



***Ab initio* Studies of Molozonide Formation in 1,3-Dipolar Cycloaddition Reactions Between C7-C10 Membered Simple Cycloalkynes and O₃**

AVAT (ARMAN) TAHERPOUR*, HADI SHAFIEE and ELAHE RAJAEIAN

Department of Chemistry, Science Faculty, Islamic Azad University, P.O.Box 38135-567, Arak (Iran).

*Corresponding author: E-mail: avatarman.taherpour@gmail.com, ataherpour@iau-arak.ac.ir

(Received: July 27, 2011; Accepted: August 30, 2011)

ABSTRACT

Huisgen's reaction of alkynes with Ozone (O₃), at its first step yielding carboxylic acids functional groups is, undoubtedly, an example of 1,3-dipolar cycloaddition reactions. Cycloadditions of 1,3-dipoles may occur by concerted mechanisms. The energy content in alkynes may be increased further by bending the normally linear triple bond, as in the small cycloalkynes. The strain energy in the cycloalkynes increases as the size of the ring decreases. In this study, the reactivity and strain energy effect of these cycloalkynes with O₃ will be discussed in light of computational studies using *ab initio* methods (RHF/6-31G*//RHF/6-31G* level). The investigation of the structural properties, theoretical thermodynamic and kinetic data i.e. Δ_rG , ΔG^\ddagger and rate constants of the reactions at 298°K will be presented.

Key words: Cycloalkynes; Ozonolysis; Molozonide; Cycloaddition reaction; 1,3-Dipolar reaction; *ab initio* calculations; molecular modeling.

INTRODUCTION

1,3-dipolar cycloaddition, also known as the *Huisgen* cycloaddition or *Huisgen* reaction, is an organic chemical reaction belonging to the larger class of cycloadditions^{1,2}. It is the reaction between a 1,3-dipole and a dipolarophile, most of which are substituted alkenes, to form a five-membered ring. 2 π -electrons of the dipolarophile and 4 electrons of the dipolar compound participate in a concerted, pericyclic shift. The addition is stereoconservative (suprafacial), and the reaction is therefore a [2_s+4_s]

cycloaddition similar to the Diels-Alder reaction. Many authors still use the term "[2+3] cycloaddition", which counts the number of involved atoms but does not follow IUPAC recommendations. IUPAC recommends the use of "(2+3)" for the number of involved atoms instead. A condition for such a reaction to take place is a certain similarity of the interacting HOMO and LUMO orbitals, depending on the relative orbital energies of both the dipolarophile and the dipole. Electron-withdrawing groups on the dipolarophile normally favor an interaction of the LUMO of the dipolarophile with

the HOMO of the dipole that leads to the formation of the new bonds, whereas electron donating groups on the dipolarophile normally favor the reverse of this interaction¹⁻⁶.

The energy content in alkynes may be increased further by bending the normally linear triple bond, as in the smaller cycloalkynes. The strain energy in simple cycloalkynes may be increased by bending the normally linear triple bond.

The strain energy and reactivity in cycloalkynes increase as the size of the ring decreases.[7-10] The strain energy of I-1 to I-4 are 31.1, 20.8, 16.4 and 9.9 kcal mol⁻¹, respectively⁷. Cycloadditions of 1,3-dipolar molecules such as O₃ (II) with simple cycloalkynes (I) may occur by concerted mechanism of 1,3-dipolar cycloaddition to produce III. The most general and mildest method of oxidatively cleaving unsaturated compounds to carbonyl compounds is ozonolysis. In this reaction, the unsaturated compounds (such as -C=C- and -C≡C-) are treated with O₃ at low temperatures in, for example, methanol. The molozonide intermediate (like III) is produced during the concerted reaction of the 1,3-dipolar cycloadditions. The isolable intermediate is an ozonide by passing from molozonides. In this study, the reactivity and strain energy effect of the simple cycloalkynes (I) with O₃ (II) for the first step of ozonolysis reaction and producing the molozonide (III) will be discussed in light of computational studies using *ab initio* methods (RHF/6-31G**/RHF/6-31G* levels). The investigation of the structural properties, theoretical thermodynamic and kinetic data i.e. ΔrG, ΔG[#] and rate constants of the reactions at 298°K will be presented.

