Original Article

Computational study of the proton transfer of phenyl urea

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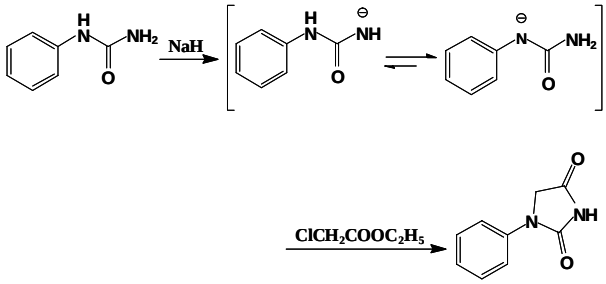
ABSTRACT: The proton transfer between two nitrogen atoms (N1 and N3) in a molecule of phenyl urea is an important process in the synthesis of 1-phenylimidazolidine-2,4-dione. Three pathways of the proton transfer have been investigated using Density Functional Theory (DFT). With negative N1 phenyl urea, the transformed double bond of N1-C2 connects N1, C2, and N3 into a benzene conjugate system, making the structure more stable than negative N3 phenyl urea. Intermolecular proton transfer was found to be the primary manner of protein transfer at 300 K. Both negative N1 and negative N3 exist and the former is primal. The proton transfer is very fast, and the diluted solution may slow down the rate but produce much more negative N1 as well.

Keywords: Proton transfer, Synthesis, DFT, B3LYP, Phenyl urea

1. Introduction

1-Phenylimidazolidine-2,4-dione is an important immediate used in the medical and chemical industries (*1*). It can be synthesized through phenyl urea and ethyl chloroacetate with the deprotonation of NaH. The proton transfer of phenyl urea is an important process in this synthesis. As this proton transfer can form two kinds of negative N phenyl urea as depicted in Scheme 1, there are always several co-products when this transfer actually occurs.

Based on actual performance, a hydrogen can be released during the reaction after the formation of the negative phenyl urea. There are three proton transfers involving negative phenyl urea: proton translocation between the hydrogen and phenyl urea anion, intramolecular proton translocation, and intermolecular proton translocation. This study sought to investigate the theoretical mechanisms of these proton transfers using Density Functional Theory and to provide theoretical suggestions for more effective synthesis.



Scheme 1. Synthesis of 1-phenylimidazolidine-2,4-dione.

2. Materials and Methods

Computations were carried out using the Gaussian 98 program (*2*). The initial structures of reagents, products, and transition states were optimized using density functional theory (DFT) at the B3LYP/6-31G* level (*3-5*). To confirm the transition states, pathways were identified by intrinsic reaction coordinate (IRC) calculation (*6*). The frequencies of these optimized structures were also calculated to obtain the enthalpy energy and the Gibbs' free energies (G). All data and structures mentioned below are related to the same level.

3. Results and Discussion

Three possible proton transfers relating to the negative nitrogen ion are shown in Figures 1-3. The relative atomic charge distributions of all states are calculated and given in Table 1. Table 2 lists the parameters for the three reaction pathways. Figure 4 shows the relative energy changes.

Following NaH deprotonation, one H_2 molecule must be produced. The proton transfer between H_2 and a phenyl urea anion is shown in Figure 1. The computed N1-C2 distances are 1.46, 1.41, and 1.35 Å in state A, TS1, and state B, respectively, and the bond lengths of C2-N3 are 1.32, 1.36, and 1.43 Å in state A,

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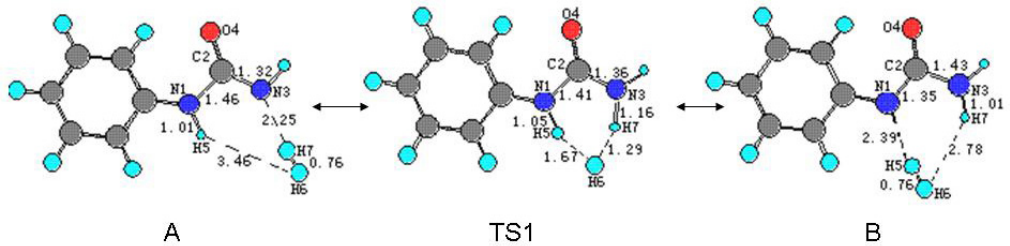

Figure 1. Proton transfer between H_2 and a phenyl urea anion and the B3LYP/6-31G* optimized structures of A, TS1, and B. Distances in Å.

