------Raf. Jour. Sci., Vol. 19, No.3, pp 18- 23 2008------

Theoretical Study of the Factors Influencing the Kinetic of 1, 3-Dipolar Cycloaddition Reactions by Regression Analysis

Walid Y.Yousif
Department of Basic Science
College of Agriculture and Foresty
Mosul University

(Received 30/3/2008 ; Accepted 31/8/2008)

ABSTRACT

The single-and multi-parametric linear regression analysis is applied for the study of the influence of different factors on the kinetic of 1,3-dipolar cycloaddition reactions. The rate constants of the addition of eight **N**-(substituted) maleimides on phthalazinium-2-dicyanomethanide(Butler *et al.*, 1996) is correlated as dependent variable with the electron densities of the carbons involved in the addition reaction, the frontier orbital energy levels, and the steric energies of the transition states and products as independent variables. Results of the analysis revealed that all mentioned factors affect the rate of the reaction, but to different extents. The steric energy of the transition state and the electron density are the most influencing factors; the energy of the lowest unoccupied molecular orbital and the steric energy of the products come next. The energy of the highest occupied molecular orbital has the least influence on the reaction.

KEYWORDS: Electron densities; frontier orbital energy levels; steric energies of transition state and product.

دراسة نظرية للعوامل المؤثرة على حركية تفاعل الاضافة الحلقى من نوع
1,3 - ثنائى القطب بواسطة التحليل الانحداري

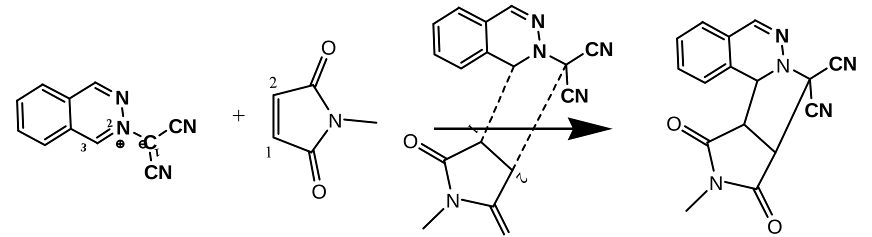
الملخص

تم استخدام طريقة التحليل الانحدارى الخطى منفرد ومتعدد الدالات لدراسة العوامل المؤثرة على تفاعل الاضافة الحلقية من نوع 1 و3-ثنائى القطب. درس الترابط بين سرع اضافة ثمانية مركبات من الماليميدات المعوضة على ذرة النتروجين الى المركب فيثالازينيم-2-داي سيانوميثنايد كدالة معتمدة مع الكثافة الالكترونية على ذرات الكاربون المشتركة فى تفاعل الاضافة ومستوى طاقة اوربتال المجابهة وطاقة الحشد الفراغى للحالة الانتقالية وللمركبات الناتجة كدالة غير معتمدة. تشير نتائج التحليل الى ان جميع هذه الدالات تؤثر على سرعة تفاعل الاضافة ولكن بدرجات متفاوتة. الكثافة الالكترونية وطاقة الحشد الفراغى للحالة الانتقالية هما اكثر الدالات تاثير, وياتى فى الدرجة الثانية طاقة اوطأ اوربتال غير مشغول وطاقة الحشد الفراغى للمركبات الناتجة وياتى فى المرتبة الاخيرة طاقة أعلى اوربتال مشغول.

INTRODUCTION

1,3-dipolar cycloaddition reactions belong to the type of reactions that involve an electron donor-acceptor interactions (Sustman and Schubert, 1972). According to molecular orbital perturbation theory (MOPT), the kinetics of these reactions are controlled by HOMO-LUMO interactions which depend on frontier orbital energies and electron density of the carbons participating in the reactions (Herndon, 1972). In addition to the mentioned two factors the steric interaction of subsistent in the transition state and product is also expected to influence the rate of the reaction.