Computational details and Calculations

The *ab initio* molecular orbital calculations were performed with the gaussian 98 program. Geometries for all structures were fully optimized by means of analytical energy gradients in RHF level with the 6-31G* basis set.[11] The synchronous Transit-guided Quasi-Newton (STQN) method was used to locate transition states and products, which were confirmed to have zero and one imaginary frequency, respectively. The frequencies were scaled by a factor of 0.8929 and used to compute the free energies (ΔG[#]) and the free energies changes of

reaction (Δ_rG) at 298°K by equations:

$$\Delta G^{\#} = \Sigma G_{TS} - \Sigma G_{Reactants} \quad \dots(1)$$

$$\Delta_r G = \Sigma G_{products} - \Sigma G_{reactants} \quad \dots(2)$$

Also, rate constants were calculated with the Eyring equation, derived from transition state theory:[12]

$$k = K_B T/h \exp(-\Delta G^*/RT) \quad \dots(3)$$

ΔG[#] is the free energy difference between transition state and reactants. The imaginary reactions were studied in two methods: RHF/6-31G*/RHF/6-31G*. In this study, the most conformations of the simple cycloalkynes (I-1 to I-4) were investigated in the 1,3-dipolar cycloaddition reactions with (II).

RESULTS AND DISCUSSION

The selected structural parameters, the heats of formation in kcal mol⁻¹ and the results of 1,3-dipolar cycloaddition reactions of I (cycloalkynes) and O₃ (II) by using RHF/6-31G**/RHF/6-31G* method and the transition states of the conversion from the reactants to isooxazoles as the products are summarized in Table 1 to Table 3 and Fig. 1 to Fig. 8. The energy surface and the barrier energy for the reactions were investigated in detail by changing the position and distances between appropriate atoms in the reaction pathway. The structural results in the level have been similar. The optimized structures are shown for reactants in Fig. 1, for transition states in Figure-2 and for products in Figure-3. The diagram of the free energies (ΔG[#]) and the free energies changes of reaction (Δ_rG) at 298°K for 1,3-dipolar cycloaddition reactions of I and II by using RHF/6-31G**/RHF/6-31G* method are shown in Figure-4 to Figure-8. The free energies of the reactants, transition states and products in reactions of cycloalkynes (I) with nitrile oxide (II) are listed in Table-3. The results show the treatment the electron correlation gives more stable energies. Table-3 shows the thermodynamic (ΔG[#] and Δ_rG in kcal mol⁻¹) and kinetic (rate constants=k, in M⁻¹Sec⁻¹ and relative constants=k') data of the 1, 3-dipolar cycloaddition reactions of I-1 to I-4 and II.

Structures for the synchronous transition state are obtained with mean bond length values of C1-O18 and C2-O20 bonds in transition states of C7, C8, C9 and C10 with O₃ (II). The bond length values of C-O for two sides of this addition are equal.

The bond length values of C1-O18 and C2-O20 for the transition states are: [2.28, 2.28], [2.19, 2.19], [2.16, 2.16] and [2.14, 2.14] in Å for 1,3-dipolar cycloaddition reactions of I-1 to I-4 (cycloalkynes) and ozone (II), respectively. Figure-2 and Table-2

Table 1: The selected structural parameters (bond length in Å and bond angle in °) of the cycloalkynes I-1 to I-4

