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Research Article

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Density functional theory (DFT) studies of the stability of tautomers and equilibrium constants of cyanuric acid (CA) in different solvents

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ABSTRACT

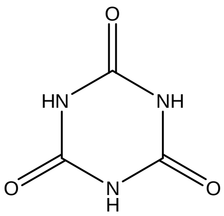
The relative energies and tautomeric equilibrium constants of Cyanuric acid (1,3,5-triazine-2,4,6-triol) have been calculated at DFT/B3LYP level of theory using 6-311++ G (d,p) basis set in gas phase and different solvents by using PCM model. The results indicate that the keto tautomer (CA1) is the most stable in the gas phase and other solvents. The order of stability of isomers was found to be CA1 > CA3 > CA2 > CA6 > CA11 > CA10 > CA7 > CA4 > CA5 > CA9 > CA8.The calculated tautomeric equilibrium constants with respect to the most stable tautomer CA1 in both gas phase and in different solvents. The mean polarizabilities were calculated and the order was Gas > THF > ethanol > DMF > water.

Key words: Cyanuric acid, DFT method, relative stabilities, equilibrium constants and solvent effects.

INTRODUCTION

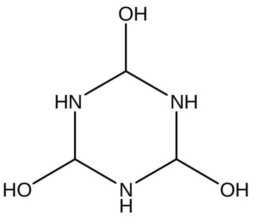
Cyanuric acid (CYA) is also a triazine-derivative and may also be described as two structural isomers, the enol-like triazine-triol and the keto-like tautomer. Cyanuric acid is a unique cyclic amide having three hydrogen bond donor and three acceptor sites, leading to a range of hydrogen bonding possibilities, both with other cyanuric acids as well as with polar solvents. Cyanuric acid, which are structurally similar to amino acids, are promising candidates to use in the investigation of non-covalent interactions in the assembly and stabilization of biological systems on a surface.CYA is commonly used as a component of bleaches in swimming pools [1,2]. Under controlled conditions CYA as well as their derivatives can form hydrogen-bonded self-assemblies with specific surface structures and these assemblies have been used as surface templates in supramolecular chemistry [3-6].Cyanuric acid is an oxytriazine melamine analogue that may be produced as a by-product in melamine synthesis. It is a USFDA-accepted component of feed-grade biuret, a ruminant feed additive, and is also found in swimming pool water as the dissociation product of dichloroisocyanurates used for water disinfection.When used for disinfection purposes in drinking-water, sodium dichloroisocyanurate is rapidly dechlorinated to cyanurate [7, 8]. Cyanuric acid derivatives are regulated in the USA as components of sanitizing solutions for use on food-processing equipment, utensils and other food contact articles.

Cyanuric acid shows keto-enol or more precisely aminoketo-iminoalcohol tautomerism. A prominent example is the isomerism between isocyanuric acid (1a) and cyanuric acid (1b) and may exist in several different tautomeric forms (Fig. 1).



1a

1,3,5-triazine-2,4,6-triol



1b

1,3,5-triazine-2,4,6- (1H,3H,5H)trione

In the present research work we were calculated relative stability, enthalpy, entropy, Gibbs free energy, equilibrium constants and polarizabilties for the theoretical possible tautomers of cyanuric acid at 298.15 K in gas phase and different solvents. We have found the tautomeric equilibrium constants with respect to the more stable tautomer both in the gas phase and in different solvents.

COMPUTATIONAL SECTION

Molecular geometries of tautomeric forms of Cyanuric acid were fully optimized by using the Gaussian quantum chemistry software package Gaussian 09 w [9] at DFT/B3LYP level of theory, using the 6-311++G (d,p) basis set. Following the geometry optimizations, analytical frequency calculations were preceded following the standard procedures, to obtain the thermochemical properties. In addition the effects of solvents on the tautomeric structure properties were studied by means of the self-consistent reaction-field (SCRF) method based on PCM developed by Tomasi and coworkers [10] , it is one of the most widely used approaches. In this model, a solute is considered inside a cavity and the solvent as a structureless medium characterized by some parameters such as its dielectric constant, molar volume and polarizability. This consideration can substantially improve the simulation results for the electronic or vibrational spectroscopy of real molecular systems [11,12].The solvents chose for this studies are polar protic solvents namely water (ε = 74.80) and ethanol (ε = 24.55) and polar aprotic solvents like tetrahydrofuran(THF) (ε = 7.50) and dimethylformamide (ε = 38.00).

