A density functionnal study of hetero-Diels-Alder reactions with substituted nitrosoalkenes

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Abstract: Two mechanisms of cycloadditions of substituted nitosoalkenes to an alkene have been theoretically studied here : the [4+2] Diels Alder cycloaddition and the [3+2] dipolar cycloaddition.The chemoselectivity and the pathways of the reactions are discussed here.Density functionnal theory (DFT) calculations have been carried out using B3LYP functionnal and 6-31G* basis sets.

Keywords: cycloaddition, nitosoalkenes, Diels Alder cycloaddition , Density functionnal theory calculations, chemoselectivity, transition states calculation , reaction pathways .

I INTRODUCTION :

The hetero cycloaddition reactions are now largely used for the synthesis of new molecules of fondamental importance for the industry and for academic interest.
The computational model reactions studied here are the cycloaddition of substituted nitrosoalkenes with ethylene :

with R= H,
C6H5,
pNO2C6H5,
CO2Et
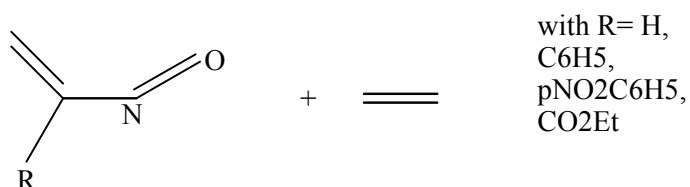
In previous experimental studies of this kind of reactions ,two types of products are obtained meaning that two mechanisms may be involved [1,2,3] :

An hetero Diels Alder type mechanism involving the s-cis nitosoalkene:[4+2] mechanism,

And a 1,3 dipolar cycloaddition involving the s-trans nitrosoalkenes:
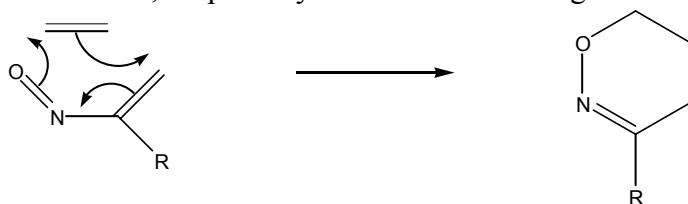
Hétéro Diels Alder [4+2]cycloaddition
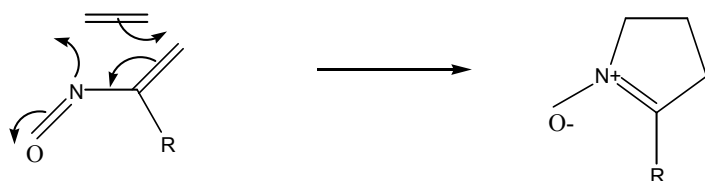
Dipolar 1,3 cycloaddition

R=H
R=C6H5
R=pNO2C6H4
R=CO2Et

We have tried here to determine the the reaction pathways for each case and to predict the favored cycloadducts.

II COMPUTATIONNAL DETAILS :

The DFT methods are now mostely used for studying structures and reactivity of chemical systems instead of traditionnal Hartree-Fock-correlation interaction calculations which are more difficult to perform.It appears in most DFT studies that hybrid funtionnals including gradient corrections and associated to the 6-31G* basis sets lead to potential energy barriers in good agreement with experiment[4-6].
In the present study the gradient corrected exchange and correlation functionnal Becke,Lee,Yang and Parr (B3LYP) [8] is used with the standard 6-31G* basis set implemented in the Gaussian 98 program[9] .
The reactants ,the products and the transition states have been studied and their structures completely optimized with the Berny analytical gradient optimisation method[10] .
The products and the reactants are checked to be minima of the reaction pathways with zero vibrationnal frequencies.
The transition states are determined using the QST2 or QST3 methods [11].Frequency calculations were performed for each transition state structure and the results checked for a single imaginary vibrational fraquency.Unrestricted calculations are performed for these states allowing so a possible biradical mechanism.

III RESULTS AND DISCUSSION

Optimized structures and characteristics of the transition states are given table 1.
The activation energies were estimated from B3LYP/6-31G* point energy calculations on the structures previously optimized (table 2).The energy pathways are drawn Scheme 1.