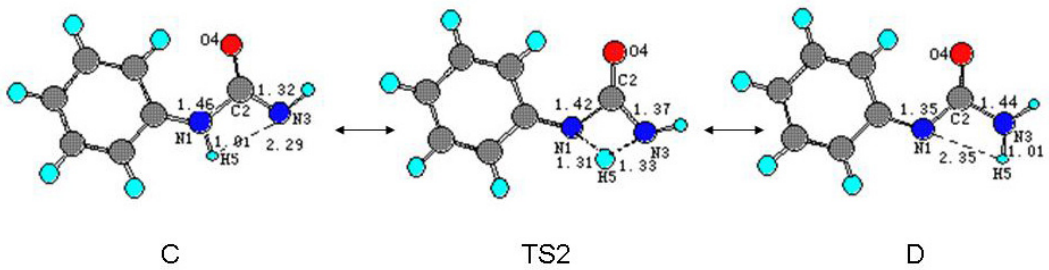

Figure 2. Intramolecular proton transfer and the B3LYP/6-31G* optimized structures of C, TS2, and D. Distances are in Å.

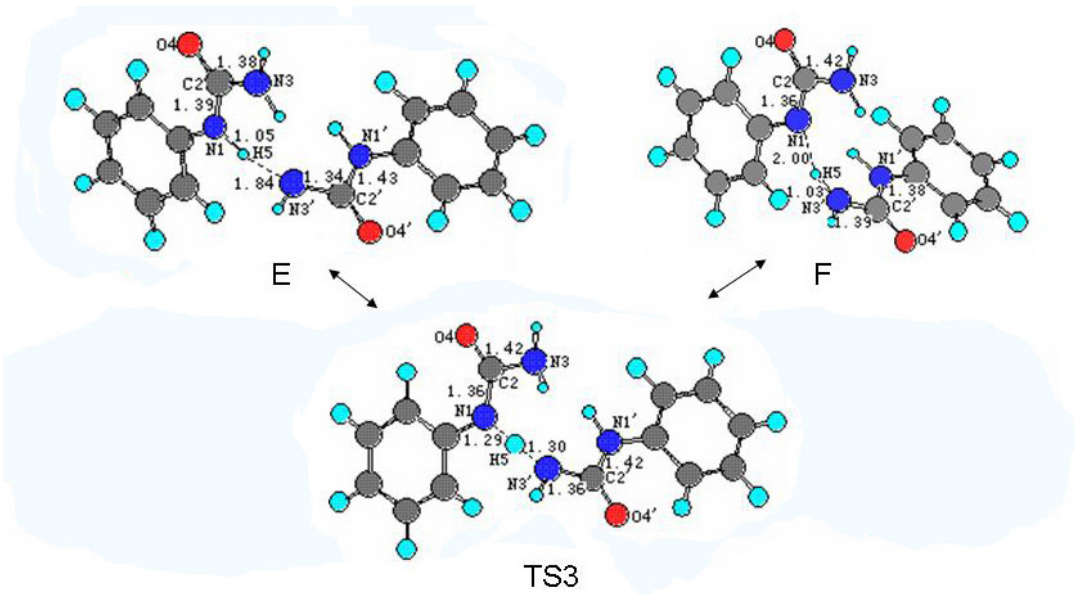

Figure 3. Intermolecular proton transfer and the B3LYP/6-31G* optimized structures of E, TS3, and F. Distances are in Å.

Table 1. The relative atomic charge distributions of all states calculated at B3LYP/6-31G*

	A	TS1	B	C	TS2	D	E	TS3	F
N1	-0.774	-0.508	-0.535	-0.723	-0.565	-0.706	-0.300	-1.007	-0.498
C2	0.876	0.715	0.694	0.843	0.722	0.748	0.723	0.957	0.767
N3	-0.969	-0.798	-0.861	-1.066	-0.840	-0.848	-0.775	-0.935	-0.888
O4	-0.697	-0.597	-0.562	-0.690	-0.614	-0.605	-0.595	-0.645	-0.642
N1'							-0.687	-0.649	-0.272
C2'							0.823	0.835	0.611
N3'							-0.720	-0.949	-0.641
O4'							-0.681	-0.634	-0.579

Charges in e.

