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Ab initio and DFT Studies on Tautomerization of Nitrosamine in Reaction of the Nitrosamine Isomers-H_2O_2

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Ab initio molecular orbital and DFT calculations have been carried out for tautomerization, 2 imino tautomers and 1 zwitter ionic to amino (most stable species of the nitrosamine isomers) in reaction of HNNOH-H_2O_2 in order to elucidate the structures and energetics. The structures and transition states were optimized using B3LYP and MP2 methods with 6-311++G(2d,2p), AUG-cc-pVDZ basis sets. The transition states of the three transformation reactions found in the study possess 3 proton-transfer processes. Energetics and thermodynamic properties of all tautomerization of nitrosamine in reaction of the nitrosamine isomers - H_2O_2 have been obtained.

Key Words: Tautomerization, Nitrosamine, H_2O_2, Proton-transfer.

INTRODUCTION

Oxidation in biological systems can damage biomolecules including nucleic acid and protein. Hydrogen peroxide (H_2O_2) generating highly reactive radicals has been proven to play a role in the oxidation reactions[1] Significant quantities of H_2O_2 can be detected as a byproduct of several metabolic pathways in human blood[2].

The H_2O_2 complexes which are important in many chemical and biochemical systems have been investigated by different research groups. The interactions of hydrogen peroxide with O_3[3,4], dimethyl ether[5], 1,3-butanediol[6], glycine[7], formamide[8], uracil[9], water[10], hydrogen halides[11], urea[12] and nitrosamine[13] were studied.

Tautomers are isomers of organic compounds that readily interconvert by a chemical reaction called tautomerization. Commonly this reaction results in the formal migration of a hydrogen atom or proton, accompanied by a switch of a single bond and adjacent double bond, nitrosamine has tautomer structure. Because NH_2NO contains N=O as well as NH_2 groups, it is expected to form a strong binary H-bonded complex with compounds such as H_2O_2 which is not only a proton donor but also a proton acceptor. To the best of our knowledge, interaction between NH_2NO and H_2O_2 as well as nature of interactions in NH_2NO-H_2O_2 complexes has not been experimentally investigated. But the theory has been studied[13]. Tautomerization of nitrosamine study has not been when a H_2O_2 with NH_2NO do complex formation.

COMPUTATIONAL DETAILS

The geometries of the complexes and transition-states were optimized using B3LYP and MP2 methods with 6-311++G(2d,2p) and AUG-cc-pVDZ basis sets by Gaussian-03 program package[14].

The thermal and corresponding zero-point vibrational energies calculations were performed for all optimized species at aforementioned levels to evaluate. Vibrational frequencies (from the analytic Hessian) were calculated to ensure that each minimum is a true local minimum (containing only positive frequencies) and that each transition state has only a single imaginary frequency (one negative eigenvalue of the Hessian).

The Mulliken electronegativity (χ), chemical hardness (η) and electronic chemical potential (μ) for all isomers of the nitrosamines were computed using orbital energies of the highest occupied molecular orbital (HOMO) and the lowes unoccupied molecular orbital (LUMO) at the B3LYP/AUG-cc-pVDZ and MP2/AUG-cc-pVDZ levels of theory. The chemical hardness, electronic chemical potential and Mulliken electronegativity were derived from the first ionization potential (I) and electron affinity (A) of the N-electron molecular system with a total energy (E) and external potential $[\nu(\vec{r})]$ using the relations:

$$\chi = -\left(\frac{\partial E}{\partial N}\right)_{\nu(\vec{r})} = -\mu \cong \frac{1}{2}(I + A) \text{ and } \eta = -\left(\frac{\partial E}{\partial N^2}\right)_{\nu(\vec{r})} \cong \frac{1}{2}(I - A)$$