In the present paper the rate of addition of eight **N**-substituted maleimides to phthalazinium-2-dicyanomethanide (Lowry *et al.*, 1996), as a dependent variable is correlated with some relevant physical properties of the dipolarophiles as independent variables via the application of the single-and multi-parametric linear regression method. These properties include the HOMO-LUMO energy levels, the electron density of the carbons participating in the addition reaction, and the steric energies of the transition states and products.The mechanism (Butler *et al.*, 2001) of the addition reaction is expected to proceed according to scheme (1).



phtalazinium-2-dicyanomethanide N-(substituted)maleinimides 10-Methyl-9,11-dioxo-8a,9,10,11,11a,11b-hexahydro-pyrrolo [3',4':3,4]pyrrolo[2,1-*a*]phthalazine-8,8-dicarbonitrile

Scheme (1)

THEORITECAL CALCULATION

The kinetic data of the reactions have been obtained from (Butler *et al.*, 2001). The quantum mechanics semiemperical method and molecular mechanics calculations for determing the HOMO, LUMO, Ecd1, Ecd2, Steric energy of transition states (TS) and products. Have been estimated using. Chem Office software version 8.0.3. Single and multiparamatric linear regression analysis have been calculated by. SPSS software version (9.0) this has been used between the rate constant of the investigated reaction as dependent variable and the frontier orbital energy levels, electron density, and steric energies of transition states (TS) and products as independent variables.

In linear regression analysis the square correlation coefficient ($\mathbf{R}^2$), and the regression coefficient ($\mathbf{a_1,a_2}$……etc) are very important for the evaluation of the regression analysis results. Multiparametric linear equation may be written in the form:

$$Y=a_0+a_1x_1+a_2x_2+.........a_n x_n$$

Where Y stands for the dependent variable (the rate constant in our case), a_0 is scaling constant that depends on the reference state, $\mathbf{X_1}$, $\mathbf{X}_2$…etc are the independent variables (the relevant physical proprieties of reactant in our case, ($\mathbf{a_1}$, $\mathbf{a}_2$….etc) are the regression coefficients that have the significance of statistical weighting factors and they describe the susceptibility of the dependent variable **Y** to the associated independent variable **x**. The quality of the linear correlation is given in terms of the square correlation coefficient

(**R^2**) which ranges between zero to one. Good correlation should possess values larger than 0.9.Even larger values than 0.9 are necessary if the aim of the application of the analysis is for prediction purposes. Smaller values than 0.9 can be helpful for the interptation of experimental results or theoretical calculations.

RESULTS AND DISCUSSION

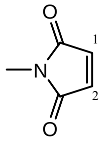
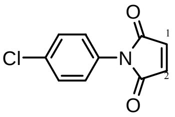
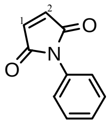
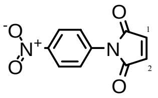
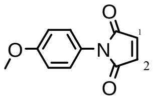
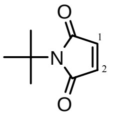
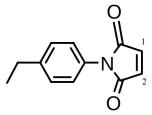
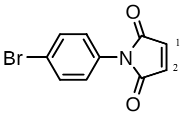
Table (1) gives the calculated values for some physical properties of the investigated dipolarophiles using semiemperical quantum mechanics and molecular mechanics methodes. Table (2) shows the results of the single-and multiparametric linear regression analysis. This reveals that the three studied molecular properties, namely, the electron density on the carbons involved in the addition reaction, the frontier orbital energy levels, and the steric energies of the transition states and products are influencing the rates of the reactions. However, the mentioned parameters affect the rate of the reaction to different extent. The most important factors are the steric energy of the transition state and electron density of the carbons participating in the addition reaction with R^2 = 0.876 and 0.846 respectively. It is generally accepted at present that the transition state of 1,3-dipolar addition reaction includes cyclic complex formed via electron donor-acceptor interaction between the reactants (Huisgen, 1976). The probability of the formation of the product as compared to the probability of dissociation of the complex to the free reactants increases with the increase of the stability of the complex and the rate of delocalization of the π-electrons to form the new σ-bonds. Both of these processes are influenced by the level of electron density and the steric energy of the transition state.

The steric energy of the product and the lowest unoccupied energy level come next in importance and are almost of equal weight as influencing factors on the reaction with R^2=0.777 and 0.75 respectively.

At last, the highest occupied molecular orbital is of the least influence on the reaction with R^2=0.376.Table (2) also shows that the consideration of two and three factors increase the correlation efficiency with correlation coefficients better than 0.95.This result suggests that the rate of the reaction is controlled by all studied factors. However, the various factors possess different weights.

Similar results have been obtained for the addition of free radicals to multiple bonds (Ibrahim, 2002) and for the Diels-Alder reaction (Yousif, 2005).