Parameter*	Cycloheptyne	Cyclooctyne	Cyclononyne	Cyclodecyne
Bond Lengths				
1C-2C	1.19	1.19	1.19	1.19
2C - 3C	1.47	1.47	1.47	1.47
3C - 4C	1.55	1.55	1.55	1.55
4C - 5C	1.55	1.54	1.55	1.53
5C - 6C	1.55	1.56	1.54	1.54
1C - 7C	1.47	-	-	-
1C- 8C	-	1.47	-	-
1C-9C	-	-	1.47	-
1C-10C	-	-	-	1.47
Bond Angles				
1C - 2C - 3C	146.52	158.10	163.45	172.22
2C - 3C - 4C	103.94	106.47	107.70	112.77
2C - 1C - 7C	146.55	-	-	-
2C - 1C - 8C	-	158.02	-	-
7C - 1C - 9C	-	-	163.47	-
2C - 1C - 10C	-	-	-	172.17
1C - 7C -6C	103.93	-	-	-
1C - 8C-7C	-	106.48	-	-
1C -9C- 8C	-	-	107.67	-
1C - 10C- 9C	-	-	-	112.76
2C - 3C - 8H	113.87	-	-	-
2C - 3C - 9H	110.18	-	-	-
1C - 7C- 16H	110.18	-	-	-
1C- 7C - 17H	113.87	-	-	-
2C-3C - 9H	-	112.67	-	-
2C-3C-10H	-	109.86	-	-
1C-8C-16H	-	109.86	-	-
1C-8C-17H	-	112.67	-	-
2C-3C - 10H	-	-	111.58	-
2C-3C-11H	-	-	109.97	-
1C-9C-16H	-	-	111.57	-
1C-9C-17H	-	-	109.98	-
2C-3C-11H	-	-	-	108.89
2C-3C-12H	-	-	-	109.88
1C-9C-16H	-	-	-	109.88
1C-9C-17H	-	-	-	108.89

*The results of the calculations in method RHF/6-31G**/RHF/6-31G*

show the structures and the data of the transition states.

The strain energy is one of the main functions in these reactions. By increasing the ring size of the cycloalkynes and decreasing the strain energy of the cycloalkynes I-1 to I-4, the internal

bond angles of C-C≡C have increased. The bond angles of C1-C2≡C3 are 146.52, 158.10, 163.45 and 172.22 for I-1 to I-4, respectively. For each cycloalkyne in these 1,3-dipolar cycloaddition reactions, the thermodynamic and kinetic stabilities of I are related to the strain energies and the structural characters particularly around the C-C≡C-

Table 2: The selected structural parameters of the transition states (bond length in Å and bond angle in °) of the 1,3-dipolar cycloaddition reactions of I-1 to I-4 and II

Parameters*/TS	TS(C7)	TS(C8)	TS(C9)	TS(C10)
Bond Lengths				
1C- 2C	1.20	1.21	1.22	1.22
2C - 3C	1.47	1.47	1.48	1.48
1C -18O	2.28	2.19	2.16	2.14
18O-19O	1.22	1.23	1.23	1.24
19O -20O	1.22	1.23	1.23	1.24
20O -2C	2.28	2.19	2.15	2.14
1C-7C	1.47	-	-	-
1C- 8C	-	1.47	-	-
1C-9C	-	-	1.48	-
1C-10C	-	-	-	1.48
Bond Angles				
18O-19O-20O	114.72	113.34	112.69	112.14
1C-18O-19O	95.28	96.56	96.61	96.94
2C-20O-19O	95.29	96.16	97.02	97.55
2C-1C-18O	100.82	101.35	101.40	101.453
1C-2C-20O	100.80	100.93	101.40	101.50
1C-2C-3C	145.04	154.55	158.73	161.15
2C-1C-7C	145.11	-	-	-
2C-1C-8C	-	154.70	-	-
2C-1C-9C	-	-	158.78	-
2C-1C-10C	-	-	-	162.21

*The results of the calculations in method RHF/6-31G**/RHF/6-31G*

Table 3: The thermodynamic (ΔG^\ddagger and $\Delta_r G$ in kcal mol⁻¹) and kinetic (rate constants= k in M⁻¹Sec⁻¹ and relative constants= k') data of the 1,3-dipolar cycloaddition reactions of I-1 to I-4 and II.

Cycloalkynes	ΔG^\ddagger (kcal.mol ⁻¹)	$\Delta_r G$ (kcal.mol ⁻¹)	k	k'
C ₇	18.44	102.58	1.88 × 10 ⁻¹	4.59 × 10 ⁵
C ₈	23.13	85.96	6.86 × 10 ⁻⁵	1.38 × 10 ²
C ₉	26.67	79.33	1.76 × 10 ⁻⁷	0.425
C ₁₀	26.16	78.69	4.10 × 10 ⁻⁷	1