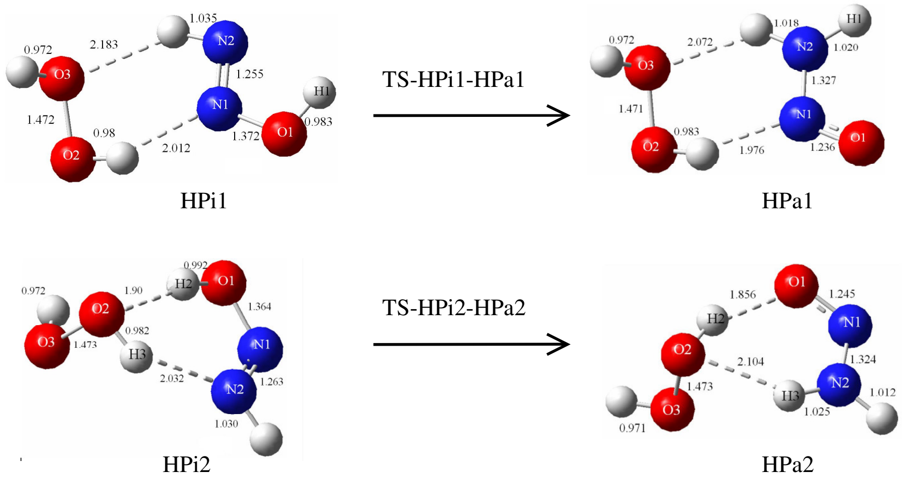
and the first ionization potential and electron affinity are I = E(N - 1) - E(N) and A = E(N) - E(N + 1)[15]. According to the Koopmans theorem[16], I and A were computed from the HOMO and LUMOenergies using the relations: $I = -E_{HOMO}$ and $A = -E_{LUMO}$.

The standard enthalpy ΔH_{298} and Gibbs free energy changes ΔG_{298} of interconversion reactions have been derived from the frequency calculations.

RESULTS AND DISCUSSION

Isomer and transition-state structures: The HNNOH nitrosamine isomers can be classified into two types namely imino (type i) and zwitter ionic (type z) isomers that reaction with H_2O_2. Nitrosamine tautomers in trace interconversions (proton transfer) convert to amino (most stable species of the nitrosamine isomers). Supplementary data, are categorized into three groups, Fig. 1 for group 1 (imino-H_2O_2): HPi_1, HPi_2, Fig. 2 for group 2 (zwitter ionic-H_2O_2): HPz and Fig. 3 for group 3 (transition-states): TS-HPi_1-HPa_1, TS-HPi_2-HPa_2, TS-HPz-HPa_3: these structures computed at the MP2/AUG-cc-pVDZ level of theory.

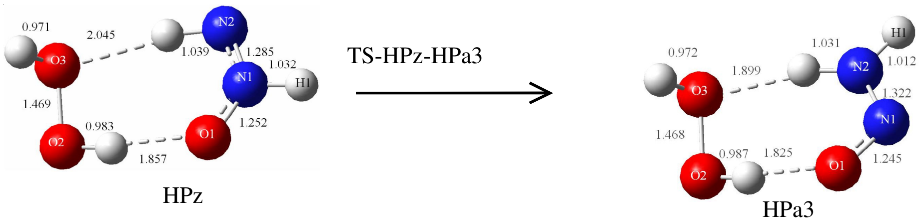
The few stable isomer of the nitrosamine-H_2O_2 is a Hi_1 which is able to convert to HPa_1 (most stable), HPi_1 *via* the transition-state TS-HPi_1-HPa_1. The structures of HPi_1, HPa_1 and transition states of their interconversion are in the MP2/AUG-cc-pVDZ-optimized geometrical parameters are shown in Fig. 1. The Ha_2 and Ha_3 complexes are the most stable complexes of the groups 2 and 3, respectively.