Table 2. Energy changes and reaction equilibrium constants of three proton transfer pathways

Pathway	$\Delta H_{reagent\text{-}product}$ (kJ/mol)	$\Delta G_{reagent\text{-}product}$ (kJ/mol)	$\Delta G_{forward}$ (kJ/mol)	$K_{forward}$ [a] (1/S)	$\Delta G_{reverse}$ (kJ/mol)	$K_{reverse}$ [a] (1/S)
A-B	-18.84	-15.94	95.60	1.11E - 04	79.66	6.86E - 02
C-D	-23.41	-22.34	140.61	1.44E - 12	118.27	1.18E - 08
E-F	-3.57	-1.75	13.79	2.38E + 10	12.04	4.83E + 10

[a] K = 6.2125*E[12 - ΔG*1000/(8.314*298.15)].

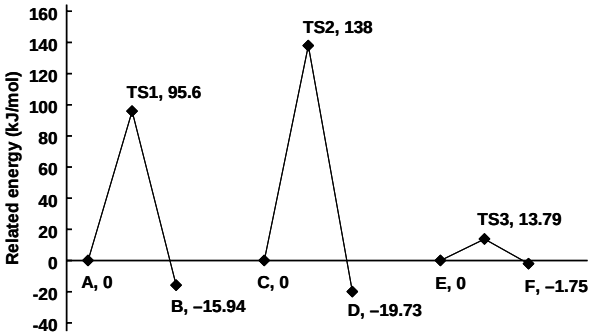

Figure 4. The relative energy changes of all pathways according to the optimized structures calculated at B3LYP/6-31G*.

TS1, and state B, respectively. Since the bond of N1-C2 is converted from a single bond to a double bond, the conjugate effect between urea and the benzene ring is enhanced. As the result, the charge values of N1, C2, and N3 decrease while the charge value for the benzene ring increases (Table 1). The charge distribution of the whole molecule becomes more uniform. Inversely, the double bond of C2-N3 becomes a single bond. In transition state 1, a planar hexatomic ring consisting of N1, C2, N3, H5, H6, and H7 connects to the conjugate area of the benzene ring.

With H5 transferred from N1 to N3, as displayed in Figure 2, intramolecular proton transfer is complete. Except for hydrogen, state C is similar to state A in terms of structure and charge distribution, while D is similar to B. In transition state 2 (TS2), N1, C2, N3, and H5 make up of a planar four-membered ring. For the bond of N1-C2 to become a double bond, the four-membered ring is conjugated with the benzene ring.

Intermolecular proton transfer is displayed in Figure 3 with the proton H5 shifting between N1 and N3'. The structures of negative molecules in states E and F are similar to those in states C and D, respectively. One can consider state C to transform into state D with the help of a phenyl urea molecule, which serves as an H-bond donator. In transition state 3 (TS3), two molecules are in different planes. N1 and N3' share H5 in a straight line. The distances of N1-H5, and N3'-H5 are 1.29 and 1.30 Å, respectively.

As shown in Table 1, the intermolecular H-bond can change the electric charge distribution. In state E, the related atoms of the negative molecule (N1', C2', N3', and O4') have lower charges than those in states A and C. This is similar to state F, where the related atomic charges of the negative molecule (N1, C2, N3, and O4) are lower than those in states B and D. Thus, the conjugate effect is stronger and the charge distribution becomes more uniform. There is a substantial correlative change between the charge and bond. An interesting finding with regard to TS3 is that all of the atomic charges have obviously risen in comparison to TS1 and TS2. This suggests that the dipolarity of the whole system is enhanced and that conjugation weakens in TS3.

According to Table 2, all proton transfers are exothermic reactions. The pathway E to F has a lower energy barrier (Figure 4) of 13.79 kJ/mol and is the main proton transfer at 300 K. The equilibrium proportion of structures E and F is 1:2. Thus, both the negative N1 and negative N3 structures can exist together. Theoretically, there are two negative phenyl urea formed, N1 (as expected) and N3. The rate of the transfer between N1 and N3 is very fast. As indicated by the current study, the concentrated solution facilitates formation of an intermolecular complex to allow proton transfer between molecules and it also allows the formation of negative N3 phenyl urea. A diluted solution was chosen to keep the molecule simple. Although this slows down the reaction rate, a much more stable negative N1 phenyl urea is produced in the solution.

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