Substituent effect on the reaction mechanism of proton transfer in formamide

2 **AUTHORS**, INCLUDING:

Mehdi Yoosefian

Kerman Graduate University of Technology

42 PUBLICATIONS **285** CITATIONS

Substituent Effect on the Reaction Mechanism of Proton Transfer in Formamide

Heidar Raissi* and Mehdi Yoosefian*

MP2 and B3LYP methods at 6-311++G** basis set have been used to explore proton transfer in keto-enol forms of formamide and to investigate the effect of substituent, i.e., H, F, Cl, OH, SH, and NH_2 on their transition states. Additionally, the vibrational frequencies of aforementioned compounds are calculated at the same levels of theory. It is proposed that the barrier heights values in kJ/mol for F, Cl, OH, and SH substituents are significantly greater than that of the bare tautomerization reaction, implying the importance of the substituents effect on the intramolecular proton transfer. © 2011 Wiley Periodicals, Inc.

DOI: 10.1002/qua.23235

Introduction

Proton transfer (PT) reactions via intermolecular hydrogen bonding (HB) have been analyzed in detail.[1,2] The double PT for the centrosymmetric dimer of formic acid has also been examined both theoretically and experimentally,[3] and that carboxylic acids possessing two equivalent hydrogen bonds were also probed.[4] An asymmetrical double potential well exists, when the product of the PT becomes identical and geometrically the same as reactants.[5] Grabowski et al.[6] studied centrosymmetric dimers of formamide (FO) and related species in which two equivalents N—H···O HB occur, proving the existence of a nonsymmetric potential energy well. Here, the products of the double PT process which are the tautomeric forms of the reactants contain O—H···N HB.

Nonetheless, there is a particular type of PT in which a substituent group can manipulate the reaction by steric or electron effects. On this basis, we have examined the effect of substituents on formamide (FO) → formamidic (FOA) conversion. We believe that the NH_2CHO (FO) → HN=CHOH (FOA) tautomerization could be used as a model to mimic PT in nucleic acids bases of guanine and uracil. Recently, the barrier energy value for the bare FO → FOA isomerization in the gas phase was derived by Wang et al.[7] as 204.6 kJ/mol. On the other hand, Bell et al.[8] performed the *ab initio* dynamics calculations based on a canonical variational transition state theory at 6-31g (d,p) basis set level using different density functional theory (DFT) methods. They tested the accuracy of different DFT methods, found the rate constant for the forward and the reverse reaction. They also evaluated the effects of different substituents on FO regarding the geometrical parameters, the activation energy reduction, and the reaction paths for FO → FOA isomerization. There have been numerous investigations on different kinds of PT reactions.[5] To the best of our knowledge, there are a few studies on the effects of substituents on the PT reactions.

Computational Methods

DFT methods are known to give reliable geometric and thermodynamic properties for hydrogen bonded clusters.[9,10] However, the superiority of DFT methods has been doubted by several recent studies.[10–12] Some commonly used gradient-corrected functionals give barriers too low values compared with post-HF and experimental methods.[10–12] The geometries of the reactants, transition states and products for the tautomerization are optimized using the B3LYP/6-311++G** level of theory.[13] For comparison, the MP2 calculations[14] are performed at chosen basis set. The vibrational frequencies were obtained at the same levels for characterization of stationary points and zero point energy (ZPE) corrections. Intrinsic reactions coordinate (IRC) paths calculations,[15,16] which connect pairs of tautomers with the corresponding transition state, were carried out. All calculations are conducted using the GAUSSIAN 03 program package.[17]

Results and Discussion

Geometries

Figure 1 compares the geometries of the reactants, transition states and products involved in the Cl, F, OH, SH, and NH_2 assisted PT reactions alongside geometries of the unsubstituted reaction. The calculated geometric parameters indicate that the MP2 and B3LYP methods at 6-311++G** basis set levels are in good agreement with each other. For example, in FO molecule, C—N, C=O bond lengths and NCO bond angle are 1.364, 1.217 Å and 124.8○ at MP2 level, respectively, which are in good consensus with B3LYP results (see Fig. 1). For simplicity, we have only listed the geometric parameters at B3LYP/6-311++G** level. The tautomerization causes significant change in bond length, in the range of about 0.09 to 0.14 Å, except for CH and NH which is about 0.01 Å. For the normal mechanism of FO → TS → FOA, the transition state (TS) assumes a coplanar four-membered ring. Our findings suggest that first NCO bond angle undergoes a compression, and then