Table 1: The calculated values for some physical properties of the investigated dipolarophiles

N-substituted dipolarophiles	**HOMO ev**	**LUMO ev**	**EdC1 ev**	**EdC2 ev**	**Steric E. TS kcal/mole**	**Steric E. Prod kcal/mole**	***K rate Constant x 10^3**
	-10.512	-1.142	4.1537	4.1540	1.01723	1.80235	**317.7**
	-9.132	-1.368	4.1509	4.1508	0.637152	1.45573	**568**
	-9.143	-1.246	4.1528	4.1526	0.766909	1.47069	**506**
	-9.933	-1.706	4.1462	4.1459	0.586879	1.53706	**650**
	-8.700	-1.224	4.1528	4.1531	0.958303	1.67071	**499**
	- -10.427	-1.030	4.1589	4.1579	1.32219	2.07242	**202.3**
	-8.901	-1.218	4.1532	4.1530	0.683887	1.49489	**488**
	-9.185	-1.395	4.1505	4.1503	0.649208	1.59975	**561**

*=Lit mol^{-1}s^{-1},taken from reference (Butler *et al.*, 2002)

Table 2: The results of single-and multiparametric regression analysis

Factor	**R^2**	**a_0**	**a_1**	**a_2**	**a_3**	**Std.Dev.**
Steric energy of the transition(TS) state	0.876	0.918	-0.537	------	--------	0.135799
Steric energy of the product	0.777	1.469.	-0.608	--------	--------	0.12792
HOMO	0.376	1.679	0.127	--------	--------	0.0889
LUMO	0.75	-0.322	-0.616	--------	--------	0.12566
Edc1	0.846	155.62	-37.365	--------	--------	0.13337
Edc2	0.835	160.79	-38.611	--------	--------	0.13263
HOMO, EdC2	0.992	143.778	0.0854	34.317	----------	0.14475
LUMO,EdC2	0.861	306.14	0.599	-73.43	---------	0.1438
HOMO,Edc1	0.982	138.229	0.0802	-32.99	--------	0.1438
LUMO,EdC1	0.848	183.271	0.121	-43.98	--------	0.13356
HOMO,TS	0.917	1.168	0.0302	-0.491	-------	0.13695
LUMO,TS	0.915	0.485	-0.238	-0.385	--------	0.1390
HOMO,Steric of product	0.77	1.456	-0.0024	-0.613	--------	0.12792
LUMO,Steric of product	0.951	0.629	-0.373	-0.389	--------	0.1415
EdC1,Steric of product	0.941	120.202	-28.65	-0.078	---------	0.14407
EdC1,TS	0.921	73.79	-17.583	-0.321	--------	0.1393
EdC2,TS	0.919	73.582	-17.541	-0.311	--------	0.1391
EdC2,Steric of product	0.945	102.948	-24.552	-0.324	--------	0.141105
EdC1,TS,HOMO	0.985	120	-28.652	-0.078	0.0708	0.14407
EdC2,TS,HOMO	0.995	135.04	-32.224	-0.0366	0.0808	0.14479
EdC1,TS,LUMO	0.922	53.801	-0.331	-12.800	-0.0763	0.13938
EdC2,Steric of product, HOMO	0.997	135.38	-32.299	0.0579	0.14485	0.14485
EdC2,Steric of product, LUMO	0.951	1.031	0.0964	-0.388	-0.372	0.14153
TS,LUMO,EdC2	0.919	58.31	-0.34	-0.0525	-13.877	0.13913

HOMO = Energy of highest occupied molecular orbital theory, .LUMO= Energy of Lowest unoccupied molecular orbital theory, EdC1=Electron density of carbon one, EdC2=electron density of carbon two, TS=Steric energy of transition state, Prod=Steric energy of product, E=Energy, Std. Dev=Stander. Deviation, eV=electron volt.

CONCLUSION

The energy of the frontier orbitals, the electronic density of the carbons participating in the 1,3-dipolar cycloaddition reaction and the steric energy of the transition states and products are the factors that influence the rate of the reaction investigated in this paper.

The steric energy of the transition states and the electron density possess the heaviest weight, followed by the energy of the lowest unoccupied molecular orbital and the steric energy of the product.The energy of the highest occupied molecular orbital has the least influence on the reaction.

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