HPi1 HPa1

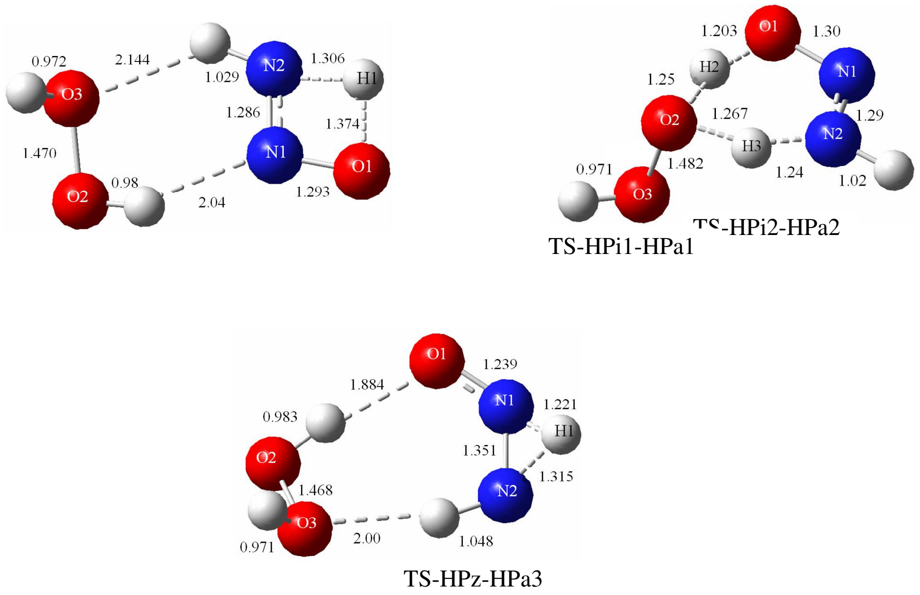
HPi2 HPa2

Fig. 1. Structures of imino-H_2O_2 group 1



HPz HPa3

Fig. 2. Structures of zwitter ionic-H_2O_2 group 2



TS-HPi1-HPa1 TS-HPi2-HPa2

TS-HPz-HPa3

Fig. 3. Structures of transition-states group 3

Energetics, thermodynamic properties: The electronic binding energies with BSSE, thermal and zero-point corrected energies for different complexes at several levels of theory are given in Table-1.

TABLE-1
BINDING ENERGIES (kcal/mol) FOR ISOMERS OF THE NITROSAMINE-H_2O_2

Complex	Method	Basis set	BSSE	De	D_e^{BSSE}	D_0	D_0^{BSSE}
HPi_1	B3LYP	6-311++G(2d,2p)	0.40	-5.91	-5.52	-4.31	-3.91
		AUG-cc-pVDZ	0.29	-5.72	-5.43	-4.14	-3.85
	MP2	6-311++G(2d,2p)	1.49	-7.63	-6.14	-6.00	-4.51
		AUG-cc-pVDZ	1.66	-7.88	-6.22	-6.25	-4.59
HPi_2	B3LYP	6-311++G(2d,2p)	1.26	-5.29	-4.03	-3.76	-2.50
		AUG-cc-pVDZ	0.46	-5.44	-4.98	-3.85	-3.40
	MP2	6-311++G(2d,2p)	1.65	-6.34	-4.68	-4.73	-3.08
		AUG-cc-pVDZ	2.22	-6.99	-4.76	-5.28	-3.05
HPz	B3LYP	6-311++G(2d,2p)	0.68	-7.61	-6.93	-6.12	-5.44
		AUG-cc-pVDZ	0.65	-7.14	-6.49	-5.60	-4.95
	MP2	6-311++G(2d,2p)	1.78	-8.69	-6.92	-6.88	-5.10
		AUG-cc-pVDZ	1.95	-9.03	-7.08	-7.23	-5.28
HPa_1	B3LYP	6-311++G(2d,2p)	0.43	-7.59	-7.16	-5.50	-5.07
		AUG-cc-pVDZ	0.57	-7.66	-7.09	-5.64	-5.07
	MP2	6-311++G(2d,2p)	1.65	-9.32	-7.67	-7.12	-5.47
		AUG-cc-pVDZ	1.87	-9.74	-7.87	-7.63	-5.76
HPa_2	B3LYP	6-311++G(2d,2p)	0.51	-7.55	-7.04	-5.97	-5.46
		AUG-cc-pVDZ	0.51	-7.48	-6.97	-5.50	-4.99
	MP2	6-311++G(2d,2p)	1.68	-8.89	-7.21	-6.85	-5.17
		AUG-cc-pVDZ	1.97	-9.54	-7.57	-7.41	-5.45
HPa_3	B3LYP	6-311++G(2d,2p)	0.64	-9.22	-8.58	-6.78	-6.14
		AUG-cc-pVDZ	0.52	-9.31	-8.79	-6.97	-6.45
	MP2	6-311++G(2d,2p)	2.01	-10.40	-8.39	-7.76	-5.75
		AUG-cc-pVDZ	2.23	-11.02	-8.79	-8.49	-6.26

D_e^{BSSE} = Electronic binding energy (D_e) + BSSE, $D_0 = D_e + \Delta ZPE$, $D_0^{BSSE} = D_0$ + BSSE.

Basis set superposition errors (BSSE)[17] introduce a significant correction in the calculation of energies and have been considered in most recent studies. From Table-1, the relative stabilities of all isomers of the nitrosamine dimers based on their D_0^{BSSE} are in decreasing order: $HPa_3 > HPa_1 > HPa_2 > HPz > HPi_1 > HPi_2$. The amines complexes are the most stable complexes.

The relative thermodynamic properties (activation energies, activation free energies, reaction enthalpies, reaction free energies) of all transition-states of their interconversions, computed at the B3LYP/AUG-cc-pVDZ and MP2/AUG-cc-pVDZ levels of theory are shown in Table-2.

