Nitrosative Guanine Deamination: A Quantum Mechanical Study of the Carbodiimide - Cyanoamine Tautomerization in the Pyrimidine Ring-Opened Intermediate.

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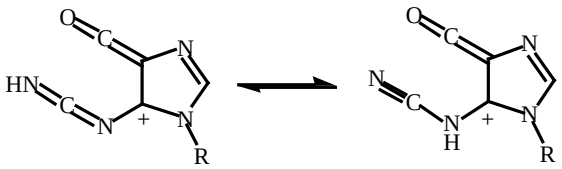
Nitric oxide[1] and nitrous acid[2] cause deamination of DNA bases and interstrand crosslinking which represent an important mechanism of genomic alteration. Chronic inflammation is associated with the increased production of nitric oxide and there seems to be a direct relationship between chronic inflammation and different types of cancers in human body.[3] Because of the considerable dietary[4] and environmental[5] exposure of humans to the oxides of nitrogen, the deamination chemistry of DNA has attracted considerable attention in recent years. We have been studying the mechanisms of these DNA base deaminations by quantum mechanical methods. The deamination of guanine leads to the formation of xanthine and oxanosine.[6] This process is believed to involve the formation of guaninediazonium ion, although the diazonium ions of DNA bases have never been isolated or observed experimentally. Our recent *ab initio* studies of DNA base deaminations have revealed that the guaninediazonium ion is kinetically and thermodynamically unstable with respect to dediazoniation leading to the formation of pyrimidine ring opened intermediate **1**.[7] This key intermediate is highly reactive and has a variety of options to react. One of these possibilities is the tautomerization to the cyano-amine **2**. The parent cyanoamine is known to be more stable than the parent carbodiimide. We have studied this tautomerization at RHF/6-31G* and B3LYP/6-31G* levels of theory for models with different R-groups (e.g. H, CH_3, CH_2OCH_3). Unexpectedly, the carbodiimide tautomer was found to be more stable than the cyano-amine in all of the model cations studied. The thermodynamics of this tautomerization process for different rotational isomers of the model cations has been determined and the results will be presented.



1 **2**

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1 (a) Ainscough, E. W.; Bridie, A. M. *J. Chem. Edu.* **1995**, *72*, 686. (b) Taylor, D. K.; Bytheway, I.; Barton, D, H. R.; Bayse, C. A.; Hall, M. B. *J. Org. Chem.* **1995**, *60*, 435.
2 Zimmerman, F. K. *Mutation Res.* **1977**, *39*, 127.
3 Ohshima, H.; Bartsch, H. *Mutat. Res.* **1994**, *305*, 253.
4 Wolff, E. A.; Wasserman, A. E. *Science* **1972**, *177*, 15.
5 O'Sullivan, D. A. *Chem. Eng. News* **1970**, *48*, 38.
6 (a) Schuster, V. H.; Wilhelm, R. C. *Biochem. Biophys. Acta* **1963**, *68*, 554. (b) Suzuki, T.; Yamaoka, R.; Nishi, M.; Ide, H.; Makino, K. *J. Am. Chem. Soc.* **1996**, *118*, 2515.
7 (a) Glaser, R.; Son, M.-S. *J. Am. Chem. Soc.* **1996**, *118*, 10942. (b) Glaser, R.; Rayat, S.; Lewis, M.; Son, M. -S.; Meyer, S. *J. Am. Chem. Soc.* **1999**, *121*, 6108.