H. Raissi, M. Yoosefian
Chemistry Department, Birjand University, Birjand, Iran
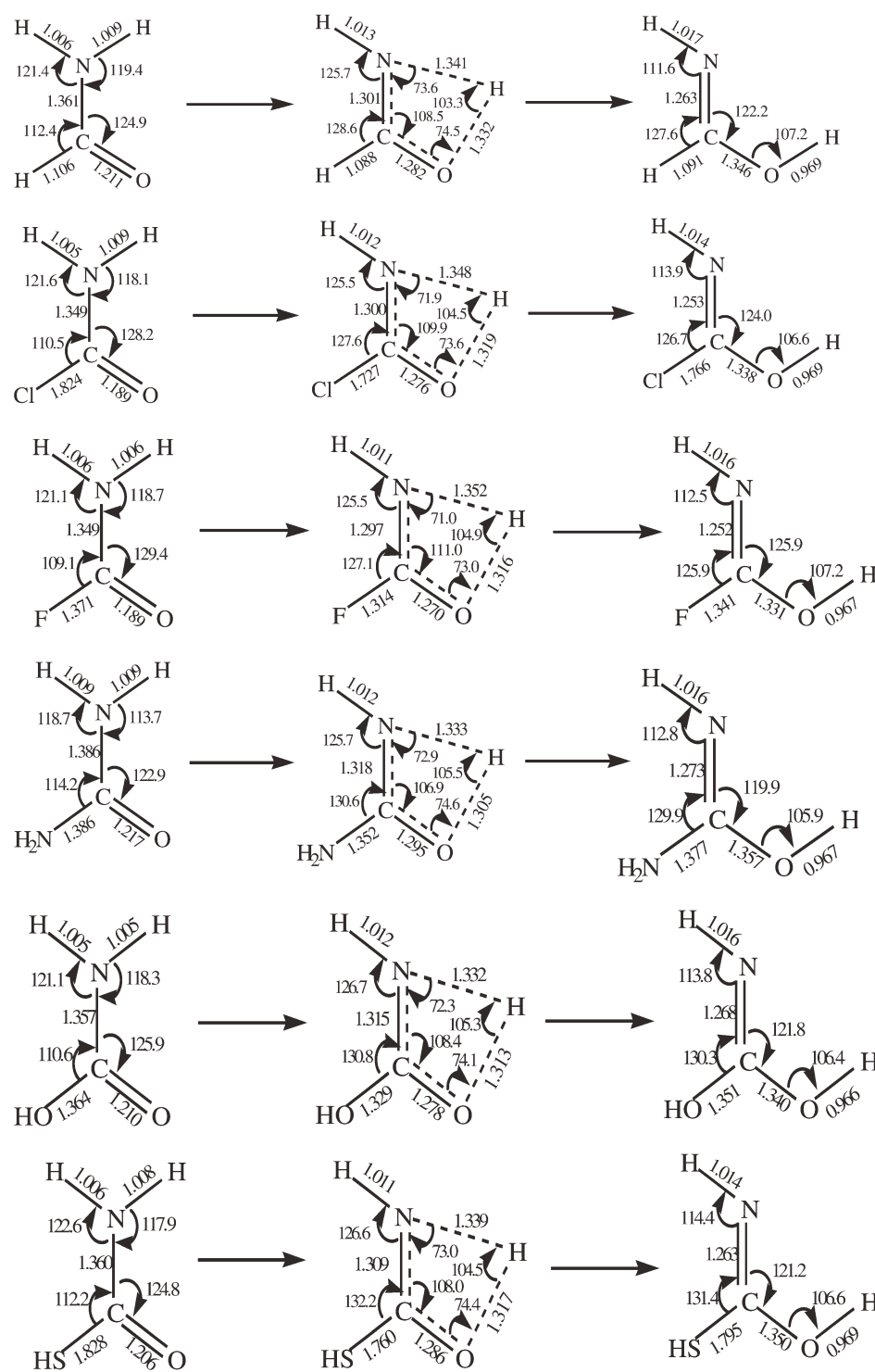*E-mail: hraissy@yahoo.com or myoosefian@yahoo.com*

Figure 1. The optimized structures of the reactants, transition states and products of the normal and substituted tautomerization. The bond lengths in Å and bond angles in degree.

state. Also as it is obvious from Figure 1, in the reaction process, the CO bond length gradually increases, while CN bond length simultaneously decreases. In general, the structural changes reflect the formation of a new O—H bond and the rupture of an old N—H bond. This means H atom has been transferred from N to O atom.