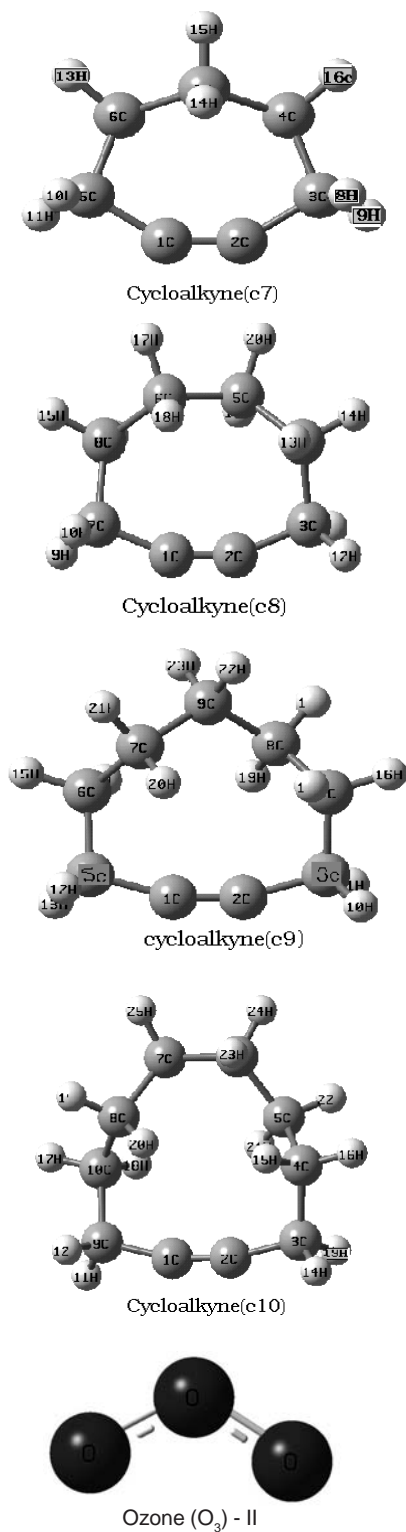


Fig. 1: Cycloalkynes 7-10 membered rings (I) and Ozone (II)

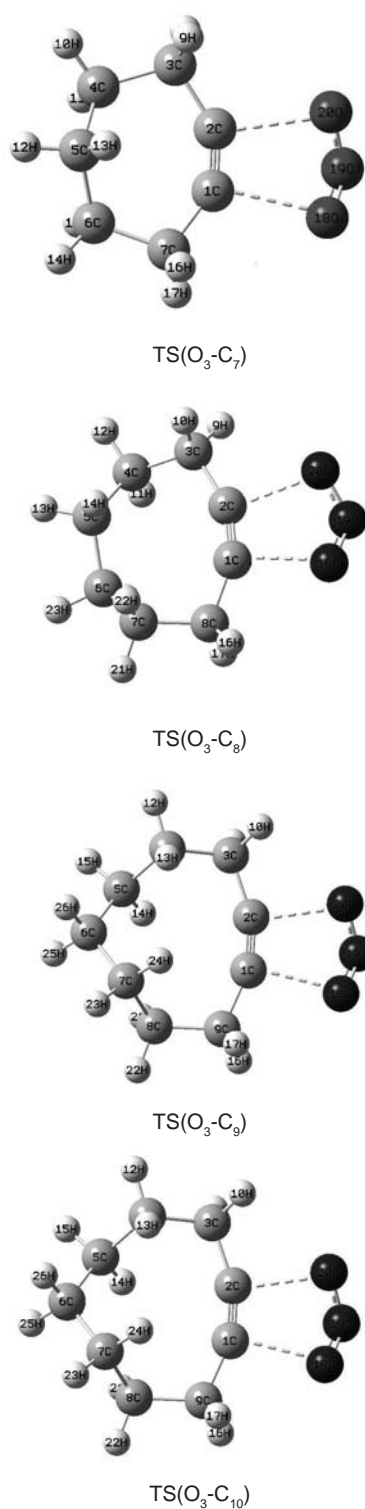


Fig. 2: Transition states of 1,3-dipolar cycloaddition of Cycloalkynes 7-10 membered rings (I) and Ozone (II)

