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Theoretical Study of Solvent Effects on 1,3- Dipolar Cycloaddition Reaction

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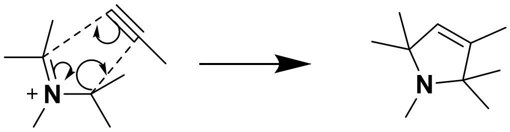
Abstract

In the present study the regression analysis of the rate constant k ^{15}with solvent parameters, for two sets of 1,3-dipolarcycloaddition reactions were done. The first was the reaction azomethine 1 with cyclooctyne 2, ynamine 3 and dimethyl acetylenecarboxylate (4) in different nonprotic solvents. The second were the reactions of the nitrones 5 and 6 with dipolarophile 7. Semiempirical calculations (PM3) were done for the reactants. The resulting quantum descriptors HOMO-LUMO and the transition state quantum descriptors (LUMO$_{dipolarophile}$ - HOMO$_{dipole}$ (HdL) and LUMO$_{dipole}$ – HOMO$_{dipolarophile}$ (LdH)) were plotted against solvent parameters, in order to obtain predictive computational models. Good to excellent correlations were obtained for these reactions. The multiparameteric models obtained were corrected for collinearity by using Ridge regression.

Keyword: solvent effects, regression analysis, 1,3-dipolarcycloaddition , HOMO-LUMO..

Introduction

The 1,3- dipolar cycloaddition(DC) reactions are versatile method for the synthesis of five-membered heterocyclics[1]. The reaction involves the cycloaddition of 1,3-dipole to a double bond(dipolarophile) to form a five-membered ring (Scheme I).



Scheme I

The addition is stereoselective, where new chiral centers are created due to the syn attack of the 1,3-dipole on the double bond[1].

DC reactions are a thermally allowed [$_{\pi}$ 4 $_{s}$ + $_{\pi}$ 2 $_{s}$] concerted reactions [3]. Hence the transition state (T.S.) is controlled by frontier orbitals of the reactants. Depending on the nature of the dipoles and the dipolarophiles, the overlap of these orbitals achieved in three manners: type I, II and III, which are controlled by HOMO-LUMO energy gap[2]. In type I or normal electron demand reactions, the reaction is controlled by the HOMO of the dipole i.e. a nucleophilic dipole. In type II, the reaction is controlled by HOMO-LUMO of the dipole and the rate of reaction does not affected by presence of EWG or EDG in the dipolarophile. The third type of reactions the inverse electron demand reactions, is LUMO-dipole controlled, the dipole behaves as electrophile.

However, azomethine yildes are of great importance in DC reactions. Its reaction with dipolarophiles produces pyrroline and pyrrolidine with high stereoselectivity[4-10]. The stereoselective addition of nitrones to dipolarophiles produces isoxazlidine a precursor of many alkaloids [10b-d, 11b].

Since most organic reactions are done in solution, the change of solvent may minimize reaction times or maximize yields. Therefore understanding solvent effects for any reaction is of vital importance to academia and industry. The effect of solvent can be categorized as general solvent effects and specific solvent effects [12]. The first are the solvent bulk macroscopic physical properties, which are long range forces such as dielectric constant (Ɛ) (usually described by Kirkwood function f(Ɛ)[12]) and refractive index (n) (usually described by Lorentz-Lorentz function $f(n^2)$[12]). Dielectric constant is a function of molecular dipole moment and polarizability. While refractive- index is a function of permittivity and polarizability. The specific solvents effects are chemical in nature depend on the structure of solvent molecule; hence they convey more information about the interactions with solute molecules. They result in the formation of solvation complexes. The strength of these interactions are usually described in terms of many empirical parameters, such as α(hydrogen bond donor)[12], β(hydrogen bond acceptor)[12], E (electrophilicity), B(nucleophilicity), DN Gutmann's donor number(Lewis basicity)[13], AN Gutmann's acceptor number (Lewis acidity)[13] …..etc.

Although DC reactions are important synthetic reactions, there are few studies on the solvent effects of these reactions in the literature [15a-c]. The correlation of rate constant with solvent parameters may convey valuable information about the solvent effects on the reaction rate [14]. Hence the rate constants of two different types of DC reactions were taken from literature, namely the reaction of azomethine yilde (1) with cyclooctyne(2), ynamine(3) and dimethyl acetylenedicarboxylate(4)[15a], and the second is the reaction of(E)-3,3,3-trichloro-1-nitroprop-1-ene(7) with ketonitrones, C,C,N-triphenylnitrone (5), and C-fluorine-N-phenylnitrone (6)[15b]. The rate constants (experimental descriptor) in different aprotic solvents were plotted against solvent parameters to produce single and multiparametric equations. Besides the plots of the ground state quantum descriptors (HOMO, LUMO) and, T.S. quantum descriptors (HdL, LdH)) against solvent parameters.

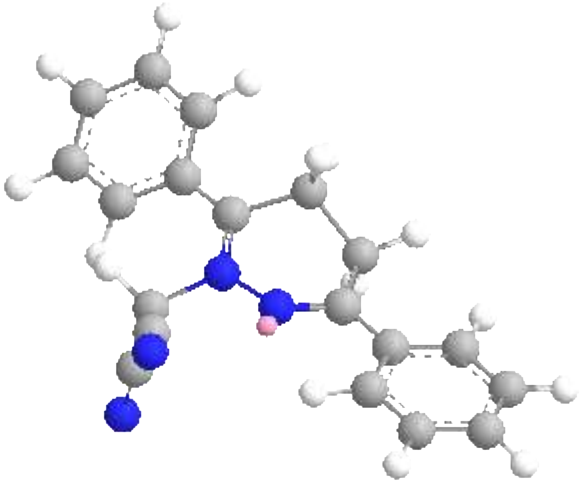
Computational and Statistical Details

The structures of the 1,3-dipoles and dipolarophiles(scheme II) were optimized with semiempirical PM3 method using Gaussian9. The calculation were carried out for each compound in the proper solvent applying continuum model (PCM) and at restricted closed shell Hartree-Fock(RHF) level.