The activation energies of the reactions are in the increasing order: $HPi_2 \rightarrow HPa_2 < HPi_1 \rightarrow HPa_1 < HPz \rightarrow HPa_3$. Activation energy di-proton transfer less than monoproton transfer, in the middle of monoproton transfer H from O to N energy less than H from N1-N2. This may be explained within the principle of the minimal

TABLE-2
THERMODYNAMIC QUANTITIES, TRANSITION-STATES OF THE NITROSAMINE-H_2O_2, COMPUTED AT THE B3LYP/AUG-cc-pVDZ AND MP2/AUG-cc-pVDZ LEVELS OF THEORY

Reactions						
B3LYP/AUG-cc-pVDZ	$\Delta E^{\ddagger}$	$\Delta H^{\ddagger}$	$\Delta G^{\ddagger}$	ΔE^{o}	ΔH^{o}	ΔG^{o}
TS-HPi$_1$-HPa$_1$	21.38	21.38	21.30	1.63	1.63	1.34
TS-HPi$_2$-HPa$_2$	8.13	8.13	10.84	2.03	2.03	1.90
TS-HPz-HPa$_3$	50.24	50.24	50.06	1.37	1.37	0.65
MP2/AUG-cc-pVDZ						
TS-HPi$_1$-HPa$_1$	28.89	28.89	29.09	1.71	1.71	0.84
TS-HPi$_2$-HPa$_2$	9.55	9.55	12.16	2.41	2.41	1.49
TS-HPz-HPa$_3$	50.52	50.52	50.43	1.68	1.68	0.58

proton affinity difference between donor and acceptor[18]. The effect of proton affinity difference between donor and acceptor on the proton transfer.

All the reactions were found to be the endothermic processes. The proton-transfer processes *via* TS-HPi$_1$-HPa$_1$, TS-HPi$_2$-HPa$_2$ and TS-HPz-HPa$_3$ occur between atoms O1, N2 and N1, O1, O2 and N1, N2, respectively. Based on the proton-transfer transition-states, the interconversions *via* transition-state structures of the nitrosamine isomers-H_2O_2 are able to be classified into two types namely (i) monoproton transfer, MPT and (ii) di-proton transfer, which imaginary frequencies of TS-HPi$_1$-HPa$_1$, TS-HPi$_2$-HPa$_2$, TS-HPz-HPa$_3$ corresponding transition-states are, respectively, 1838.4i, 1612.88i, 2033.61i (Table-3).

TABLE-3
TYPES OF TRANSITION-STATE STRUCTURES COMPUTED AT THE MP2/AUG-cc-pVDZ LEVEL OF THEORY

Types of transition-state (TS)			
Mono-proton transfer TS^{a,b}		Di-proton transfer TS^{a,c}	
TS-HPi$_1$-HPa$_1$	1838.4i	TS - HPi2- HPa2	1612.88i
TS-HPz-HPa$_3$	2033.6i	–	–

a: Transition-state, imaginary frequency in cm^{-1}. b: Intramolecular proton transfer. c: Intermolecular proton transfer.

Frontier MO energies and chemical indices: The energies of the lowest unoccupied molecular orbital (LUMO), E_{LUMO} and the highest occupied molecular orbital (HOMO), E_{HOMO} at the B3LYP/AUG-cc-pVDZ and MP2/AUG-cc-pVDZ levels and frontier molecular orbital energy gap, $\Delta E_{HOMO-LUMO}$, chemical hardness, chemical potential and Mulliken electronegativity of all isomers of the nitrosamine isomers-H_2O_2 computed at the B3LYP/AUG-cc-pVDZ and MP2/AUG-cc-pVDZ levels are shown in Table-4.

The chemical hardness, electronic chemical potential and electronegativity are important tools to study the relative stabilities of different isomers of a molecular system. The chemical reactivities and electronegativity of all the isomers of the nitrosamine isomers -H_2O_2 based on their frontier molecular energy gaps are in decreasing order: HPa_3 > HPa_1 > HPa_2 > HPz > HPi_2 > HPi_1.