It appears that for the first three cases of substituents ,the cycloaddition occurs via a one step mechanism, only one transition state has been detected : they are concerted and synchroneous mechanisms(for R=H,the mechanism seems to be concerted but asynchrone since the bond distances R1 and R2 of the transition state are very different) .For the system involving the CO_2Et substituent ,the cycloaddition involves at least two transition states meaning that a non concerted mechanism occurs.In this case the reaction pathway seems more complicated and is not completly drawn.
The HOMO-LUMO energy gaps of the transition states calculated table 2 are large and this forbids stable biradical structures in all cases of substituents.

According to the calculated activation energies , it seems that the [4+2] Diels Alder mechanism occurs preferentially for H and pNO_2-C_6H_4 substituents leading to a six membered ring and that the one step 1,3 dipolar cycloaddition is favored for the C_6H_5 substituent leading to a five membered ring.
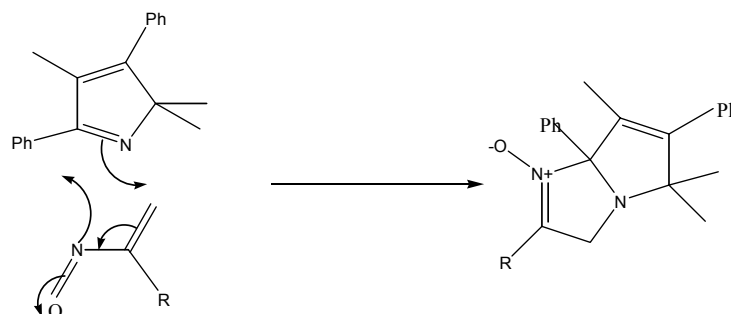For R= CO_2Et the favored cycloadduct is the six membered ring according to the energy pathway drawn scheme 1.
In real experimental synthesis, the substituents are generally bigger and ethylene plays here the role of a double bond of a complex organic molecule [1] , the Diels Alder mechanism is favored for the four cases.The two mechanisms occur , two types of cycloadducts exist except for R= CO_2Et .

Our results can be compared with those of the following experimental reactions involving this type of mechanisms [1] :
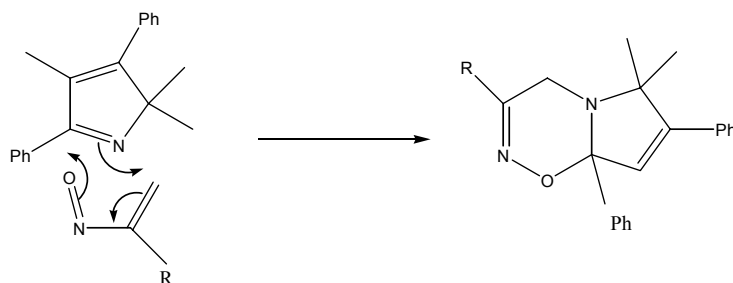
Hétero-Diels Alder [4+2] cycloaddition

Dipolar 1,3 cycloaddition

Our calculations are in agreement with experiment for R=H, pNO$_2$-C$_6$H$_4$,CO$_2$Et : the cis cycloaddition is favored ,but for R= C$_6$H$_5$ the favored cycloadduct is not the same.
Since the molecules are different some factors which are not taken into account in the computation may change the conclusion ,the comparison between experiment and theory could not be done, the stereochemistry and the electronic properties of the substituents have an important role in the reactionnal mechanisms .Moreover , the dienophyl componant in the experimental reactions is a C=N bond as it is a C=C bond in the computationnal model.

The solvant effect ,not taken into account here, may also change the chemoselectivity of the reactions and favor the dipolar 1,3 cycloaddition. If we consider the dipole moments (table 2), they are different for each species and the activation energies may change differently for the different reactions if a polar solvent is used. However , the solvent used experimentally is the dichloromethane which is a non polar solvent and would not have any influence on the activation energies.

The organic molecules of the experimental reactions are, however ,too big to be studied with quantum chemistry methods, especially pathways and transition states calculations are difficult to perform.