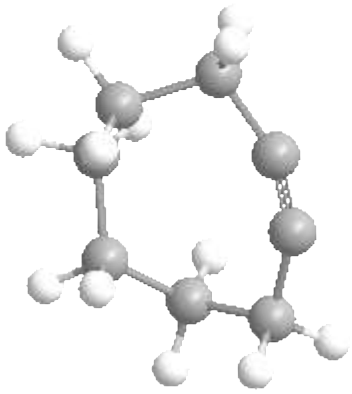
The single and multiparametric equations were calculated using SPSS version 20. Correlations between variables were considered significant at $p< 0.05$ and following the higher R^2[16]. Analyses of variance (ANOVA) were also done to assess the uncertainty. Multiparameter models were subjected to Ridge regression in order to avoid collinearity. Only models with variance inflation factor VIF< 10 were considered.

Results and Discussion

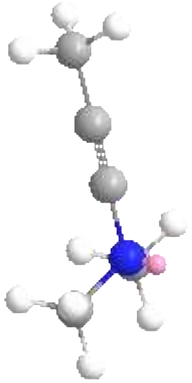
The rate constant, the calculated HOMO-LUMO for each dipolarophile and the dipole, and the energy difference HdL and LdH, in the corresponding solvent together with the solvent parameters are listed in tables 1,2 ,3,4, and 5.



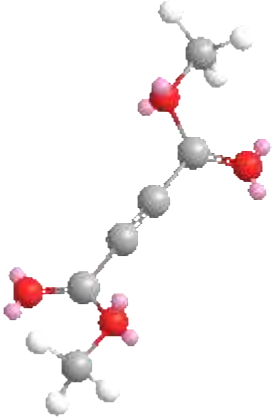
Dipole 1



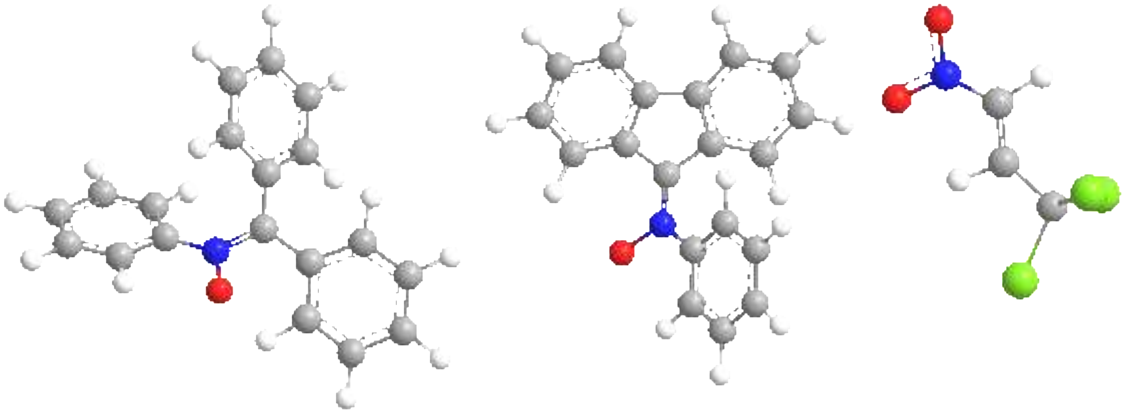
Cyclooctyne 2



Ynamine 3



Dimethyl acetylenedicarboxylate 4



Nitrone 5 Nitrone 6 Dipole 7

Scheme II

The reaction of azomethine 1

The output of the regressions of logk with single experimental descriptors (solvent parameters) or single quantum descriptors (ground state descriptors HOMO-LUMO dipolarophiles, and HOMO-LUMO dipole, T.S. descriptors HdL and LdH) of the reaction of the 1,3-dipole 1 with cyclooctyne 2,ynamine 3 and dimethyl acetylenecarboxylate 4 are shown in tables 6. Since the three reactions were between one dipole and three different dipolarophiles, logically the solvation appears may be mainly the impact of solvent on the dipolarophiles, at least for those obeyed the same mechanism. Although results indicate mainly poor correlations $R^2 <0.9$, still many of them are significant $p< 0.05$. Hence only cases with $p<0.05$ were taken into consideration. It seems that there are two modes of solvation for these reactions. The first in case of the reaction of compounds 2 and 4 with 1 where a negative solvation are shown for solvent polarization and polarizability (negative coefficients for E_T 30and f(ε)). While logk for the reaction of compound 3 with 1 increase as the solvent polarization and polarizability increase (positive coefficients for E_T30 and f(ε)). This result is in agreement with the different mechanisms that have been explained for these reactions [15a-c]. A stereospecific concerted one for the reaction of compounds 2 and 4 with 1and a nonstereospecific two step reaction via zwitterionic intermediates for the reaction of the ynamine 3 with 1. A concerted mechanism leads to a less polar T.S. which obviously needs negative solvation through the solvent polarization. In contrast more polarized medium needs for the generation of a zwitterionic intermediate i.e. positive solvation through the solvent polarization.

However the following multiparametric equations were obtained for the reaction of dipolarophile 2 with the dipole 1:

$$logk = -.749 - .023AN - .0065DN - 1.404f(\varepsilon) \dots (1)$$

R^2 =.9905, F=69.587, sig. =.0142.

$$logk = -1.997 - .027AN - .0082DN + 3.104f(n2) \dots (2)$$

R^2 =.9749, F=25.88, sig. =.0374.

