

A DFT study on the effect of position of functional group on the kinetics and mechanism of 1,3-dipolar cycloaddition of benzonitrile oxide and dihydrofuran

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Abstract: A theoretical study on the effect of position of functional groups on the kinetics and mechanism of Cycloaddition of benzonitrile oxide and Dihydrofuran was performed using DFT methods at the B3LYP level of the theory with 6-31G (d, p) basis set at 298.15K. Equilibrium molecular geometries and harmonic vibrational frequencies of the reactants, transition state and product were calculated. Natural bond orbital analysis was used to analysis charge changes on the atoms during the reaction. Thermodynamic and kinetic parameters of the reaction were investigated. Solvent effect on the kinetic and thermodynamic parameters of the reaction was investigated. Non polar solvent enhances the rate. But the reaction in polar solvent was slower than gas phase. These calculations indicated that the reaction proceeds through a synchronous concerted mechanism. Putting the methyl functional group on the phenyl ring changes the reaction rate, but changing the position of it in ortho, meta or para position has no change in the rate.

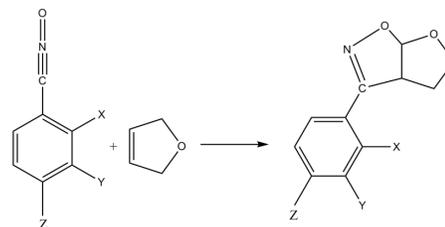
Keywords: DFT, Kinetics, Dipolar cycloaddition, Thermodynamics.

Introduction

Heterocyclic compounds are the most important molecules of organic chemistry that have been used in a lot of applications, especially in pharmacology [1-4]. There are a lot of advanced methods for making any type heteroatom rings [5,6]. Dipolar Cycloaddition, DC, is one of these methods for designing different kinds of heterocyclic compounds that have a significant using to the organic synthesis. Products of DC reactions are very numerous. They consist of compounds with different ring size and atoms. 1,3-DC is one type of dipolar cycloadditions that is used to synthesize of varies five-member ring heterocycles. Usually in 1, 3-DC reaction a carbon-carbon double bond reacts with a three member group of polar atoms [7]. Applications of dipolar cycloaddition are enormous, so spatial attentions have been paid to these

classes of reactions and kinetics and mechanism of them were studied [8-10] and the study of mechanism of them continues.

In continue our study about dipolar cycloadditions [11] and because of the importance of these classes of reactions we performed a detailed investigation on the effect of position of functional groups on the kinetics and mechanism of dipolar cycloaddition of benzonitrile oxide and Dihydrofuran (Scheme 1).

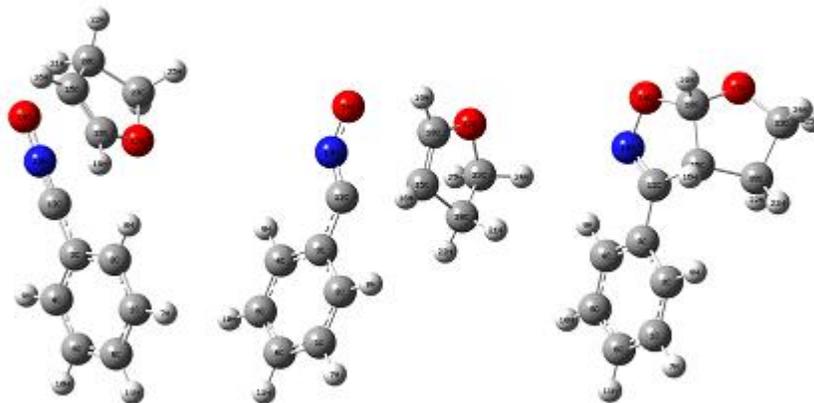


Scheme 1: Dipolar cycloaddition of benzonitrile oxide and Dihydrofuran.