Table 1:characteristics of the transition states

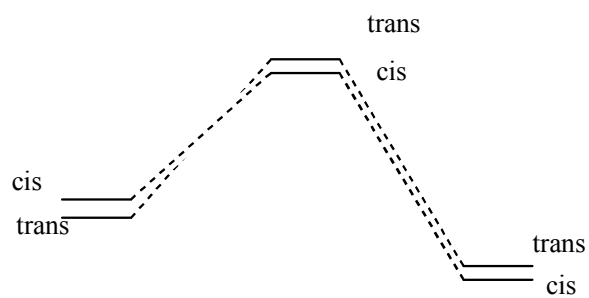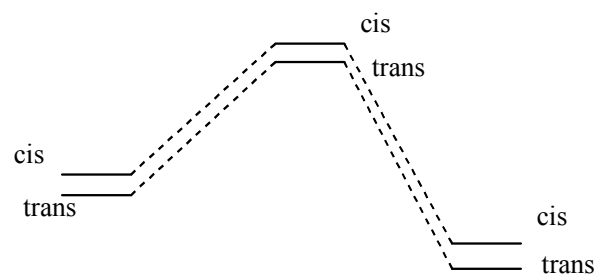| Dienes	R1(Å)	R2(Å)	R3(Å)	R4(Å)	Q1 $_O$	Q2 $_N$	Q3 $_C$	Q4 $_C$	Q5 $_C$
R=H cis	4.04	2.26			-0.35	-0.04	0.07	0.001	0.14
trans			2.48	2.19	-0.03	0.03	0.03	-0.01	0.10
R=C$_6$H$_5$ Cis	3.20	3.67			-0.28	0.01	0.13	-0.01	0.02
trans			2.60	2.11	-0.33	-0.05	0.001	0.01	0.11
R=pNO$_2$-C$_6$H$_4$ Cis	2.29	2.26			-0.33	-0.09	0.03	0.02	0.14
trans			2.63	2.10	-0.32	-0.05	0.02	0.01	0.13
R=CO$_2$Et Cis	2.24	2.26			-0.34	-0.06	0.06	-0.001	0.15
trans			3.63	4.16	-0.28	-0.02	0.08	-0.01	0.02
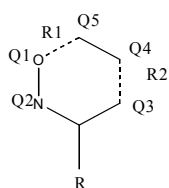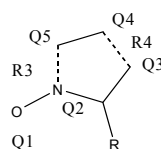
CIS CYCLOADDITION   TRANS CYCLOADDITION

Table 2 :Activation energy of the different cycloadditions ,dipole moments(Debye) and HOMO –LUMO gaps of the transition states.

Diènes		ΔE (kcal/mol)	$\mu_{reactant}$	μ_{TS}	$\mu_{product}$	ΔE$_{(HOMO-LUMO)TS}$ eV
1 R=H	Trans	29.08	3.11	3.57	4.06	2.92
	cis	10.43	2.77	3.58	3.56	3.34
2 R=C$_6$H$_5$	Trans	27.26	2.98	3.32	3.59	2.74
	Cis	46.20	2.69	2.57	3.07	3.24
3 R=pNO$_2$-C$_6$H$_4$	Trans	25.62	4.69	7.19	7.13	2.76
	Cis	4.81	4.29	6.06	6.69	3.20
4 R=CO$_2$Et	Trans	3.33	4.09	4.15 ; 4.96	4.99	2.47
	Cis	11.02	5.15	6.69 ; 3.71	3.75	5.72

R=H or R=C6H4NO2

trans
cis

cis
trans

trans
cis

R=C6H5

cis
trans

cis
trans

cis
trans

R=CO2Et

trans
cis
cis
trans

cis
trans

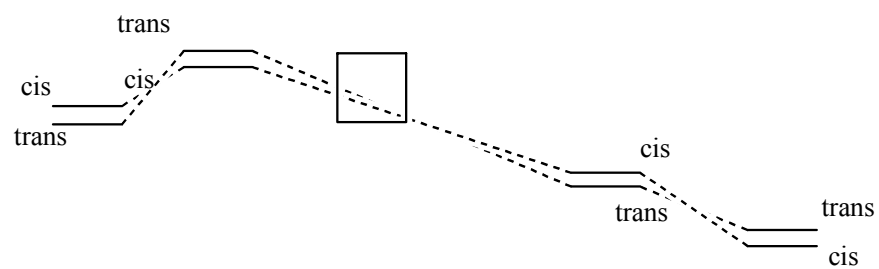trans
cis

Scheme 1 : Energy pathways for the different cycloadditions

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