Equation 1 clearly suggests that the reaction is retarded by both the specific solvation (Lewis acidity-basicity, negative AN, DN) and the general polarization solvation (negative f(ε)). In table 6 $LUMO_1$ showed a negative and $HOMO_2$ showed positive correlation with logk. This is accordance with experiment [15a-c]. Since the reaction is an inverse demand type i.e. as $LUMO_1$ decrease and $HOMO_2$ increase the rate of the reaction increase.

A collinear significant correlation was obtained for the reaction of the dipolarophile 4 with the dipole 1 (table 6):

$$logk = -3.408 - 0.017AN \ldots.(3)$$

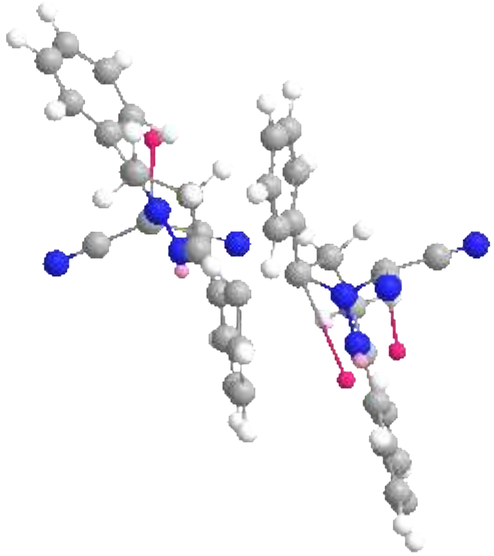
R^2 =0.789, t=3.351, sig.=0.044.

The best dual parameteric equation obtained for the reaction of 4 was:

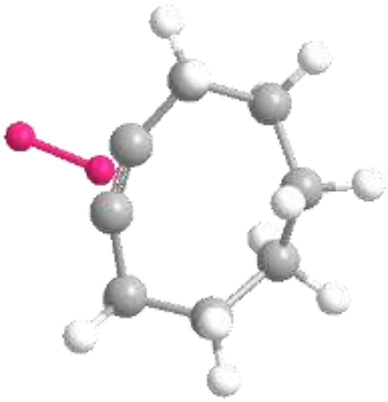
$$logk = -2.977 - .0344\, AN - .01137\, DN \ldots (4)$$

R^2 =.8985, F=13.272, sig. =.0324.

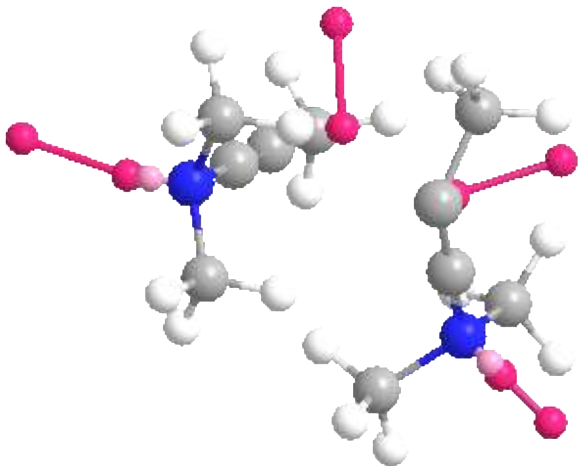
It seems that dimethyl acetylenecarboxylate 4 is strongly solvated (reaction retardation) through the resonance structures (scheme IV); these are the LUMO of the dipolarophile 4 which is attacked by the HOMO of the dipole[15].This was consistent with the negative correlation of $LUMO_4$ and positive correlation of $HOMO_1$ with logk found (table 6). Also the electrophilic triple bond (scheme III) needs desolvation prior to attack by the electron-poor azomethine 1 (negative DN and AN):



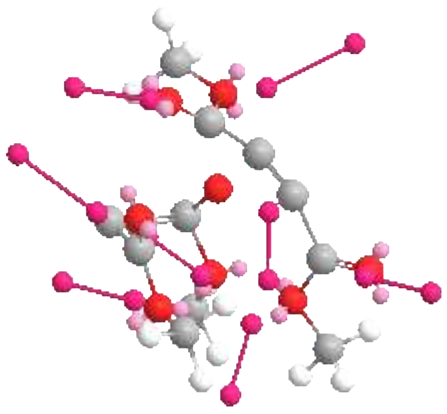
The dipole 1 in resonance, the solvent shown in pink. E_T30(-ve), AN(+ve), DN (-ve), π*(-ve) HOMO1 and E_T30(+ve),AN (-ve), DN(+ve), π*(+ve) for LUMO1



Cyclooctyne 2 ,HOMO2 E_T30(-ve), AN(+ve), π*(-ve)



HOMO3 LUMO3
Yenamine 3, AN(+ve), E_T30(-ve) π*(-ve) for HOMO3 and LUMO3.



LUMO4 HOMO4
Dimethyl actylenedicarboxylate 4 AN(-ve), DN(+ve), E_T30(+ve), π*(+ve) for both HOMO4 and LUMO4.

Scheme III

$$logk = -6.12 + 0.151ET30 \ldots.(5)$$

R2=0.945, t=9.271, t $_{table}$=5.208, sig.=0.001

$$logk = -2.701 + 6.478f(\epsilon) \ldots.(6)$$

R2=0.746, t=3.832,t $_{table}$=2.447, sig.=0.012

$$logk = -6.0176 + .1428ET30 + .0135AN \ldots(7)$$

R^2 =.9896, F=142.5105, sig. =.001.

$$logk = -6.4759 + .1631ET30 - .0129DN \ldots(8)$$

R^2 =.9654, F=55.8735, sig. =.001.