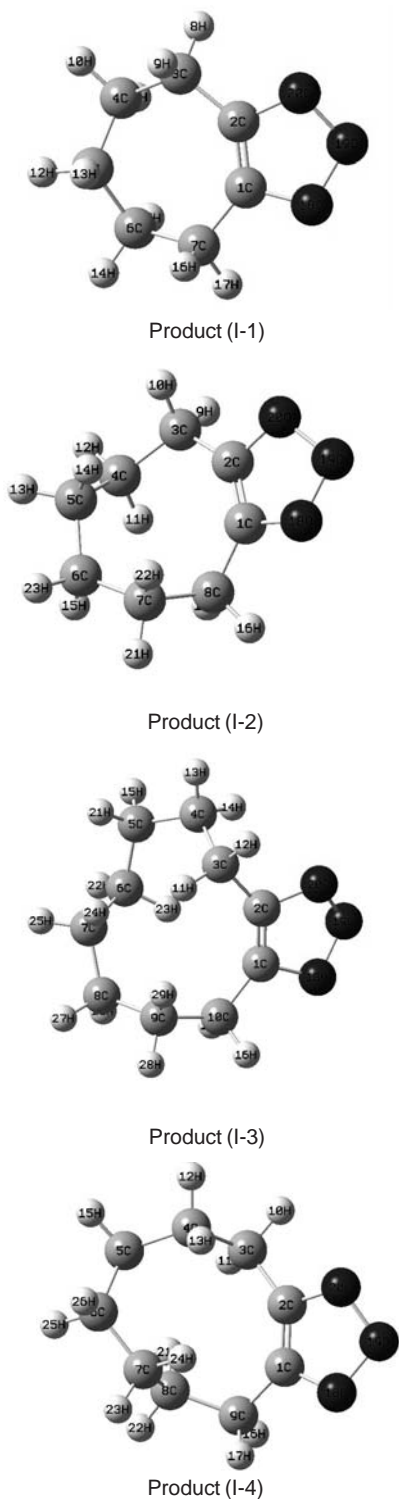


Fig. 3: Products of 1,3-dipolar cycloaddition of cycloalkynes 7-10 membered rings (I) and Ozone (II)

C. The bond angles of C1-C2≡C3 have reached to 145.04, 154.55, 158.73 and 161.15 for I-1 to I-4, respectively, in the transition states (TS) during the reaction of I and II. In this case, the bond angles of O18-O19-O20 have reached to 114.72, 113.34, 112.69 and 112.14 for I-1 to I-4, respectively. It seems that the bond angles were affected with the ring sizes of cycloalkynes (I) at the TS stage as well. The kinetic stabilities were decreased by decreasing the ring sizes, subsequently increasing the strain energies of cycloalkynes I. Table-3 shows the calculated rate constants (k , in $M^{-1}Sec^{-1}$) by utilizing the RHF/6-31G**/RHF/6-31G* (k) methods

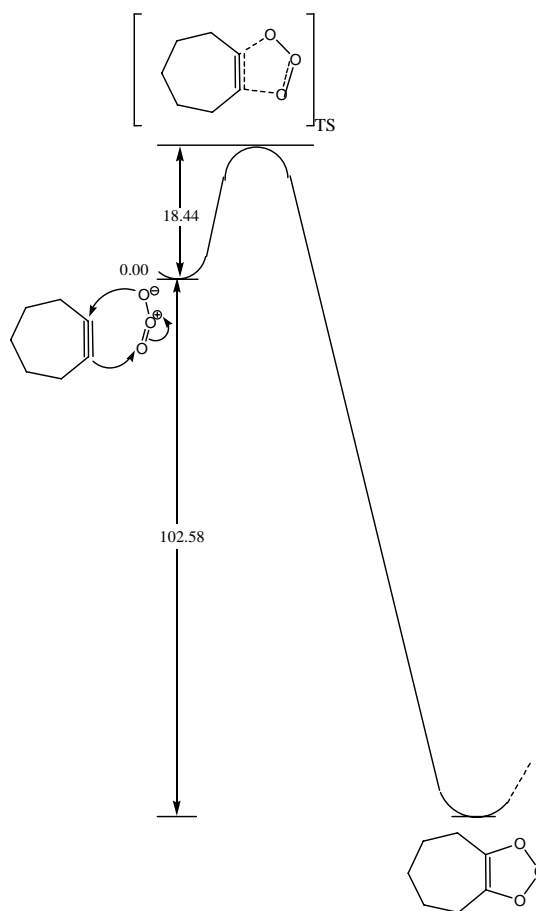


Fig. 5: The diagram of the free energies (ΔG^\ddagger) and the free energies changes of reaction ($\Delta_r G$) at 298°K for 1,3-dipolar cycloaddition reactions of I-1 (cycloheptyne) and II by using RHF/6-31G**/RHF/6-31G* method

