solvent.
5. The strongest bonding interactions have been found for metalated thymine with heavy alkali metals.
6. The C1–O1 distance in (2, metalated), (4, metalated) and (5, metalated) and C3–O3 distance in (1, metalated) and (3, metalated) decreases with increasing atomic number of alkali metal.
7. The C1–N2 distance in (1, metalated), (3, metalated) decreases and in (2, metalated), (4, metalated) and (5, metalated) increases with increasing atomic number of metal. The N2–C3 distance in (2, metalated), and (5, metalated) decreases and in (3, metalated) and (5, metalated) increases with increasing atomic number of metal. The C3–N4 distance in (4, metalated) and (5, metalated) decreases and in (1, metalated), (2, metalated) and (3, metalated) increases with increasing atomic number of metal.

5 REFERENCES

- [1] G. L. Eichhon, *Adv. Inorg. Biochem.* **1981**, *3*, 1.
- [2] R. B. Martin, *Acc. Chem. Res.* **1985**, *18*, 32.
- [3] H. Sigel, *Chem. Soc. Rev.* **1993**, *22*, 255.
- [4] (a) M. Monajjemi, et al. *Main Group Metal Chemistry.* **2002**, *25*, 733; (b) M. Monajjemi, R Ghiasi, *Appl.*

- Orgmetal. Chem.* **2003**, 17, 635–640.
- [5] J. E. Del Bene, *J. Phys. Chem.* 1983, 87, 367.
- [6] J. E. Del Bene, *J. Phys. Chem.* 1984, 88, 5927.
- [7] (a) J. V. Burda, J. Sponer, P. Hobza, *J. Phys. Chem.* **1996**, 100, 7250; (b) M. T. Rodgers, P. B. Armentrout, *J. Am. Chem. Soc.* **2000**, 122, 8548; (c) N. U. Zhanpeisov, J. Leszczynski, *J. Phys. Chem. A.* **1998**, 102, 6167; (d) J. Sponer, P. Hobza, *J. Phys. Chem.* **1994**, 98, 3161.
- [8] M. Monajjemi, et al. *J. Mol. Struct. (Theochem)* **2002**, 581, 51.
- [9] J. Sponer, J. E. Sponer, L. Gorb, J. Leszczynski, B. Lippert. *J. Phys. Chem. A.* **1999**, 103, 11406.
- [10] M. J. Clarke. *J. Am. Chem. Soc.* **1978**, 100, 5068 and references there in.
- [11] B. Lippert, H. Schollhorn. *J. Am. Chem. Soc.* **1986**, 108, 6616.
- [12] (a) F. Pichierri, F. Hoithenrich, E. Zangrando, B. Lippert, L. Randaccio. *J. Biol. Inorg. Chem.* **1996**, 1, 439; (b) J. Muller, E. Zangrudo, N. Pahlke, E. Freisinger, L. Randaccio, B. Lippert. *Eur. J. Chem.* **1998**, 4, 397; (c) J. Muller, F. Glahe, E. Freisinger, B. Lippert. *Inorg. Chem.* **1999**, 38, 3160.
- [13] (a) S. J. Lippard, J. M. Berg, *Principle of Bioinorganic Chemistry*; University Science Books: Mill Valley, CA, 1994; (b) W. Kaim, B. Schwedersky, *Bioinorganic Chemistry: Inorganic elements in the Chemistry of Life*; John Wiley & Sons: Chichester, 1994.
- [14] L. A. Lobew, A. R. Zakour, *In Nucleic Acid–Metal Ion Interactions*; John Wiley & Sons; New Yourk, 1980: pp 115–144.
- [15] Y. C. Jean, Y. G. Gao, A. H. Wang, *J. Biochem.* **1993**, 32, 381.
- [16] A. Gordon, A. R. Katritzky, *Tetrahedron Lett.* **1968**, 2767.
- [17] J. Rank, A. R. Kartitzkt, *J. Chem. Soc., Perkin Trans.* **1976**, 2, 1428.
- [18] M. Kuzuya, A. Noguchi, T. Okuda, *J. Chem. Soc., Perkin Trans.* **1985**, 2, 1428.
- [19] P. Cieplak, P. Bash, U. C. Singh, Kollman P.A, *J. Am. Chem. Soc.* **1987**, 109, 6283.
- [20] C. J. Cramer, Truhlar, *J. Am. Chem. Soc.* **1991**, 113, 8552.
- [21] M. Szafam, Karelson, Ktritzky, J. Koput, M. C. Zerner, *J. Comput. Chem.* **1993**, 14, 371.
- [22] S. Miertus, E. Scrocco, *J. Chem. Phys.* **1981**, 55, 117.
- [23] S. Miertus, E. Tomasi, *J. Chem. Phys.* **1982**, 65, 239.
- [24] R. Cammi, B. Mennucci, *J. Chem. Phys.* **1999**, 110, 9877.
- [25] Gaussian 98, Revision A.7, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, Jr., R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, A. G. Baboul, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, J. L. Andres, C. Gonzalez, M. Head-Gordon, E. S. Replogle, and J. A. Pople, Gaussian, Inc., Pittsburgh PA, 1998.
- [26] T. Clark, J. Chandrasekhar, G. W. Spitznagel, P. V. R. Schlegel. *J. Comp. Chem.* **1983**, 4, 294.
- [27] (a) A. Schaefer, H. Horn, R. Ahlrichs. *J. Chem. Phys.* **1992**, 93, 2571; (b) P. J. Hay and W. R. Wadt. *J. Chem. Phys.* **1985**, 82, 270; (c) P. J. Hay, W.R. Wadt. *J. Chem. Phys.* **1985**, 82, 284; (d) P. J. Hay, W.R. Wadt. *J. Chem. Phys.* **1985**, 82, 299.
- [28] (a) J. E. Carpenter, F. Weinhold. *J. Mol. Struct. (Theochem)* **1988**, 169, 41; (b) J. P. Foster, F. Weinhold. *J. Am. Chem. Soc.* 1980, **102**, 7211; (c) A. E. Reed, F. Weinhold. *J. Chem. Phys.* **1983**, 78, 4066; (d) A. E. Reed, L. A. Curtiss, F. Weinhold. *Chem. Rev.* **1988**, 88, 899; (e) A. E. Redd, R. B. Weinstock, F. Weinhold. *J. Chem. Phys.* **1985**, 83, 735.
- [29] M. W. Wong, K. B. Wiberg and M. J. Frisch, *J. Amer. Chem. Soc.* **1992**, 114, 1645.
- [30] S. Miertus and J. Tomasi, *J. Chem. Phys.* **1982**, 65, 239.
- [31] M. Cossi, V. Barone, R. Cammi and J. Tomasi, *Chem. Phys. Lett.* **1996**, 255, 327.
- [32] A. D. Becke, *J. Chem. Phys.* **1993**, 98, 5648.
- [33] C. Lee, W. Yang, R. G. Parr, *Phys. Rev.* **1988**, B 37, 785
- [34] Alkorta I, Rozas I, Eleguero J. *J. Mol. Struct. (Theochem)* **2001**, 537, 139.
- [35] J. E. Huheey, E. A. Keiter and R. L. Keiter, *Inorganic Chemistry, Principles of structure and Reactivity*, Fourth Edition, Harpar And Row, New York, 1994 pp 348–350, 518–519.