RESULTS AND DISCUSSION

The optimized structures of the tautomers of titled compound calculated by ab initio method DFT/B3LYP at level of 6-311++G (d,p) basis set, in accordance with atom numbering scheme given in Figure.1 in gas phase and different solvents. Isocyanuric acid 1a has ten tautomeric forms: two mono hydroxy, six di-hydroxy and two tri-hydroxy isomers, these are differ in the mono proton, di proton and tri proton transfer and orientation of the hydroxyl groups. The isomers are labelled, CA1: Cyanuric acid (1,3,5-triazinane-2,4,6-trione), CA2 and CA3: 6-hydroxy-1,3,5-triazine-2,4(1H,3H)- dione , CA4, CA5, CA6, CA7, CA8 and CA9: 4,6-dihydroxy-1,3,5-triazin-2(1H)-one and CA10 and CA11: 1,3,5-triazine-2,4,6-triol.

Table1. The energies of tautomers (a.u) at DFT/6-311++G(d,p) level in different media and the relative energies compared to the most stable isomer CA1.The relative energies in brackets in kcal mol^{-1}

Tautomer	gas	THF	ethanol	DMF	water
CA1	-506.290024(0.00)	-506.304423(0.00)	-506.306820(0.00)	-506.307341(0.00)	-506.307628(0.00)
CA2	-506.247645(26.59)	-506.270440(21.32)	-506.274749(20.12)	-506.275690(19.86)	-506.274750(20.63)
CA3	-506.262850(17.05)	-506.279191(15.83)	-506.282074(15.53)	-506.282696(15.46)	-506.282984(15.46)
CA4	-506.232431(36.14)	-506.253799(31.77)	-506.257861(30.72)	-506.258749(30.49)	-506.259162(30.41)
CA5	-506.230261(37.50)	-506.252788(32.40)	-506.257139(31.18)	-506.258094(30.90)	-506.258538(30.80)
CA6	-506.245276(28.08)	-506.261172(27.14)	-506.264016(26.86)	-506.264630(26.80)	-506.264915(26.80)
CA7	-506.241349(30.54)	-506.259534(28.17)	-506.262957(27.52)	-506.263704(27.38)	-506.264052(27.34)
CA8	-506.196117(58.93)	-506.230196(46.58)	-506.237554(43.47)	-506.239190(42.77)	-506.239956(42.46)
CA9	-506.212707(48.52)	-506.240013(40.42)	-506.245463(38.50)	-506.246666(38.07)	-506.247227(37.90)
CA10	-506.241407(30.51)	-506.253835(31.74)	-506.256155(31.79)	-506.256660(31.80)	-506.256895(31.84)
CA11	-506.243090(29.45)	-506.254413(31.38)	-506.256439(31.61)	-506.256873(31.67)	-506.257111(31.70)

Relative Energies

The relative energies of various tautomers and isomers of isocyanuric acid studied with respect to the most stable isomer CA1 are reported in Table 1. In Table 1, results are presented for the absolute and relative electronic energy in gas and different (THF, ethanol, DMF and water) solvents phase respectively. The isocyanuric acid isomer CA1 is the most stable isomer in both gas phase and different solutions because of CA1 is keto isomer. In order of stability in gas phase was CA1 > CA3 > CA2 > CA6 > CA11 > CA10 > CA7 > CA4 > CA5 > CA9 > CA8.