Now for substitution-assisted tautomerization of FO-R → TS-R → FOA-R, when R = F, we have the most stable geometry. TS-R is the transition state for the substituted tautomerization, which shows concerted hydrogen transfer processes along the ringy skeleton. The breaking of the N—H bond is accompanied by the transfer of H atom from N to O, forming FOA-R as the product.

As shown in Figure 1, the trend of changes in the geometrical parameters for fluorine-assisted proton transfer (FAPT) reactions is similar to that of the bare FO tautomerization. However, in comparison with the normal tautomerization, the discrepancy in NCO angle in FAPT is 18.4° (for FO → FOA, it is 16.4°). At the same time, the N—H bond lengthening increases by about 1.49% which is another factor contributing to the higher energy barrier of reaction FO(-F) → TS(-F) → FOA(-F).

For FO-R and FOA-R in which R = NH₂, we have the most unstable geometry. In comparison with the normal tautomerization, the discrepancy in NCO angle in FO-NH₂ is 16°. Again, the N—H bond length decreases by about 0.8% which is another factor contributing to the lower

the NH bond starts to lengthen. The reason is that after tautomerization occurrence, the FO undertakes larger structural change which is energetically disfavored. Then, the NCO bond angle is compressed from an equilibrium value of 124.9° to 108.5° at B3LYP/6-311++G** level, i.e., 13.1% decrease in bond angle. The NH bond is stretched from 1.009 to 1.341 Å, i.e., an increase of 32.9% in bond length to reach the transition

energy barrier of FO(-NH₂) → TS(-NH₂) → FOA(-NH₂) process. We found out that in TS, the framework of FO monomer changes more than the NH₂-TS, OH-TS, and SH-TS. Moreover, due to vital role of the intramolecular HB in the PT, we studied the effect of substituents on geometrical parameters. The result of our calculations shown in Figure 1 indicates, in TS of the chlorinated and fluorinated compounds, both the N···H

Table 1. The activation energies, changes of enthalpy and free energy and binding energies (kJ/mol) for the FO → FOA tautomerization.

	B3LYP				MP2			
Substitution	E_a	ΔH	ΔG	Binding	E_a	ΔH	ΔG	Binding
H	202.986 (189.979)	55.225	57.262	54.349 (56.359)	197.749 (184.701)	51.368	51.129	47.826 (51.182)
Cl	232.287 (218.696)	80.172	82.514	80.785 (81.398)	222.242 (208.326)	74.310	74.126	72.161 (74.113)
F	241.294 (228.251)	84.331	86.865	84.676 (85.599)	238.635 (225.328)	83.588	83.189	81.478 (83.278)
NH$_2$	200.607 (184.848)	67.575	67.801	68.546 (67.730)	202.232 (187.419)	65.112	65.086	66.547 (65.110)
OH	242.128 (227.778)	96.243	100.055	96.847 (97.708)	241.296 (226.116)	92.047	91.874	93.632 (92.011)
SH	215.914 (203.686)	76.801	76.735	74.350 (76.657)	209.281 (194.844)	66.635	66.622	67.797 (66.798)

The values in parenthesis are including zero point vibrational energy (ZPE) corrections.

distance and the $\theta_{(NHO)}$ angle are larger, whereas O···H and N···O distances are smaller, in comparing to the corresponding values of the unsubstituted compounds. There is a clear relationship between the aforementioned parameters and the strength of the HB. In the TS form, the smaller the N···H and N····O distances, the larger the O···H bond length and the $\theta_{(NHO)}$ angle leading to the stronger the intramolecular HB.[18–21] In addition, the substituent groups in FO weaken the intramolecular HB.

