

Theoretical study of the heterocyclic molecules reactivity in the normal electron demand Diels-Alder reaction

SAMEH AYADI¹, KHALED ESSALAH,
SLAHEDDINE KRICHANE and MANEF ABDERRABBA

¹Unite de recherche Physico-Chimie Moleculaire. IPEST,
Boite postale 51, 2070 la Marsa, Tunisie.

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ABSTRACT

The purpose of this work is a theoretical study of the Diels-Alder reactions between, a diene 2 like 2,3-dimethylbutadiene 2a₁ and 2-trimethylsilyloxybuta-1,3-diene 2b₁ with a series of 6-nitrobenzofuroxane 5a-c. From a thermodynamic and orbital point view, we discuss the possibility and the stereoselectivity of these kinds reactions.

Key words: normal electron demand Diels-Alder (NEDDA), DFT method, DNBF.

INTRODUCTION

Experimental study done by auteurs shows that the addition of 2,3-dimethylbutadiene to a solution of 4-aza-6-nitrobenzofuroxan 1 in CDCl₃ gives the product 3a₁ and 3'a₁. The auteurs carry out another experience, under similar conditions, but with a longer reaction time this reaction did not allow the isolation of 3a₁ and 3'a₁, but in adding advantage water in the solution, he obtained the hydrate 4, likes pale yellow solid, resulting from the reaction of 3a₁. The structure of 4 was determined by X-ray crystallography, which confirm that the addition of H₂O has taken place at the C₁₀=N₉ double bond¹.

Recently, it has been showed that the nitrobenzofuroxan (DNBF) are able to react as a dienophile or heterodiene in the Diels-Alder reactions [2-5]. In first stage, we have choice the 6-nitrobenzofuroxane molecules which looks like the 4-aza-6-nitrobenzofuroxan 1. We have only substitue the nitrogen atome number 4 of the molecule 1 by the C-R₃ groupment, then we obtient the molecules 5a-c (figure 2) which seems

particularly interessants for experimental study. The diene substitution was studied by substitution of 2,3-dimethylbutadiene 2a₁ by the 2-trimethylsilyloxybuta-1,3-diene 2b₁. In order to find the better calculation method which lead to better convergence for these kind of system, we have optimized molecule 4 by two different method SCF/6-31G and DFT/B3LYP with the basis set 3-21G. In second stage, we have studied the addition of diene 2a₁-b₁ on the 6-nitrobenzofuroxane 5a-c. In the end, from thermodynamic and orbital point of view we have discussed the possibility and the stereoselectivity of normal electron demand Diels-Alder reaction.

Theoretical study of the compound 4 Calculation method

Calculations are done at SCF level with standard basis sets 6-31G of GAUSSIAN 98 program⁶ and while using the DFT method of the same program with The B3LYP hybrid functional⁷⁻⁸ and basis sets 3-21G. The choice of this last method is justified by its efficiency in the treatment of system type⁹. The geometry of the various critical points on the potential energy surface was fully optimized with

the gradient method available in GAUSSIAN 98. Calculations of harmonic vibrational frequencies were carry out to determine the nature of each critical point.

RESULTS

In order to determine the reliability calculation methods in the treatment of this system type, we optimized the geometry of the compound 4. Putting in mind the stereochemistry of this molecule 4, we compare our theoretical results with the experimental data of the X-ray [1]. Table 1 regroups some geometric parameters of the optimized molecule and the X-ray data. The figure 2 shows the stereochemistry of the molecule 4 optimised at DFT level.

The SCF/6-31G and DFT method give result which agree with the experimental X-ray data of the compound 4. We noticed that the DFT method gives the best results. Therefore the calculation method of DFT/B3-LYP with the standard basis set 3-21G is more reliable with this system type⁹.