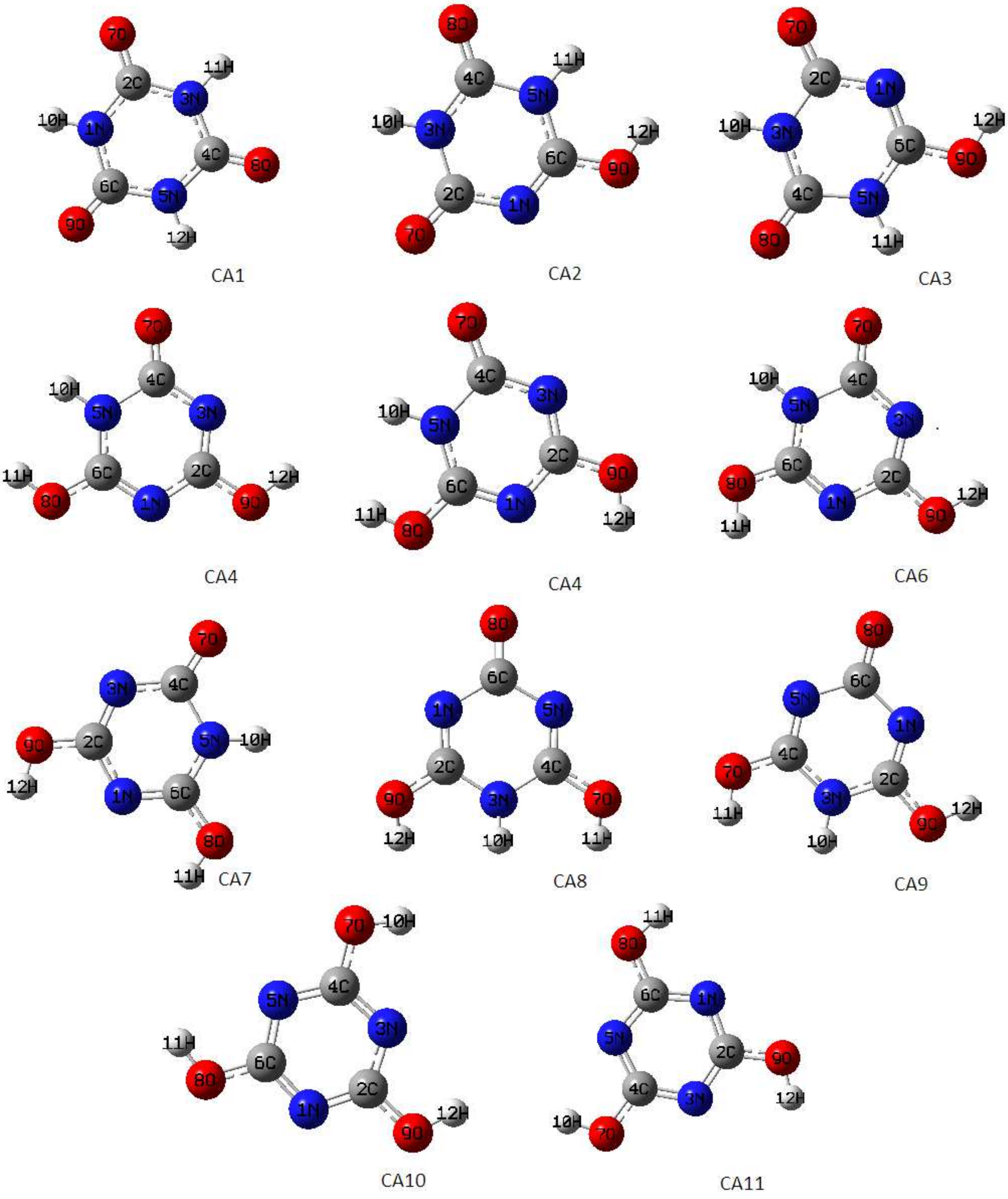

CA1 CA2 CA3
CA4 CA4 CA6
CA7 CA8 CA9
CA10 CA11

Fig.1. Leven structural isomers of $C_3N_3O_3H_3$ comprising Cyanuric acid (1,3,5-triazinane-2,4,6-trione) (labeled (1)), 6-hydroxy-1,3,5-triazine-2,4(1H,3H)- dione ((2) and (3)), 4,6-dihydroxy-1,3,5-triazin-2(1H)-one ((4), (5),(6) (7),(8)and (9)), and 1,3,5-triazine-2,4,6-triol ((10) and (11)) in gas phase. Each atom is colored and numbered. Grey is carbon, blue is nitrogen, red is oxygen and white is hydrogen

Solvent effects are relevant to tautomer stability phenomena, since polarity differences among tautomers can induce significant changes in their relative energies in solutions. For this purpose, the PCM calculations were employed to analyze the solvent effects on tautomerism of Cyanuric acid.