In the above there are single and multiparametric equations belongs to the reaction of the ynamine 3 with the dipole 1which is claimed to occur via zwitterionic intermediate rather than concerted mechanism found for the other two dipolarophiles 2 and4[15].However equation 4 and 5 showed that the reaction is accelerated by solvent polarization(positive sign shown for E_T30 and f(ε)). The biparametric equations 6 and 7 indicates that the reaction is positively solvated by solvent acidity AN (or electrophilicity) and negatively solvated by solvent basicity DN (or nucleophilicity) . This result can be rationalized in terms of the solvation-complexes of both reactants (scheme III).

Two trend of solvation required by the reaction scheme III. The resonance structure of the dipole ($LUMO_1$) is positively solvated by polarization acidity and basicity (positive sign of f(ε),DN and AN) table 9 . On other hand, the free ynamine ($HOMO_3$) (negative sign of f(ε),E_T30,DN and AN table) is required to attack the $LUMO_1$. This is compatible with inverse electron demand reaction found for the reaction [15a] (table 2).

To obtain a predictive computational model for these reactions the quantum descriptors of the reactants plotted against the solvents parameters and the rate constant k. From tables 1, 2 and 3, one can deduce that the reaction of 2 and 3 with 1 are LUMOdipole-controlled and that of 4 with 1 is HOMOdipole- controlled i.e. from the values of LdH and HdL . However the best parametric equations found for the ground state quantum descriptors for the reaction of 2 with 1 were:

$HOMO2 = -0.365 - 0.001ET30 - 6.8 * E - 5DN + 0.001AN - 0.013\pi * \ldots (9)$

R^2 =.999, F_{cal}=338.309, F_{table}=244.583, sig. =.041

$LUMO1 = -.068 + .001ET30 + 2.0 * E - 5DN - 6.0 * E - 5\ AN + .005\pi * \ldots (10)$

R^2=1.0,F_{cal}=14351.5, F_{table} =5624.583, sig.=.006.

$LdH = .297 + 8.8 * E - 5\ DN - .001\ AN + .018\pi *$... (11)

If we subtract equation (9) from equation (10), we obtain equation (11). From which we can conclude that LdH decreased (rate increase) as reactants solvated through acidity parameter (scheme III). While solvation of the dipole through DN and π* retarded the rate. The T.S. quantum descriptor LdH showed a positive correlation (positive sign for E_T30 and f(ε) for the dipolarophile 2. Hence as the polarizing ability of the solvent increase LdH increase i.e. the rate of the reaction decrease. This is compatible with the equation 14 and 15.

$LdH = 0.303 + 0.001E_T30 \ldots\ldots\ldots..(12)$

$R^2 = 0.822,\ \ t = 4.803\ , sig = 0.005$

$LdH = 0.31 + 0.001f(\varepsilon)\ \ \ldots\ldots\ldots\ \ \ldots(13)$

$R^2 = 0.992\ , t = 25.185\ , sig = 0.001$

$LdH = 0.3 + 0.001E_T30 - 5.* 10^{-5}AN \ldots\ldots\ldots.\ldots(14a)$

$R^2 = 0.878\ , t = 10.785\ \ \ sig = 0.043$.

$LdH = .3 + .000468ET30 - 5.0868 * E - 5AN \ldots (14b)$

R^2 =.872, F=10.2173, sig.=.0458.

$LdH = .305 + 9.95 * E - 5DN + .00021ET30 + .00066\pi * \ldots (14c)$

R^2 =.9429, F=16.5183, sig.=.0227.

$logk = 43.452 - 141.942\ LdH\ \ \ldots\ldots\ldots\ldots(15)$

$R^2 = 0.687\ \ \ , t = 3.315\ , sig = 0.021$

The reaction of dipolarophile 4 is HOMO dipole-controlled as deduced from table 3 and claimed in ref.15a. Two excellent multiparametric equations were obtained for the reaction of the dipolarophile 4:

$LUMO4 = -.046 + .001ET30 + 4.9 * E - 5DN - 8.9 * E - 5AN + .01\pi * ..(16)$

R^2 =1.0, F_{cal} =504.062, F_{table} =224.58, sig.=.033.

$HOMO1 = -.288 - .001ET30 - .001DN + .703AN - 1.002\pi * \ldots (17)$

R^2 =.999, F_{cal} =327.55, F_{table} =224.58, sig.=.041.

Upon subtraction of equation (16) from equation (17) HdL is obtained:

$HdL = .242 + .0051DN - .702AN + .99\pi *$…(18)

This indicates that the reaction is positively solvated by solvent acidity AN, solvation of dipolarophile , and retarded by solvation of the dipole by DN and π*.

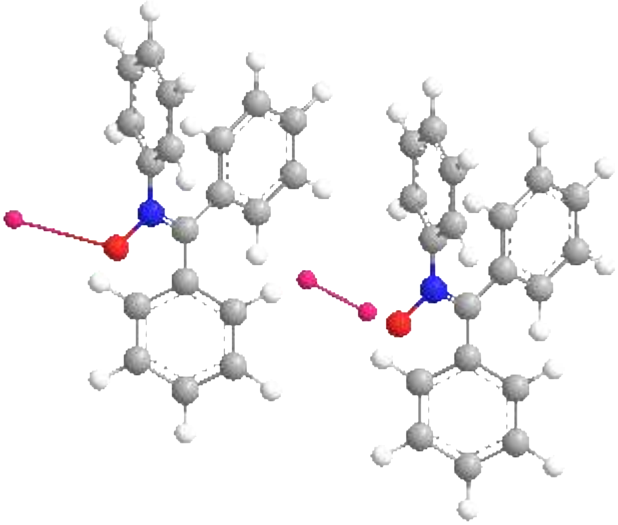
Also inverse correlation found for logk with HdL (negative sign of HdL equation 12) means that the reaction becomes faster as HdL decrease.