Energetics

Owing to small size of all substituents, one can reasonably assume that the influence of each substituent on the chemical properties of FO will be mainly due to their electronic effects, not to steric effects. The activation energy values, enthalpy and free energy changes for the FO → FOA tautomerization (kJ/mol) are presented in Table 1. The values in parenthesis are for zero point vibrational energy (ZPE) corrections. Here, the PT is characterized by high-activation energy values. Our calculated E_a values and the zero point vibrational energies are in good agreement with that of the previous study by Wang et al.[7] at CISD (Configuration Interaction Singly and Doubly excited) level. As shown in Figure 2, for substituted compounds the barrier height of the tautomerization are 42 kJ/mol more with respect to unsubstituted ones, except for FO (—NH$_2$), suggesting that the PT occurs with more difficulty for F, Cl, OH, and SH substituted compounds. Regarding NH$_2$ substituted compound, the energy barrier decreases by amount of about 3 kJ/mol indicating that NH$_2$ enhances the accelerate the PT. The standard enthalpy and free energy changes are also listed in Table 1. The positive standard enthalpy change demonstrates that the FO → FOA process is endothermic ($\Delta G° = 57.26$ kJ/

mol at B3LYP/6-311++G** level). On large basis set, the calculated $\Delta H°$ was about 55.22 kJ/mol at 298.15 K. The equilibrium constant is also calculated using the standard formula $K = \exp(-\Delta G°/RT)$ ($K = 9.29 \times 10^{-11}$ for the formation of FOA). On F, Cl, OH, SH, and NH$_2$ substitutions, the calculated $\Delta G°$ were 86.86, 82.51, 100.06, 76.74, and 67.80 kJ/mol, respectively. The calculated $\Delta G°$ and $\Delta H°$ values for FO → FOA are higher than those values for FO-R → FOA-R process. The $\Delta G°$ and $\Delta H°$ discrepancy between the two processes is responsible for change in activation energies. For any highly endothermic reaction, the transition state is located closer to the product. So, the energy barrier diminishes significantly. The large positive $\Delta G°$ values indicate that the PT process is quite disfavored, i.e., it is a nonspontaneous. Therefore, for the formamide → FOA acid isomerization, all of the six reaction processes are endothermic. Regarding the respective substituted compounds, they cannot possess higher positive standard free energy, although they have elevated activation energy. Hence, the environmental condition changes such as, increase in concentration of the unfavored substituents will impose its effect on reaction mechanism enhancing the process spontaneity, whereas for the OH-FO tautomerization, its $\Delta G°$ value has been nearly doubled.
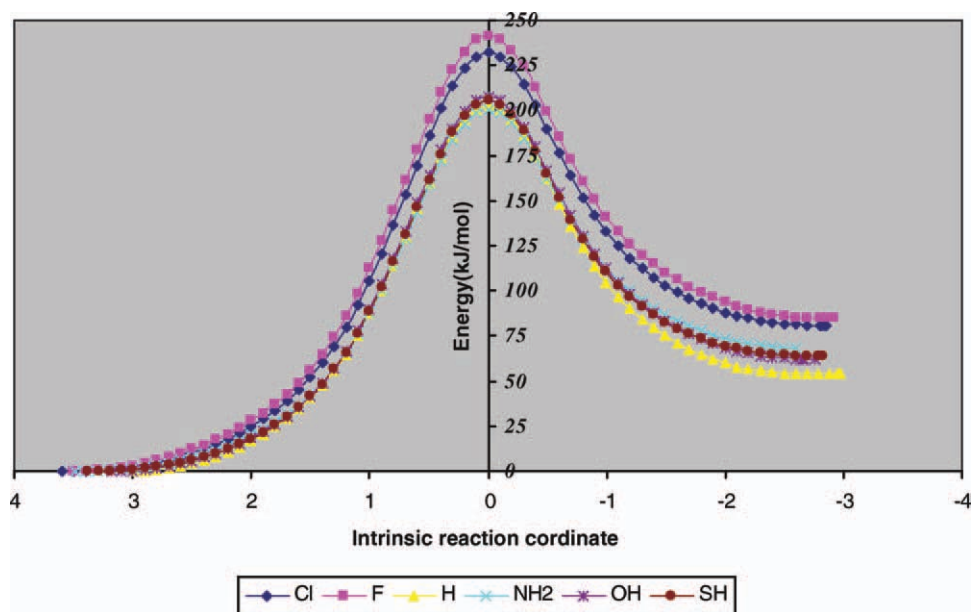

Figure 2. Comparison of energies related to the intrinsic reaction coordinate (IRC) path in the formamid and its substitutions. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Such large positive $\Delta G°$ value implies that this reaction in gas phase is both thermodynamically and kinetically unfavored, meaning that the reverse reaction is both thermodynamically and kinetically favored.