The geometry parameters data assigned to 4 is in complet agreement with our theoretical results. The distance ($d_{H7-H10} = 2.47 \text{ \AA}$) calculated by DFT/B3Lyp with the standard basis set 6-31G was in good accordy with the distance obtained by X-Ray crystallography : $d_{H7-H10} = 2.186 \text{ \AA}$.

Vibrational analysis

IR spectra calculate by DFT/3-21G method are also in accord with the experimental one ($\nu_{C6=C5(\text{theo})} = 1755 \text{ cm}^{-1}$ et $\nu_{C6=C5(\text{exp})} = 1609 \text{ cm}^{-1}$).

Table 1 : Selected optimized geometrical parameters for the compound 4

	SCF/ 6-31G	DFT/3 -21G	X-ray [6]
N4-C5	1.457	1.455	1.445
C7-C10	1.525	1.526	1.537
C11-C12	1.348	1.347	1.327
N2-C6	1.565	1.563	1.536
C5-O5	1.414	1.412	1.408
N4-C9	1.354	1.391	1.366
C13-C12	1.487	1.489	1.499
C6-C7	1.473	1.474	1.543
C5-C6	1.449	1.448	1.547
N4-H4	1.001	1.001	0.86
C9-N4-C5	115.373	115.377	115.8
N4-C5-C6	124.34	124.257	109.37
C5-C6-C7	119.587	119.585	111.81
C6-C7-C8	109.287	109.285	105.06
C11-C12-C13	121.030	121.050	122.55
C10-C11-C12	118.347	118.415	123.16
C7-C10-C11	108.642	108.768	116.39
C7-C8-C9	125.381	125.546	125.72

Distances are in Angstrom (\AA) and Angles in degrees ($^{\circ}$)

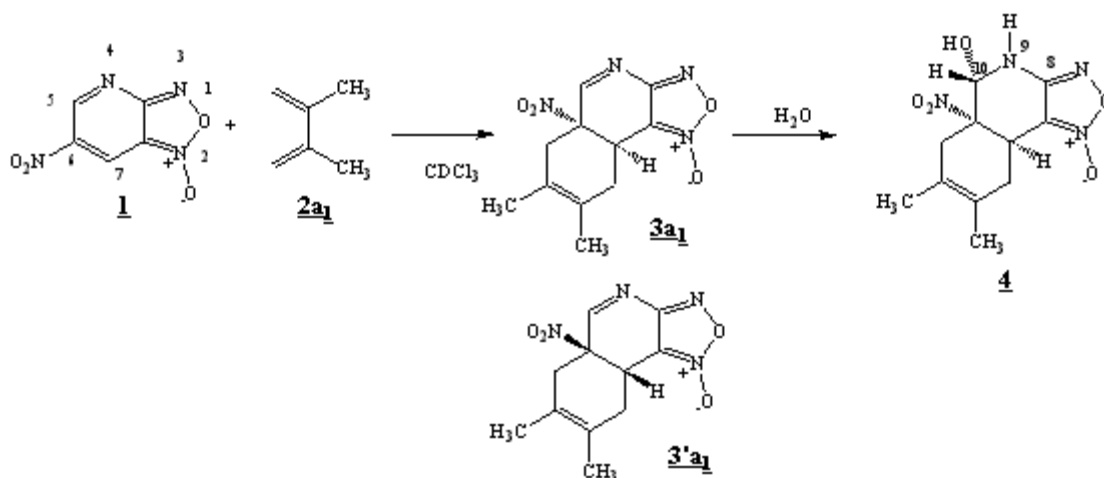


Fig. 1:

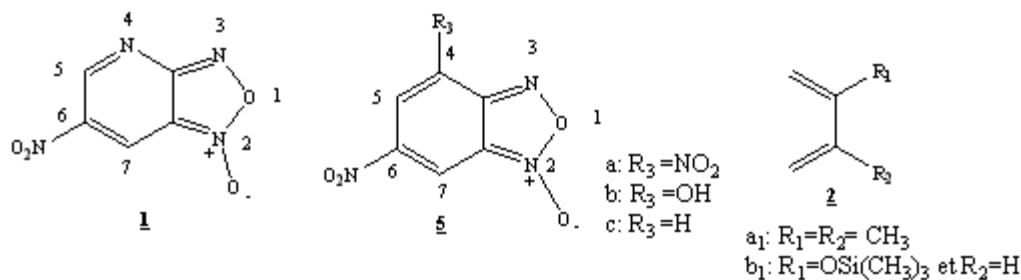


Fig. 2:

We noticed that the DFT method using the functional B3LYP and the standard basis set 3-21G gives the most results with this type of heterocyclic molecules. Therefore, we continue the thermodynamic study on Diels-Alder reaction between the heterocyclic molecules such as 4-aza-6-nitrobenzofuroxan 1 and 6-nitrobenzofuroxan 5a-c with the diene 2a₁-b₁, by using the DFT method with the functional B3LYP and the standard basis set 3-21G of the GAUSSIAN 98 program⁶.

DFT study of Diels-Alder reaction

Like the figure 4 shows, we have studied the possibility and also the stereoselectivity of normal electron demand Diels-Alder reaction between heterocyclic molecules such as 4-aza-6-nitrobenzofuroxan 1 and 6-nitrobenzofuroxan 5a-c with the diene 2a₁-b₁. The diene is activated by the substituent groupement – (CH₃) or – (OSi(CH₃)₃).

In the case of diene 2a₁-b₁ addition on the 6-nitrobenzofuroxane 5a-c, we have focused our attention to study the R₃ groupement on the Diels-Alder reaction. This study seems to be interesting from synthetic point of view.

The orbitals border study

We have determined the LUMO and the HOMO of diene 2a₁-b₁, by DFT/B3LYP with standard basis set method, and as well the LUMO and the HOMO of molecules 1 and 5a-c see table I. In each case of these reactions, the orbital diagram between the molecules 1 and the diene 2a₁-b₁, give a very good quantitative indication about the reactivity of our system. The most predominant interaction exists between the LUMO of dienophile and the HOMO of diene 2a₁-b₁. Therefore these reactions could be considered like the Diels-Alder reaction with normal electron demand^{10,11}. As example, we present Fig 5.

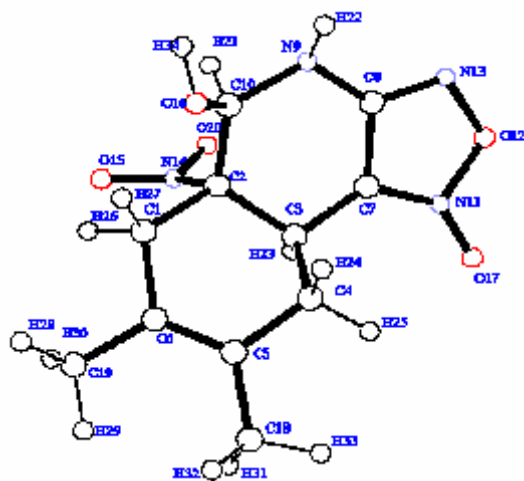


Fig. 3: DFT/ B3-LYP optimized geometries of the compound 4

Table 1: The LUMO and the HOMO of diene 2a₁-b₁ and heterocyclic molecules such as 4-aza-6-nitrobenzofuroxan 1 and 6-nitrobenzofuroxan 5a-c

	LUMO	HOMO
1	-0.132	-0.254
5a	-0.179	-0.289
5b	-0.149	-0.256
5c	-0.151	-0.264
2a ₁	-0.005	-0.225
2b ₁	-0.021	-0.217

The table 1 shows, that the difference of energy HOMO-LUMO is smaller in the case of the diene $2b_1$ reaction with the molecule $5a$ that in the case of the reaction between $2b_1$ with $5c$. Therefore the reaction should be easier in the case of the diene $2b_1$ addition on the molecule $5a$.