and the Eyring equation (Eq.-3). The chemical affinity and the calculated rate constants in the method increased by decreasing the ring size of the cycloalkynes and the bond angles of triple bonds and increasing the strain energies of I. The rate constants with RHF/6-31G**/RHF/6-31G* for the reactions of I and II are 1.88×10^{-1} , 6.86×10^{-5} , 1.76×10^{-7} and 4.10×10^{-7} , respectively. The bond angle strain release is a motive force for these reactions. Another one is reaching to the aromatic state of the molozonide III as the favored products of the reaction.

The free energy differences between transition states and reactants ΔG^\ddagger by RHF/6-31G**/RHF/6-31G* for the reactions of I and II, are 18.44,

23.13, 26.67 and 26.16 kcal.mol⁻¹, respectively. The results in the method (RHF/6-31G**/RHF/6-31G*) shows increasing in the ΔG^\ddagger of the 1,3-dipolar cycloaddition reactions of I-1 to I-4 and II, by increasing the ring size and decreasing the strain energy of cycloalkynes (I). Table 3.

The free energy changes of reactions ($\Delta_r G$) are shown in Table-3. The values of $\Delta_r G$ were obtained by the use of two RHF method and Eq.-2. The values of $\Delta_r G$ by RHF/6-31G**/RHF/6-31G* for the exothermic reactions of I and II, are 102.58, 85.96, 79.33 and 78.69 kcal.mol⁻¹, respectively. The gap in the free energies between reactants and products have been decreased by the thermodynamic stability of bigger cycloalkynes (I).

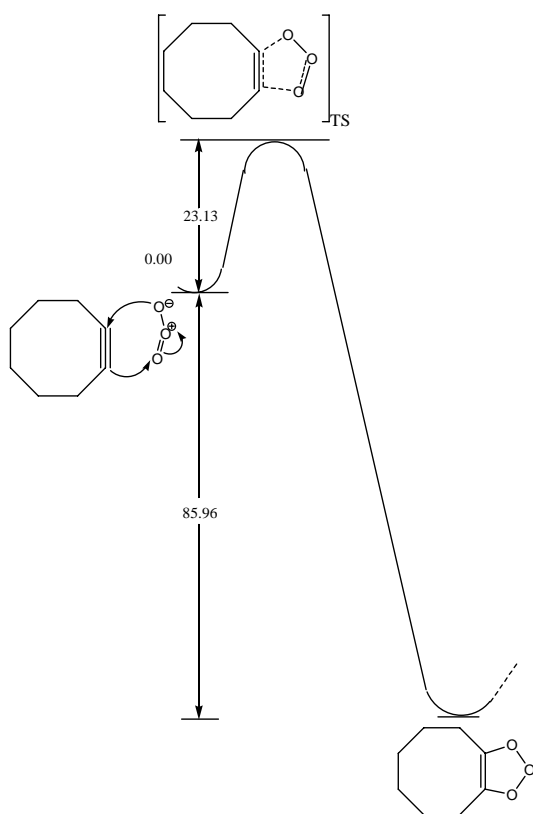


Fig. 6: The diagram of the free energies (ΔG^\ddagger) and the free energies changes of reaction ($\Delta_r G$) at 298 K for 1,3-dipolar cycloaddition reactions of I-2 (cyclooctyne) and II by using RHF/6-31G**/RHF/6-31G* method