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Results and discussion

Scheme 2 shows the optimized structures of reactants, TS, and product with the selected



Scheme 2: Optimized geometries of reactants, TS, and product for the studied reaction at B3LYP/6-31G(d,p) level at 298.15 K.

The concerted mechanism is initiated with the C12-N13, and C15-C18 π bonds cleavage and continues with O14-C18 and C12-C15 bond formation. The calculation shows that the C15-C18, and C12-N13 bonds are elongated to form the TS. According to Table 1 the transition structure has breaking of C15-C18 and C12-N13 π bond distances of 1.37 and 1.22 angstrom and forming O14-C18 and C12-C15 bond distances of 2.49 and 2.39 angstrom, respectively. The Pauling relation [12] was used to determine the related partial bond orders and the values of 0.875, 0.830, 0.054, and 0.028 were obtained for C15-C18, C12-N13, C12-C15, and C18-O14, respectively. The obtained partial bond orders indicate that 12.5% of C15-C18 and 17.0% of C12-C15 bonds are broken, whereas C12-C15 and C18-O14 have only 5.4% and 2.8% reaching to the transition state, respectively. The extent of broken and formed bonds in transition state shows that a synchronous concerted mechanism has occurred for the studied reaction.

Table 1: Key geometrical parameters of reactants, TS, and product at the B3LYP/6-31G(d,p) level of theory.

	C12-N13	O14-N13	C15-C18	C15-C12	C18-O14
Reactants	1.161	1.215	1.330	--	--
TS	1.217	1.233	1.372	2.389	2.492
Product	1.284	1.401	1.543	1.514	1.422

Table 2 shows the charge distribution in the reactants, TS and the charge difference between TS

geometrical parameters at the B3LYP/6-31G (d,p) shown in Table 1.

and reactants (Δ charge) by means of NBO analysis. The results at the TS indicate that a small negative charge developed on C15 and N13. The charge difference indicates that electron donor groups at C15, and N13 accelerate the reaction. However, at C18 position opposite result is observed (Table 2).

Table 2: Distributed NBO charges on the reactants and TS at the B3LYP/6-31G (d, p) level of theory (the numbering of atoms is like that in Scheme 3).

	C12	C15	N13	C18	O14
Reactants	0.2395	-0.3360	0.1681	0.1138	-0.4085
TS	0.2058	-0.4060	0.1008	0.1762	-0.3756
Δ (Charge)	0.0337	0.0700	0.0673	-0.0624	-0.0329

B3LYP/6-311G(d,p) results for the reaction path are given in Fig 1. This figure demonstrates the energy as a function of the reaction coordinate, C15-C12, and represents the minimum energy path which connects the reactants to the product through the saddle point.

The imaginary frequency for the transition structure was calculated to confirm the TS at B3LYP/6-31G (d,p). Table 3 presents, $\Delta G^{0,\#}$, $\Delta H^{0,\#}$, $\Delta S^{0,\#}$, E_a , and Arrhenius pre-exponential factor for the studied reaction. As can be seen from the activation energies putting the methyl substitution on the benzene ring decreases the rate, but changing the position of it has no effect on the rate. Because the ring is not too close to the atoms take part in the reaction and also calculated charges in the reactants and the TS showed no charge increasing or decreasing in the three given

positions. The calculated activation free energies indicate that the reaction can take place in room temperature and kinetically can be done without any help. We calculated ΔG^0 for the reaction and $-32.8 \text{ kcal mol}^{-1}$ was obtained. This value indicates that the reaction is thermodynamically favored. ΔG^0 was calculated by the $\Delta G^0 = G^0_{\text{P}} - G^0_{\text{R}}$.