Study of regioselectivity reaction

The study of $(2p_z)$ coefficients of the border orbitals by DFT/3-21G level for the 4-aza-6-nitrobenzofuroxan 1 and 6-nitrobenzofuroxan $5a-c$

show that the LUMO coefficient of carbone C5 is always less then carbone C7 (Table II). This means that the addition of diene $2a_1$, appear more reactif on the molecules 1 and the $5a-c$ is obtained firstly on carbone C7. This constatation is agree with experimental resultats in the case of diene $2a_1$ add on the 4-aza-6-nitrobenzofuroxan 1^1 .

In purpose to determine the stereoselectivity of the reaction between the molecules $5a-c$ and the diene $2b_1$, we have

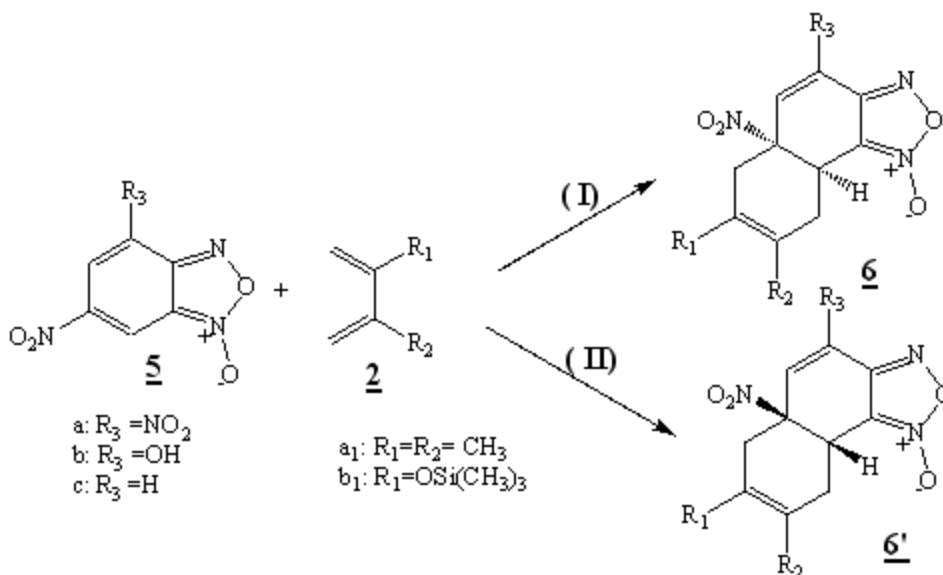


Fig. 4:

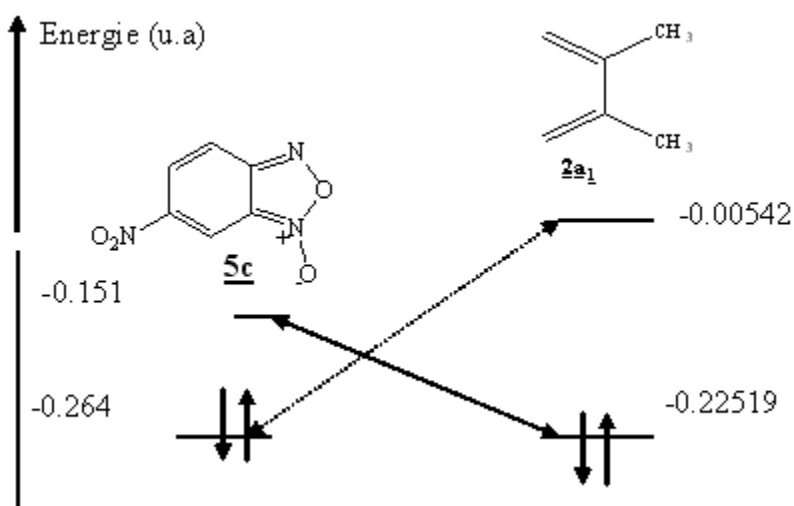


Fig. 5 : orbital diagram between molecule $5c$ with le diene $2a_1$. DFT/3-21G

calculated the (2pz) coefficient of LUMO for diene $2b_1$ and also the 2pz coefficient of LUMO which correspond to carbons C7 and C6 of molecules 5a-c and this leads to the formation of product 6. The formation of (1')-(7) and (4')-(6) liaisons are more favored. See the example on Fig 5