The results obtained for different solutions have been reported in Table 1 and compared with those obtained from the gas phase calculations. It is evident that the electronic energies of tautomers decrease in comparison with gas phase. As the dielectric constant of solvent increases the isomer relative energy is decreases because of the solvation stabilizes all the species. Obviously, larger dipole moment leads to larger stabilization in solution phase. Moreover, the solvent with larger dielectric constant results in larger stabilization energy for the polar species. The order of stability of tautomers was found in the different solvents to be similar to gas phase. In the all phases the tautomer CA1 is more stable and CA8 is less stable tautomer, have high dipole moment because of all hydroxy hydrogen's are same direction.

Thermodynamic properties

The thermodynamic parameters of the conversion processes, ΔH, ΔG, and ΔS were calculated from the results of quantum mechanical calculations of electronic, vibrational, rotational, and translational energy components. The change of enthalpies (ΔH), Gibbs free energies (ΔG) and entropies (ΔS) of various tautomers, studied with respect to the most stable isomer CA1 are reported in Table 2, in different solvents. From Table 2 the change of enthalpy (ΔH) and the free energy (ΔG) change are positive in all phases of the conversion from CA1 to other tautomers and are endothermic and non spontaneous process respectively. The ΔG values are negative and high values, so the products negligible.

Table 2. The themodynamic properties of equilibrium states between cyanuric acid tautomers in gas phase and different solvents at DFT/B3LYP theory of 6-311++G (d,p) basis set

Tautomer	gas			THF			Ethanol			DMF			water		
	ΔH	ΔG	ΔS	ΔH	ΔG	ΔS	ΔH	ΔG	ΔS	ΔH	ΔG	ΔS	ΔH	ΔG	ΔS
CA1↔CA2	25.87	25.23	2.16	20.92	20.26	2.20	19.74	19.37	1.24	19.46	14.20	1.08	20.27	19.87	1.33
CA1↔CA3	16.75	16.90	-0.482	15.52	15.61	-0.31	15.25	15.38	-0.43	15.18	11.27	-0.45	15.19	15.29	-0.33
CA1↔CA4	35.44	35.54	-0.332	31.18	30.93	0.841	30.21	30.26	-0.18	29.98	22.18	-0.37	29.92	30.02	-0.33
CA1↔CA5	36.74	36.79	-0.19	31.97	32.21	-0.78	30.77	31.06	-0.98	30.49	22.77	-1.01	30.40	30.66	-0.90
CA1↔CA6	27.72	28.17	-1.504	26.69	27.01	-1.07	26.45	26.79	-1.17	26.38	19.64	-1.18	26.40	26.71	-1.06
CA1↔CA7	30.06	30.41	-1.183	27.73	28.03	-1.00	27.12	27.45	-1.11	26.97	20.12	-1.13	26.94	27.24	-1.01
CA1↔CA8	57.56	57.11	1.513	45.78	45.27	1.68	42.75	42.11	2.17	42.07	30.87	1.38	41.79	41.43	1.23
CA1↔CA9	47.38	46.15	4.119	39.61	38.92	2.32	37.77	37.53	0.81	37.34	27.51	0.60	37.18	36.98	0.64
CA1↔CA10	30.31	31.05	2.488	31.39	31.93	-1.80	31.44	31.99	-1.84	31.44	23.45	-1.84	31.48	31.99	-1.71
CA1↔CA11	29.30	30.07	2.587	31.06	31.62	-1.87	31.27	31.82	-1.85	31.31	23.33	-1.84	31.38	31.92	-1.81