$\log k = 14.523 - 64.5\ HdL \ldots\ldots$.......... (19)

$R^2 = 0.504\ , t = 2.256, sig = 0.074.$
In case of ynamine 3 the following equations were obtained:
$HOMO3 = -.308 - .001ET30 - .001DN + .022AN + .001\pi * \ldots (20)$
R^2 =.999, Fcal=356.335, F_{table} =224.58, sig. =.04.
$LUMO1 = -.068 + .001ET30 + 2.0 * E - 5\ DN - 6.0 * E - 5\ AN + .005\pi * \ldots (21)$
R^2 =1.0, F_{cal} =14351.504, F_{table} =5624.58, sig.=.006.
The best model obtained for the reaction of ynamine 3 is different from those obtained for the reaction of dipolarophiles 2and 4, which may suggest different mechanism[17].

Reaction of nitrones

Table 7 showed the single regression of logk, of the reaction of the nitrone 5 with the alkene 7, with solvent parameters. It appears that the reaction is highly retarded by polarization and polarizability; negative f(ε) coefficient R^2 =0.984 sig.=.008, negative E_T30 coefficient R^2=0.953 sig.=0.024 and negative π^* coefficient R^2=0.909 sig.=0.47. High retardation of the reaction are also shown by Lewis acidity of the solvent, since a free negative oxygen is required for reaction (scheme V); excellent negative correlation with AN was found, R^2=0.998 t_{cal}=21.676 sig.=0.029.



Solvated oxygen and free oxygen

Scheme IV

Dual parametric equations showed excellent but less significant correlations:
$logk = 2.109 - ..005E_T30 + .379f(\varepsilon) \ldots. (23)$
R^2=1.0, F=2094.348, sig.=..015.
$logk = 2.231 - .007E_T30 - 0.218\pi * \ldots. (24\ )$
R^2=0.996, F=118.88, sig. =0.065.

Again similar effects were shown for the solvent on the ground state quantum descriptors HOMO-LUMO. Where polarization and polarizability parameters showed negative coefficients ($HOMO_5$) tables 20; f(ε) R^2=.999 t_{cal}=44.641 sig.=.001,E_T30 R^2=.903 t=4.319 sig.=.05, and π^* R2=.946 t5.946 sig.=.027. The excellent negative correlation shown by the acidity parameter AN, R^2 =1.0 t=84.051 sig. =.008, indicate that the electron pair of the $HOMO_5$ needs to be free (desolvated) in order to react. Since the reaction is a normal electron demand type (as shown from table 4; $\Delta E = H_5L_7 < L_5H_7$), the $HOMO_5$ orbital rather than the $LUMO_5$ worth to be considered. The T.S.quantum descriptor Hd_1L showed positive correlation with the polarization and polarizability solvents parameters; f(ε) R^2=.998, t_{cal} =35.663 ,sig.=.001, E_T30 R^2=.909 t=4.468 sig.=.047, π^* R^2=.941 t=5.644 sig.=.03. This indicates a polar T.S.[14b]. While the excellent correlation of the acidity parameter AN (R^2=1.0 t_{cal}=29676.474 sig.=.004) indicate that T.S. is stabilized by more acidic solvents.

$HOMO5 = -.338 - 6.27 * E - 5ET30 - .032f(\varepsilon) \ldots (25)$

R^2 =1.0, F=4072.215, sig. =.011.

$HOMO5 = -.338 - .034f(\varepsilon) - .001d \ldots (26)$

R^2=1.0, F=1696.472, sig. =.017.

$LUMO7 = -.0644 + 7.57\ ET30 + .0156\ f(\varepsilon) \ldots (27)$

R^2 =.9964, F=136.5932, sig. =.060392.

The solvation of the two reacting orbitals seems to oppose each other (equations 25 and 27), which result in reaction retardation, since the rate increase as $HOMO_5$ increase and $LUMO_7$ decrease.

However the reaction of the nitrone 6 seems to behave opposite. Although the correlation of logk with solvent parameters are poor, they show positive correlation with the polarization and polarizability parameters (f(ε), E_T30 and π^*) table 7. While the more significant correlation shown by AN indicates that the solvation of the dipolarophile prevails. In which the solvent polarizes the double bond and solvated the nitro group of the dipolarophile 7.

$logk = .823 + .02237\ DN + .237\ f(\varepsilon) \ldots (28)$

R^2 =.9628, F=25.893, sig. =.0372.

Equation 28 reflected a positive correlation through the solubility of the dipole 6. This is confirmed by the fair correlation found for the $LUMO_7$ with solvent acceptor number AN, R^2= .918 t_{cal}=4.736 sig. =.042(table 23).

On other hand the quantum descriptors showed good to excellent correlation with the polarization and polarizability parameters table 12. Which indicate a polar T.S.[15b]. The $LUMO_6$ is lowered by solvent polarization and polarizability, whereas the $HOMO_7$is raised (equation 28 and 29). This is in accord with inverse electron demand shown by this reaction table 5($L_6H_7<H_6L_7$).

$LUMO6 = -.022 - .011\ \pi * -.0001\ ET30 \ldots (29)$

R^2 =.962, F= 25.317, sig. =.038.

$HOMO7 = -.419 + .0009\ \pi * +.0001\ ET30 \ldots (30)$

R^2 =.956 F=21.695, sig. =.044.