Conclusions

The PT in intact FO, its substituents, and their effects on the transition state structures using both second-order Moller–Plesset Perturbation (MP2) and B3LYP hybrid density functional methods with a large basis set of 6-311++G** have been investigated. ΔH, ΔG, binding and activation energy values for FO → FOA process were calculated. The E_a values for this reaction at B3LYP and MP2 levels of theory were 202.9 and 189.9 kJ/mol, respectively. Using the same levels of theory, the activation energy was increased to 241.3 and 228.3 kJ/mol (for F substituent), and 242.1 and 227.8 kJ/mol (for OH substituent), whereas it was diminished to 200.6 and 184.8 kJ/mol for NH_2 substituent. Furthermore, our findings showed that for FO → FOA process, the calculated barrier heights values for all of substituted compounds (except NH_2) were significantly higher than of the bare tautomerization reaction, implying the importance of the substituents effect on the intramolecular PT. In this work, we have demonstrated that the formation of FOA acid is dramatically endoergic, especially for the OH-FO tautomerization, which is in consistent with the fact that FOA acid is too thermodynamically unfavored with respect to FO, inferring that the reverse reaction, i.e., FOA → FO is thermodynamically and kinetically favored.

Keywords: proton transfer · formamide · substitution effect · IRC · DFT

[1] M. Coll, J. Frau, B. Vilanova, A. Llinas, J. Donoso, *Int. J. Chem.* **1999**, *2,* 18.

[2] C. L. Perrin, J. B. Nielson, *Annu. Rev. Phys. Chem.* **1997**, *48,* 511.

[3] Y. J. Kim, *Am. Chem. Soc.* **1996**, *118,* 1522.

[4] T. Loerting, K. R. Liedl, *J. Am. Chem. Soc.* **1998**, *120,* 12595.

[5] J. T. Hynes, J. P. Kliman, H. H. Limbach, R. L. Schowen, Hydrogen-Transfer Reactions; V. Wiley Verlag Gmbh & Co. KGaA: Weinheim, **2007**.

[6] S. J. Grabowski, W. A. Sokalski, LJ. eszczynski, *J. Phys. Chem. A* **2006**, *110,* 4772.

[7] X. C. Wang, J. Nichols, M. Feyereisen, *J. Phys. Chem.* **1991**, *95,* 10419.

[8] R. L. Bell, D. L. Taveras, T. N. Truong, J. Simons, *Int. J. Quant. Chem.* **1997**, *63,* 862.

[9] D. Q. Wei, D. R. Salahub, J. Gao, Mark Thompson, Eds. Combined Quantum Mechanical and Molecular Mechanical Methods; Wiley: New York, **1998**

[10] D. Q. Wei, E. I. Proynov, A. Milet, D. R. Salahub, *J. Phys. Chem.* **2000**, *104,* 2384.

[11] Y. J. Kim, *Am. Chem. Soc.* **1996**, *118,* 1522.

[12] S. Sirois, E. I. Proynov, D. T. Nguyen, D. R. Salahub, *J. Chem. Phys.* **1997**, *107,* 6770.

[13] A. D. Becke, *J. Chem. Phys.* **1993**, *97,* 5648.

[14] C. Moller, S. M. Plesset, *Phys. Rev.* **1934**, *46,* 618.

[15] C. Gonzalez, H. B. Schlegel, *J. Chem. Phys.* **1989**, *90,* 2154.

[16] C. Gonzalez, H. B. Schlegel, *J. Chem. Phys.* **1989**, *94,* 5523.

[17] M. J. Frisch, et al. (**2003**) Gaussian Inc, Pittsburgh, PA.

[18] M. Fazli, A. F. Jalbout, H. Raissi, M. Yoosefian, *J. Theor. Comput. Chem. (JTCC)* **2009**, *8,* 713.

[19] E. S. Nadim, M. Yoosefian, H. Raissi, *J. Sulfur. Chem.* **2010**, *31,* 275.

[20] H. Raissi, A. F. Jalbout, M. Yoosefian, M. Fazli, A. Nowroozi, M. Shahini, Leon, De A. *Int. J. Quantum Chem.* **2010**, *110,* 821.

[21] E. S. Nadim, H. Raissi, M. Yoosefian, F. Farzad, A. Nowroozi, *J. Mol. Struct.: THEOCHEM* **2010**, *960,* 1.