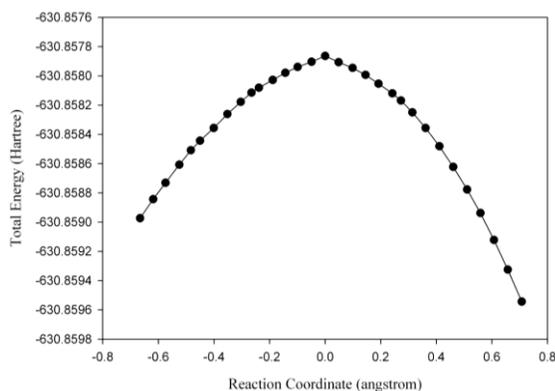


Figure 1: Schematic energy profile of the potential energy surface for the studied reaction at B3LYP/6-31G(d,p) level of theory.

Table 3: Theoretical kinetic and activation parameters for the studied reaction with B3LYP/6-31G (d,p) at 298.15 K in gas phase. ΔG^\ddagger , ΔH^\ddagger and E_a are in kcal mol^{-1} and ΔS^\ddagger , in $\text{cal mol}^{-1}\text{K}^{-1}$.

	ΔG^\ddagger	ΔH^\ddagger	E_a	ΔS^\ddagger	$\log A$
No substitution	16.7	17.6	18.8	2.9	12.6
Ortho -CH ₃	20.7	16.2	17.4	-14.9	9.8
Meta-CH ₃	20.0	15.8	16.9	-14.2	10.1
Para-CH ₃	20.1	15.9	17.1	-14.1	10.1

In order to study solvent effect on the studied reaction, we performed the CPCM calculations in water and toluene. The results are tabulated in the Table 4. As can be seen water decreased and toluene increased the rate. The reason seems to be polarity of the reactants respect to the TS. In this reaction the reactants are more polar than the TS and polar solvent stabilizes them more than the TS, so depresses the rate.

Table 4: Theoretical kinetic and activation parameters for the studied reaction in different solvents at 298.15K. ΔG^\ddagger , ΔH^\ddagger and E_a are in kcal mol^{-1} and ΔS^\ddagger is in $\text{cal mol}^{-1}\text{K}^{-1}$.

Solvent	ΔG^\ddagger	ΔH^\ddagger	ΔS^\ddagger	E_a	$\log A$
Water	17.4	16.0	-5.0	17.1	12.1
toluene	15.7	17.1	4.5	18.2	14.2

Conclusion

We studied effect of the position of alkyl group on the phenyl ring on dipolar cycloaddition of benzonitrile oxide and Dihydrofuran by DFT method with B3LYP/6-31G (d,p) level of the theory. The calculation indicated that the reaction had a synchronous concerted mechanism. Substituting methyl group on the ring decreased the rate respect to non substituted reactant but ortho, meta and para had the same rate. Non polar solvent increases the rate.

Computational

The structures corresponding to the reactants, TS and product were optimized and electronic structures and harmonic vibrational frequencies of all stationary points along the reaction pathway were calculated using Gaussian 03 computational package [13] with DFT methods.

Optimization of geometries of the stationary points on the potential energy surfaces were performed using Becke's three-parameter hybrid exchange functional with the correlation functional of Lee, Yang, Parr (B3LYP) [14,15] with the 6-31G(d,p) [16] basis sets. The synchronous transit guided quasi Newton (STQN) method [17] was used to locate the TS. The intrinsic reaction coordinate (IRC) method [18, 19] was also applied in order to check and obtain the profiles connecting the TS to the two associated minima of the proposed mechanism. The natural bond orbital (NBO) analysis [20, 21] was applied to determine the charge changes occurring in the studied process. All minimum and transition state structures are verified by vibrational frequency analysis. To take the solvent into account, we performed our calculations using cosmo polarizable continuum model (CPCM) [22].

The activation energies and Arrhenius factors were computed using eqns. (1) and (2), respectively, derived from the transition state theory [23,24].

$$E_a = \Delta H^\ddagger + RT \quad (1)$$

$$A = (ek_B T / h) \exp(\Delta S^\ddagger(T) / R) \quad (2)$$

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