Tautomeric equilibria in the gas phase and solution

Cyanuric acid exists mainly in eleven tautomeric forms (CA1 - CA11) that are in equilibrium. CA1 has a keto form and can be converted to CA2 and CA3 tautomers through a proton transfer and rotation around the C-O bond, simultaneously. The CA4 to CA9 isomers give the dihydroxy form by two protons transfer and considering the orientation of the hydroxyl hydrogen's. CA10 and CA11 are converted try hydroxyl isomers through three proton transfer. Therefore, only eleven isomers were considered in the present study.

The DFT/B3LYP method calculated tautomeric equilibrium constants with respect to the most stable tautomer CA1 of Cyanuric acid both in the gas and in different solution are listed in Table 3. The tautomeric equilibrium between tautomers a and b is described as

$$a \overset{K_T}{\rightleftharpoons} b \qquad (1)$$

Equilibrium constants for each species were calculated by using the following equation

$$K_T = e^{-(\Delta G/RT)} \qquad (2)$$

where K_T is the tautomeric equilibrium constant between the tautomers, the gas constant R is 1.987 X 10^{-3} kcal/mol; and the temperature T is 298.15 K. The pK_T values of the studied molecules were calculated by means of the following equation

$$pK_T = \frac{\Delta G}{2.303RT} \qquad (3)$$

The equilibrium between the tautomers 1 and 3 of cyanuric acid values for show that the CA2 is more dominant than the CA3, both for the gas and different solvents with a pK_T value of 12.39, (gas) and 11.44 (THF) , 11.27 (ethanol), 8.26 DMF and 11.21 (water) respectively. This is confirming to thermodynamic data of CA1↔CA3, see the table 3. The remaining tautomers are not detectable amounts because of the pK_T values are very high.

Table 3. The of equilibrium constants and pK_T for Cyanuric acid tautomers in gas phase and different solvents at DFT/B3LYP theory of 6-311++G (d,p) basis set

Tautomer	**gas**		**THF**		**Ethanol**		**DMF**		**water**	
	K	pK_T	**K**	pK_T	**K**	pK_T	**K**	pK_T	**K**	pK_T
CA1↔CA2	3.2×10^{-19}	18.50	1.4×10^{-15}	14.85	6.3×10^{-15}	14.20	3.9×10^{-11}	10.41	2.7×10^{-15}	14.57
CA1↔CA3	4.1×10^{-13}	12.39	3.6×10^{-12}	11.44	5.3×10^{-12}	11.27	5.5×10^{-9}	8.26	6.2×10^{-12}	11.21
CA1↔CA4	8.8×10^{-27}	26.05	2.1×10^{-23}	22.67	6.6×10^{-23}	22.18	5.5×10^{-17}	16.26	9.8×10^{-23}	22.01
CA1↔CA5	1.1×10^{-27}	26.97	2.4×10^{-24}	23.61	1.7×10^{-23}	22.77	2.0×10^{-17}	16.69	3.3×10^{-23}	22.48
CA1↔CA6	2.2×10^{-21}	20.65	1.6×10^{-20}	19.80	2.3×10^{-20}	19.64	4.0×10^{-15}	14.40	2.6×10^{-20}	19.58
CA1↔CA7	5.1×10^{-23}	22.29	2.8×10^{-21}	20.55	7.5×10^{-21}	20.12	1.8×10^{-15}	14.75	1.1×10^{-20}	19.97
CA1↔CA8	1.4×10^{-42}	41.87	6.5×10^{-34}	33.19	1.3×10^{-31}	30.87	2.3×10^{-23}	22.63	4.2×10^{-31}	30.37
CA1↔CA9	1.5×10^{-34}	33.83	2.9×10^{-29}	28.53	3.1×10^{-28}	27.51	6.8×10^{-21}	20.17	7.8×10^{-28}	27.11
CA1↔CA10	1.7×10^{-23}	22.76	3.9×10^{-24}	23.41	3.5×10^{-24}	23.45	6.4×10^{-18}	17.19	3.5×10^{-24}	23.45
CA1↔CA11	9.0×10^{-23}	22.04	6.6×10^{-24}	23.18	4.7×10^{-24}	23.33	7.9×10^{-18}	17.10	4.0×10^{-24}	23.40