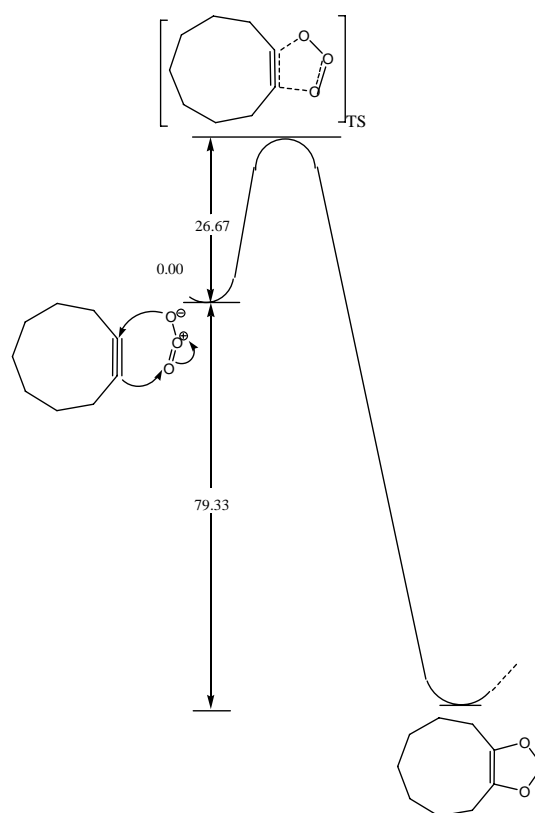


Fig. 7: The diagram of the free energies (ΔG^\ddagger) and the free energies changes of reaction ($\Delta_r G$) at 298°K for 1,3-dipolar cycloaddition reactions of I-3 (cyclononyne) and II by using RHF/6-31G**/RHF/6-31G* method

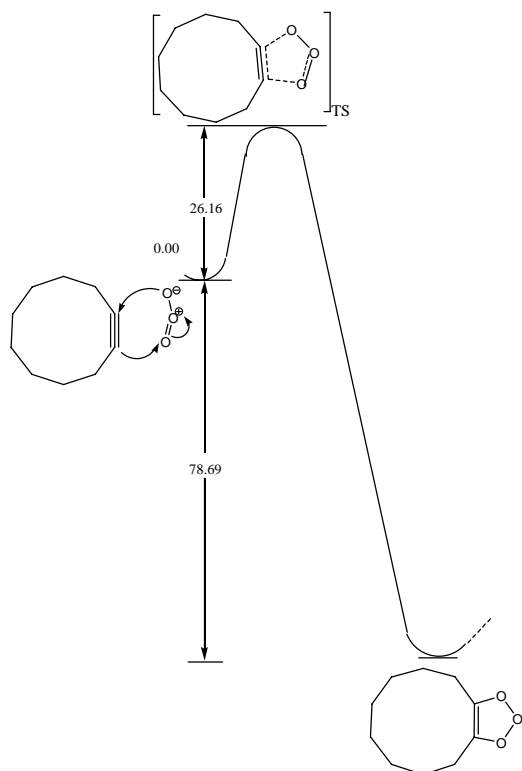


Fig. 8: The diagram of the free energies (ΔG^\ddagger) and the free energies changes of reaction ($\Delta_r G$) at 298°K for 1,3-dipolar cycloaddition reactions of I-4 (cyclodecyne) and II by using RHF/6-31G**/RHF/6-31G* method

Table 4: The free energies (G) in Hartree of the reactants, transition states and products in reactions of cycloalkynes (I) with O₃ (II)

Species	G ^a (H)
O ₃	-224.276315
Cycloheptyne	-270.668626
Cyclooctyne	-309.691463
Cyclononyne	-348.703017
Cyclodecyne	-387.705862
TS (C ₇)	-494.915558
TS (C ₈)	-533.930915
TS (C ₉)	-572.936822
TS (C ₁₀)	-572.936822
Product (C ₇)	-495.108411
Product (C ₈)	-534.104759
Product (C ₉)	-573.105756
Product (C ₁₀)	-612.104744

See Table-3 and Fig.-4 to Fig.-8. These results suggest that, the relative constants of reaction rates increased by decreasing the size of the rings and increasing the strain energies and chemical affinity of cycloalkynes I to take part in the 1,3-dipolar cycloaddition reactions of I-1 to I-4 and II for producing of the molozonide III.

CONCLUSION

Comparing results show that in the 1,3-dipolar cycloaddition reactions of I-1 to I-4 and II for producing III the rate constant and the free energies changes in reactions increases as the size of the ring decreases. The comparison of the strain energies, thermodynamic and kinetic data of the Huisgen reactions 7-10 member rings of cycloalkynes with O₃ (II) showed that the chemical affinity of I increases by increasing the bond angle strain around the triple bonds.