TABLE-4

E_{LUMO} AND E_{HOMO} ENERGIES AND FRONTIER MOLECULAR ORBITAL ENERGY GAP, $\Delta E_{HOMO\text{–}LUMO}$ OF ALL ISOMERS OF THE NITROSAMINE DIMERS COMPUTED AT THE B3LYP/AUG-cc-pVDZ AND MP2/AUG-cc-pVDZ LEVELS OF THEORY

Complex	E_{HOMO}^{a}	E_{LUMO}^{a}	$\Delta E_{HOMO\text{-}LUMO}$^{a}	$\eta^{a,b}$	$\mu^{a,c}$	$\chi^{a,d}$	ρ^e
B3LYP/AUG-cc-pVDZ							
HPi_1	-7.94	-2.00	5.94	2.97	-4.97	4.97	2.20
HPi_2	-7.90	-2.03	5.87	2.94	-4.97	4.97	1.46
HPz	-7.97	-2.20	5.77	2.88	-5.08	5.08	2.61
HPa_1	-7.22	-2.00	5.23	2.61	-4.61	4.61	3.60
HPa_2	-7.18	-1.92	5.26	2.63	-4.55	4.55	2.23
HPa_3	-7.28	-2.06	5.22	2.61	-4.67	4.67	3.75
TS-HPi_1-HPa_1	-8.22	-2.27	5.95	2.97	-5.24	5.24	2.66
TS-HPi_2-HPa_2	-7.50	-2.24	5.26	2.63	-4.87	4.87	2.52
TS-HPz-HPa_3	-7.91	-0.28	7.63	3.82	-4.09	4.09	3.05
MP2/AUG-cc-pVDZ							
HPi_1	-12.63	1.02	13.64	6.82	-5.81	5.81	2.21
HPi_2	-12.62	0.94	13.56	6.78	-5.84	5.84	1.58
HPz	-11.58	1.04	12.63	6.31	-5.27	5.27	2.87
HPa_1	-11.98	0.83	12.82	6.41	-5.57	5.57	3.57
HPa_2	-11.94	0.88	12.82	6.41	-5.53	5.53	2.36
HPa_3	-12.04	0.76	12.79	6.40	-5.64	5.64	3.72
TS-HPi_1-HPa_1	-11.96	0.91	12.88	6.44	-5.53	5.53	2.82
TS-HPi_2-HPa_2	-11.97	0.90	12.88	6.44	-5.53	5.53	2.64
TS-HPz-HPa_3	-12.68	0.21	12.89	6.45	-6.23	6.23	3.30

a: In eV. b: chemical hardness, $\eta = \Delta E_{HOMO}$–LUMO/2. c: electronic chemical potential, $\mu = (E_{HOMO} + E_{LUMO})/2$. d: The Mulliken electronegativity, $\chi = \Delta(E_{HOMO} + E_{LUMO})/2$. e: In debye.

As the acceptor strength is the inverse of the E_{LUMO} energy, the acceptor strength of the nitrosamine isomers at the B3LYP/AUG-cc-pVDZ level of theory is in the decreasing order: HPz > HPa_3 > HPi_2 > HPi_1 > HPa_1 > HPa_2. On the other hand, as the donor strength relatives to the E_{HOMO} energy, the donor strength is in the decreasing order: HPz > HPi_1 > HPi_2 > HPa_3 > HPa_1 > HPa_2. The relative reactivity based on their frontier molecular orbital energy gap is in the decreasing order: HPa_3 > HPa_1 > HPa_2 > HPz > HPi_2 > HPi_1.

The nitrosamine isomers-H_2O_2 computed at the B3LYP/AUG-cc-pVDZ and MP2/AUG-cc-pVDZ levels are shown in Table-4 that the Hi2 complex is the least polar molecule.

Conclusion

Ab initio molecular orbital and DFT calculations have been carried out for tautomerization, 2 imino tautomers and 1 zwitter ionic to amino (most stable species of the nitrosamine isomers) in reaction of HNNOH-H_2O_2. The structures and transition states were optimized using B3LYP and MP2 methods with 6-311++G(2d,2p), AUG-cc-pVDZ basis sets.

The amines complexes are the more stable than imino and zwitter ionic complexes. The activation energies of the reactions are in the increasing order: $HPi_2 \rightarrow HPa_2 <$ $HPi_1 \rightarrow HPa_1 < HPz \rightarrow HPa_3$. Activation energy di-proton transfer less than monoproton transfer, in the middle of monoproton transfer H from O to N energy less than H from N1 to N2. This may be explained within the principle of the minimal proton affinity difference between donor and acceptor[18]. The effect of proton affinity difference between donor and acceptor on the proton transfer. The chemical reactivities and electronegativity of all isomers of the nitrosamine isomers-H_2O_2 based on their frontier molecular energy gaps are in decreasing order: $HPa_3 > HPa_1$ $> HPa_2 > HPz > HPi_2 > HPi_1$.

The relative reactivity based on their frontier molecular orbital energy gap is in the decreasing order: $HPa_3 > HPa_1 > HPa_2 > HPz > HPi_2 > HPi_1$. The Hi2 complex is the least polar molecule.

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