Conclusion

The change in rate of the reaction of 2 and 4 with 1 are not huge upon changing the solvent. 2 reacts a little slower in polar acidic solvents such as acetonitrile, chloroform, and dichloroethane. Also solvents with high AN and DN retard the reaction of 4. In contrast the the ynamine 3 reacts faster in polar acidic solvents.

On other hand, the nitrones 5 and 6 showed different solvent effects behavior . Nitrone 5 was faster in nonpolar solvents such as toluene (E_T30 is –ve equation 23). While nitrone 6 was faster in polar solvent such as nitromethane (f(ε) is positive equation 28).

Conflict of Interests.
There are non-conflicts of interest .

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Table 1: cycloaddition between dipolar azomethine ylide with dipolarophiles cyclo octyne:-

solvent	k^{a}	log k	E_T30^b	π^c	f(ε)^{d}	f(n^{2})^{e}	DN^{f}	AN^{g}	HOMO	LUMO	HOMOd	LUMOd	HdL	LdH
toluene		-1.15366	33.9	.49	.241	.293	.1	3.3	-.37649	.03863	-.31063	-.06163	.34926	.31486
PhCl	.04020	-1.39577	36.8	.68	.377	.306	3.3		-.37834	.03593	-.31429	-.06098	.35022	.31736
THF	.02330	-1.63264	37.4	.55	.405	.245	20.2	8.0	-.3787	.0354	-.31502	-.06078	.35042	.31792
CHCl3	.01520	-1.81816	39.1	.69	.356	.265	4.00	23.1	-.37802	.03637	-.31367	-.06115	.35004	.31687
Dichloro ethane	.01500	-1.82391	40.7	.73	.420	.255	1.00	20.4	-.37892	.0351	-.31545	-.06066	.35055	.31826
acetone	.01480	-1.82974	42.2	.62	.465	.220	17.00	12.5	-.37955	.03419	-.3167	-.0602	.35089	.31935
CH3CN	.01220	-1.91364	45.6	.66	.480	.212	14.10	18.9	-.37977	.03388	-.31714	-.06003	.35102	.31974

a.ref.14, b.ref.11and12, c.ref.11, d.ref.11^{b}, e.ref.11^{b}, f.ref.12, g.ref.12

Table 2: cycloaddition between dipolar azomethine ylide with dipolarophiles ynamine:-

solvent	HOMO	LUMO	HOMOd	LUMOd	HdL	LdH	k^{a}	logk	E_T30^b	π^c	f (ε)^{d}	f(n^{2})^{e}	DN^{f}	AN^{g}
toluene	-.32592	.0599	-.31063	-.06163	.3705	.26429	.08380	-1.08	33.9	.49	.241	.293	.1	3.3
PhCl	-.32892	.05711	-.31429	-.06098	.3714	.26794	.49300	-.31	36.8	.68	.377	.306	3.3	
THF	-.32953	.05657	-.31502	-.06078	.37159	.26875	.22000	-.66	37.4	.55	.405	.245	20.2	8.0
CHCl3	-.3284	.05758	-.31367	-.06115	.37125	.26725	.70100	-.15	39.1	.69	.356	.265	4.0	23.1
Dichloro ethane	-.32984	.05624	-.31545	-.06066	.37169	.26918	1.28000	.11	40.7	.73	.420	.255	1.0	20.4
acetone	-.33087	.05533	-.3167	-.0602	.37203	.27067	1.56000	.19	42.2	.62	.465	.220	17.0	12.5
CH3CN	-.33119	.05501	-.31714	-.06003	.37215	.27116	5.79000	.76	45.6	.66	.480	.212	14.1	18.9

Table 3 :cycloaddition between dipolar azomethine ylide with dipolarophiles dimethyl acetylene dicarboxylate :-

solvent	HOMO	LUMO	HOMOd	LUMOd	HdL	LdH	k^{a}	log k	E_T30^b	π^c	F (ε)^{d}	F(n^{2})^{e}	DN^{f}	AN^{g}
toluene	-.43202	-.03621	-.31063	-.06163	.27442	.37039	.000914	-3.04-	33.9	.49	.241	.293	.1	3.3
PhCl	-.43118	-.03486	-.31429	-.06098	.27943	.3702	.000482	-3.32-	36.8	.68	.377	.306	3.3	
THF	-.43099	-.03455	-.31502	-.06078	.28047	.37021	.000304	-3.52-	37.4	.55	.405	.245	20.2	8.0
CHCl3	-.43134	-.03511	-.31367	-.06115	.27856	.37019	.000163	-3.79-	39.1	.69	.356	.265	4.0	23.1
Dichloro ethane	-.43088	-.03437	-.31545	-.06066	.28108	.37022	.000157	-3.80-	40.7	.73	.420	.255	1.0	20.4
acetone	-.43054	-.0338	-.3167	-.0602	.2829	.34034	.000215	-3.67-	42.2	.62	.465	.220	17.0	12.5
CH3CN	-.43042	-.03359	-.31714	-.06003	.28355	.37039	.000223	-3.65-	45.6	.66	.480	.212	14.1	18.9

Table 4:- cycloaddition of C,C,N-triphenylnitrone and (E)-3,3,3-trichloro-1-nitroprop-1-ene.

solvent	HOMO d1	LUMOd1	HOMO	LUMO	HdL	LdH	k^a	log k	E$_T$30^b	π^c	F (ε)^d	f(n^2)^e	DN^f	AN^g
PhCH3	-.34688	-.01525	-.40938	-.05844	.28891	.3939	73.74	1.86770	33.9	.54	.241	.2264	.1	3.3
PhCl	.34712	-.01523	-.04092	-.05821	.2964	.3917	62.67	1.79706	37.5	.71	.377	.23450	3.3	
CH3NO2	-.35202	-.01519	-.40697	-.0556	.3026	.3900	52.16	1.71734	46.3	.80	.481	.18790	2.7	20.5
CH2ClCH2Cl	-.35595	-.01541	-.40547	-.05335	.29958	.3909	57.16	1.75709	41.3	.81	.431	.25500	.0	16.7