From the Table 3, the pK_T values are decreasing with increase in polarity of solvents but expect in the case of DMF. Tautomeric equilibrium is influenced by the dielectric constant of the medium and solvents to hydrogen bond with each tautomer favoring the more polar tautomer. Solvent effects have been ascribed to two major components [13], electrostatic solvent-solute interaction and hydrogen bonding. The hydrogen bonding effects cannot be estimated in a quantitative manner from the salvation model, and needs further large-scale calculations. The electrostatic solvent-solute effects, however, are readily estimated by the reaction field continuum model [14] using the dipole moments and molecular polarizabilities. Application of the reaction field continuum model leads to an explanation of the change in order of tautomeric stability on going from gas phase to solution. However, such a treatment lacks explicit consideration of base-water hydrogen bonding effects [15]. The order of the pK_T values are: Gas < THF < ethanol < water < DMF.

Molecular polarizability

The Polarizability calculations carried out for gas phase and different solvents of cyanuric acid tautomers are summarized in table 4. Here, α is a second rank tensor property called the dipole Polarizability and mean Polarizability $\langle \alpha \rangle$ are evaluated using

$$\langle \alpha \rangle = \frac{1}{3}(\alpha_{xx} + \alpha_{yy} + \alpha_{zz}) \tag{4}$$

When a molecule is placed in a liquid environment, it is polarized, i.e., its electrostatic moments are changed giving rise to induced multipole moments. The amount of polarization will depend on several factors including, of course, the Polarizability of the solute and the electric field provided by the environment.

Table 4. The mean Polarizability $\langle \alpha \rangle$ for Cyanuric acid tautomers in gas phase and different solvents at DFT/B3LYP theory of 6-311++G (d,p) basis set

Polarizability(α)	**Tautomers**										
	CA1	CA2	CA3	CA4	CA5	CA6	CA7	CA8	CA9	CA10	CA11
gas	64.470	66.112	65.919	67.439	67.561	67.231	67.355	68.161	67.177	67.033	67.024
THF	79.410	81.984	81.700	83.540	83.706	83.393	83.532	83.790	83.459	83.025	83.050
Ethanol	82.357	85.158	84.834	86.801	86.985	86.639	86.788	87.154	86.821	86.251	86.271
DMF	83.000	85.859	85.528	87.524	87.715	87.357	87.510	87.911	87.570	86.965	86.984
water	83.315	85.158	85.852	87.862	88.057	87.695	87.848	88.266	87.924	87.298	87.343

As seen from the Table 4, in the gas phase the polarizabilities are low and in all the solvents are high values, the order of polarizabilities is Gas > THF > ethanol > DMF > water, due to increase of dielectric constant of solvents. The largest Polarizability was observed for CA8 tautomer in all phases.CA8 tautomer is more polarizable than other tautomers because of its dipole moment is high value in all solvents.

CONCLUSION

Tautomers of Cyanuric acid acid have been studied by using DFT method at level of B3LYP/6-311++G(d,p), in the gas phase and in different solvents by using of PCM model. The following conclusions have been drawn from the present study: All the optimized tautomers present at the stationary points are corresponding to local minima in the potential energy surface. The keto form CA1 was found to be the most stable form over than all enol forms in the gas phase and different solvents. The influence of the polar environment substantially enhanced the dipole moment for all the tautomers in going from the gaseous to solvents phase, which indicates that there is an increase in stability of the molecular system due to the solvent-molecule interaction and redistribution of the charge. The pK_T values are decreasing to increase the polarity of solvents. The mean polarizabilities in the gas phase were low and in all the solvents are high values, the order of polarizabilities is Gas > THF > ethanol > DMF > water, due to increase of dielectric constant of solvents.

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