The free energies (ΔG^\ddagger and $\Delta_r G$) of the reactants, transition states and products in the reactions of cycloalkynes (I) with O₃ are recorded by using RHF/6-31G**/RHF/6-31G* calculations at 298°K. The kinetic data (rate constants= k in M⁻¹Sec⁻¹ and relative constants= k') were calculated by the Eyring equation, which is derived from transition state theory.

In these exothermic reactions, the k and k' of the reactions increased by decreasing the size of the rings and increasing the strain energies and chemical affinity of cycloalkynes I to participate in the 1,3-dipolar cycloaddition reactions of I with II for producing of the molozonide III as the first step of oxidation of cycloalkynes I. Two factors i.e bond angle and strain release for reaching to molozonide as the favored intermediate of the exothermic reaction is the main motive forces of these 1,3-dipolar cycloaddition reactions of I with II.

ACKNOWLEDGMENTS

The corresponding author gratefully acknowledges the colleagues in Chemistry Department of The University of Queensland-Australia, for their useful suggestions during the sabbatical opportunity.

REFERENCES

1. Huisgen, R. , *Angewandte Chemie International Edition*, **2**(11): 633-645 (1963).
2. Huisgen, R., *Angewandte Chemie International Edition*, **2**(10): 565-598 (1963).
3. Huisgen, R., "Cenetary Lecture-1,3-Dipolar Cycloadditions". *Proceedings of the Chemical Society of London.*; 357 (1961).
4. G. C. Patton, *Development and Applications of Click Chemistry*, November 8, 2004. (and the literature cited there in). <http://www.scs.uiuc.edu> , Online
5. D. J. V. C. van Steenis, O. R. P. David, G. P. F. van Strijdonck, J. H. van Maarseveen and J. N. H. Reek, *Chemical Communications*, **34**: 4333 - 4335 (2005). (and the literature cited there in).
6. A. J. Dirks, S. S. van Berkel, N. S. Hatzakis, J. A. Opsteen, F. L. van Delft, J. J. L. M. Cornelissen, A. E. Rowan, J. C. M. van Hest, F. P. J. T. Rutjes, R. J. M. Nolte, *Chemical Communications*, **33**: 4172-4174 (2005). (and the literature cited there in).
7. K. P. C. Volhard, *Organic Chemistry*, W. H. Freeman, p.525 (1987).
8. F. A. Cary and R. J. Sundberg, *Advanced Organic Chemistry*, 4th Ed., Kluwer Academic/ Plenum Publishers (2000).
9. J. March, *Advanced Organic Chemistry, Reactins, Mechanisms and Structure*, 4th Ed., John Wiley and Sons, (1999).
10. A. A. Taherpour and E. Rajaeian, *Theochem*, **849**: 23-24 (2008).
11. Gaussian 98 Revision A.7, Frisch, M.J., Trucks, G.W., Schlegel, H.B., Scuseria, G.E., Robb, M.A., Cheeseman, J.R., Zakrzewski, V.G., Montgomery, Jr., J.A., Stratmann, R.E., Burant, J.C., Dapprich, S., Millam, J.M., Daniels, A.D., Kudin, K.N., Strain, M.C., Farkas, O., Tomasi, J., Barone, V., Cossi, M. Cammi, R., Mennucci, B., Pomelli, C., Adamo, C., Clifford, S., Ochterski, J., Petersson, G.A., Ayala, P.Y., Cui, Q., Morokuma, K., Malick, D.K., Rabuck, A.D., Raghavachari, K., Foresman, J.B., Cioslowski, J., Ortiz, J.V., Baboul, A.G., Stefanov, B.B., Liu, G., Liashenko, A., Piskorz, P., Komaromi, I., Gomperts, R., Martin, R.L., Fox, D.J., Keith, T., Al-Laham, M.A., Peng, C.Y., Nanayakkara, A., Gonzalez, C., Challacombe, M., Gill, P.M.W., Johnson, B., Chen, W., Wong, M.W., Andres, J.L., Gonzalez, C., Head-Gordon, M., Replogle, E. S., Pople, J.A. Gaussian, Inc., Pittsburgh PA, (1998).
12. D.A. McQuarrie and J.D. Simon, *Physical Chemistry*, University Science Books, Sausalito, CA (1999).