Table 5:- cycloaddition of C-fluorine-N-phenylnitrone and 3,3,3-trichloro-1-nitroprop-1-ene.

solvent	HOMO$_{d2}$	LUMO$_{d2}$	HOMO	LUMO	Hd1L	Ld2H	k^a	log k	E$_T$30^b	π^c	f (ε)^d	f(n^2)^e	DN^f	AN^g
PhH	-.38635	-.03525	-.40938	-.05844	.37413	.32791	8.96	.95231	34.5	.59	.23200	.22670	.1	8.2
PhCH3	-.38626	-.03545	-.04092	-.05821	.37375	.32942	8.78	.94349	33.9	.54	.24100	.22640	.1	3.3
PhCl	-.38502	-.03836	-.40697	-.0556	.36488	.33095	11.81	1.07225	37.5	.71	.37700	.23450	3.3	
CH3NO2	-.3843	-.04059	-.40547	-.05335	.3667	.33013	11.4	1.05690	46.3	.80	.48100	.18790	2.7	20.5

Table 6: Reaction of dipole 1 with dipolarophiles 2,3 and 4; regression of logk with solvent and quantum parameters.

	R^2 2	R^2 3	R^2 4	Sign 2	sign 3	sign 4	t 2	t 3	t 3	Sig 2	Sig 3	Sig 4
HOMO	0.706	0.742	0.485	+	-	-	3.465	3.794	2.168	0.018	0.013	0.082
LUMO	0.71	0.748	0.481	+	-	-	3.501	3.855	2.153	0.017	0.012	0.084
ET30	0.784	0.945	0.538	-	+	-	4.263	9.271	2.412	0.008	0.001	0.061
π*	0.414	0.484	0.546	-	+	-	1.88	2.164	2.452	0.119	0.083	0.058
LdH	0.687	0.756	0.124	-	+	+	3.315	3.935	0.841	0.021	0.011	0.439
HdL	0.699	0.758	0.504	+	-	-	3.408	3.959	2.256	0.019	0.011	0.074
f(ε)	0.715	0.746	0.524	-	+	-	3.538	3.832	2.348	0.017	0.012	0.066
f(n^2)	0.659	0.507	0.406	+	-	+	3.107	2.266	1.849	0.027	0.073	0.124
DN	0.199	0.086	0.072	-	+	-	1.113	0.687	0.624	0.316	0.523	0.56
AN	0.682	0.535	0.782	-	+	-	2.928	2.147	3.787	0.043	0.098	0.019
HOMO$_{dipole}$	0.707	0.751	0.513	+	-	+	3.477	3.883	2.297	0.018	0.012	0.07
LUMO$_{dipole}$	0.629	0.77	0.386	-	+	-	2.912	4.095	1.774	0.033	0.009	0.136

Table 7: Reaction of C,C,N-triphenylnitrone 5, and C –fluorine-N-phenylnitrone 6 with (E)-3,3,3-trichloro- 1-nitroprop-1-ene 7, regression of logk with solvent and quantum parameters.

	R^2 5	R2 6	Sign 5	Sign 6	t 5	t 6	sig. 5	sig. 6
ET30	0.953	0.453	-	+	6.357	1.578	0.024	0.213
π*	0.909	0.566	-	+	4.464	1.978	0.047	0.142
f(ε)	0.984	0.669	-	+	10.944	2.46	0.008	.091
f (n^2)	0.826	0.067	+	-	3.077	.463	0.091	0.675
DN	0.162	0.821	-	+	0.622	3.713	0.597	.034
AN	0.998	0.922	-	+	21.676	4.878	0.029	0.04
HOMO5	.99		+		14.384		.005	
LUMO7	.994		-		19.00		.003	
H$_5$L$_7$	.992		-		15.869		.004	
LUMO$_6$		.674		-		2.491		0.088
HOMO$_7$		.68		+		2.569		0.083
L$_6$H$_7$		.68		-		2.525		0.086

Table 8: reaction of dipole 1 with cyclooctyne 2, regression of LUMO$_1$, HOMO$_2$ and L$_1$H$_2$with solvent parameters

	R^2 LUMO$_1$	R2 HOMO$_2$	R2 L$_1$H$_2$	Sign LUMO$_1$	Sign HOMO$_2$	Sign L$_1$H$_2$	T LUMO$_1$	t HOMO$_2$	t L$_1$H$_2$	Sig. LUMO$_1$	Sig HOMO$_2$.	Sig. L$_1$H$_2$
ET30	.853	.793	.822	+	-	+	5.391	4.38	4.803	.003	.007	.005
π*	.171	.285	.246	+	-	+	1.014	1.413	1.279	.357	.217	.257
f(ε)	.946	1.00	.992	+	-	+	9.32	130.786	25.185	.001	.001	.001
f(n2)	.736	.637	.677	-	+	-	3.748	2.96	3.236	.013	1.871	.023
DN	.435	.412	.424	+	-	+	1.961	1.871	1.918	.107	.12	.113
AN	.161	.249	.219	+	-	+	.875	1.15	1.06	.431	.314	.349

Table 9: reaction of dipole 1 with ynamine 3, regression of LUMO$_1$, HOMO$_3$ and L$_1$H$_3$ with solvent parameters.

	R^2 HOMO$_3$	R2 LUMO$_1$	R2 L$_1$H$_3$	Sign HOMO$_3$	Sign LUMO$_1$	Sign L$_1$H$_3$	t HOMO$_3$	t LUMO$_1$	t L$_1$H$_3$	Sig. HOMO$_3$	Sig. LUMO$_1$	Sig. L$_1$H$_3$
ET30	.853	.785	.809	+	-	+	5.391	4.276	4.597	.003	.008	.006
π*	.171	.282	.256	+	-	+	1.014	1.403	1.311	.357	.22	.247
f(ε)	.946	1.0	.996	+	-	+	9.32	175.279	35.906	.001	.001	.001
f(n2)	.738	.635	.665	-	+	-	3.748	2.948	3.148	.013	.032	.025
DN	.435	.418	.426	+	-	+	1.961	1.896	1.927	.107	.116	.112
AN	.161	.245	.225	+	-	+	.875	1.139	1.079	.431	.318	.341

Table 10: reaction of dipole 1 with dimethyl acetylenedicarboxylate 4,regression of $HOMO_1$, LUMO4 and H_1L_4 with solvent parameters.

	R^2 $HOMO_1$	R^2 $LUMO_4$	R^2 H_1L_4	Sign $HOMO_1$	Sign $LUMO_4$	Sign H_1L_4	t $HOMO_1$	t $LUMO_4$	t H_1L_4	sig. $HOMO_1$	Sig. $LUMO_4$	Sig. H_1L_4
ET30	.794	.82	.802	-	+	+	4.389	4.78	4.503	.007	.005	.006
π*	.284	.251	.275	-	+	+	1.41	1.294	1.376	.218	.252	.227
f(ε)	1.0	.994	.999	-	+	+	136.86	28.145	65.911	.001	.001	.001
f(n2)	.639	.676	.65	+	-	-	2.973	3.227	3.045	.031	.023	.029
DN	.413	.424	.645	-	+	+	1.875	1.917	1.888	.12	.113	.118
AN	.249	.224	.242	-	+	+	1.151	1.075	1.129	.314	.343	.322

Table 11: Reaction of C,C,N-triphenylnitrone 5 with (E)-3,3,3-trichloro-1-nitroprop-1-ene 7, regression of $HOMO_5$,$LUMO_7$ andH_5L_7 with solvent parameters.

	R^2 $HOMO_5$	R^2 $LUMO_7$	R^2 L_5H_7	Sign $HOMO_5$	Sign $LUMO_7$	Sign L_5H_7	t $HOMO_5$	t $LUMO_7$	t L_5H_7	Sig. $HOMO_5$	Sig. $LUMO_7$	Sig. L_5H_7
ET30	0.903	.919	0.909	-	+	+	4.319	4.761	4.468	0.05	.041	0.047
DN	0.184	.194	0.187	-	+	+	0.671	.693	.679	0.571	.56	0.567
AN	1.0	1.0	1.000	-	+	+	84.051	47.993	2886.174	0.008	.013	0.001
π*	0.946	.93	0.941	-	+	+	5.946	5.171	5.649	0.027	.035	0.03
f (ε)	0.999	.997	0.998	-	+	+	44.641	24.367	35.663	0.001	.002	0.001
f(n2)	0.885	.877	0.883	+	-	-	3.932	3.783	3.882	0.059	.063	0.06
LUMO	.999			-	+	+	41.585			.001		

Table 12:- Reaction of C –fluorine-N-phenylnitrone 6 with (E)-3,3,3-trichloro-1-nitroprop-1-ene 7, regression of LUMO6,$HOMO_7$ and $L_6H_7$with solvent parameters.

	R^2 $LUMO_6$	R2 $HOMO_7$	R2 L_6H_7	Sign $LUMO_6$	Sign $HOMO_7$	Sign L_6H_7	t $LUMO_6$	t $HOMO_7$	t L_6H_7	Sig $LUMO_6$	Sig $HOMO_7$	Sig L_6H_7
E_T30	.908	.889	0.9	-	+	-	5.454	4.906	5.209	0.012	0.016	0.014
DN	0.319	.324	0.321	-	+	-	1.185	1.199	1.191	.321	0.317	0.319
AN	0.918	.913	0.916	-	+	-	4.736	4.572	4.668	0.042	0.045	0.043
π*	0.931	.934	0.933	-	+	-	6.366	6.53	6.447	0.008	0.007	0.008
f(ε)	1.0	.999	1.0	-	+	-	172.287	56.503	123.675	0.001	0.001	0.001
f (n^2)	.058	.047	0.053	+	-	+	0.431	.383	.411	0.696	0.727	0.709
d	.796	0.696	0.713	-	+	-	2.817	2.623	2.732	.067	0.079	0.072

الخلاصة

في هذه الدراسة تم اجراء التحليل الانحداري لثابت التفاعل [15] مع معاملات المذيبات لمجموعتين من تفاعلات الاضافة الحلقي ال1و3-ثنائي القطب. الاولى هي تفاعل الازوميثاين(1) مع السايكلواوكتاين (2),و البينامين(3), و ثنائي مثيل اسيتيلين كاربوكسيليت(4). والمجموعة الثانية هي تفاعل النيترونات 5و6 مع الدايبولاروفيل 7 . كما تم اجراء الحسابات الشبه تجريبية للمتفاعلات حيث رسمت القيم الكمية الناتجة ضد معاملات التفاعل وضد معاملات المذيبات. وتم الحصول على نتائج متباينة الجودة لهذه التفاعلات. واجري تحليل رج الانحداري لغرض تصحيح الشذوذ الخطي للنماذج ذات المعاملات المتعددة. الغرض من هذه الدراسة هو الحصول على نموذج او نماذج والتي بواسطتها يمكن التنبؤ بالظروف المثالية للتفاعل قبل العمل المختبري.