Thermodynamic approach

As it shows in figure 6, we studied the interaction of this heterocyclic molecules 1 and 5a-c with the diene $2a_1$ - b_1 . The heterocyclic molecules react as dienophile and the molecules of 2,3-dimethylbutadiene $2a_1$ and 2-trimethylsilyloxybuta-1,3-diene $2b_1$ react as a diene, Therefore we have a normal electron demand Diels-Alder (NEDDA). We found, it is interesting to examine from a thermodynamic approach the possibility and the stereoselectivity of Diels-Alder reactions. In each case of these reactions, we calculated by the DFT / B3LYP with the standard basis set 3-21G, the

variation of free energy $\Delta_f G$ (Kcal.mol⁻¹) correspond to every type of reaction. The table III regroups the different values obtained by the DFT method.

The reactions (I) and (II) between the 2,3-dimethylbutadiene $2a_1$ with the benzofuroxane molecules 5a-c and molecule 1 are possible, since the variation of free energy are negative. On the other hand, we study the add of the 2-trimethylsilyloxybuta-1,3-diene $2b_1$ to the molecules 5a-c and 1. We notice that reactions (I) and (II) are possible and favored thermodynamically.

We also notice that the variation of free energy corresponding to reaction (I) are more important in absolute value, than the variation of free energy relative to reaction (II). This is confirm the possibility of these reactions. Therefore the reactions (I) give always the main product.

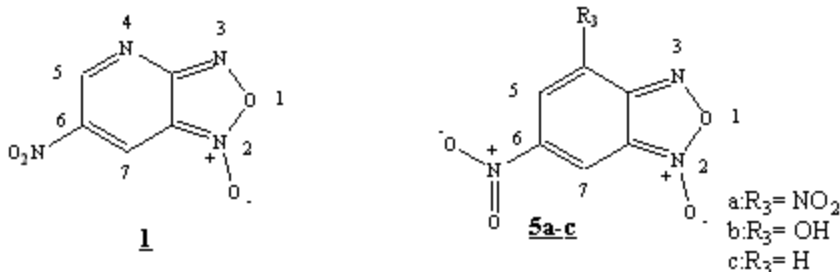


Table 2 : The LUMO Coefficient of carbons C5, C6 and C7 of molecule 1 and 5a-c, The HOMO coefficient of carbons C'1 and C'4 of diene $2a_1$ - b_1 .

	LUMO coefficient of C7	LUMO coefficient of C6	LUMO coefficient of C5
1	0.241	0.255	-0.145
5a	0.201	0.241	-0.145
5b	0.183	0.226	-0.134
5c	0.153	0.186	-0.138
	HOMO coefficient of C'1	HOMO coefficient of C'4	
2a	0.285	0.285	
2b	0.236	0.264	

From these results, we can give answer about some experimentally question¹. In fact, the addition of H₂O molecule could be done only on the majority of the reaction product. For this reason, the addition of H₂O is done only on the C₁₀=N₉ bond of product 3a₁ which could be considered from our calculation as the majority reaction product.

In each case of reactions (I) and (II), we have determine the energy which leads to the formation of reaction product. We have make the follow constatation that the energy formation of endo products 6 is more weak then the energy formation of exo products 6'. This is a new confirmation of the stability of endo products which is considered as major product part of Diels-Alder reaction between the molecules 1 and 5a-c with the diene 2a₁-b₁.

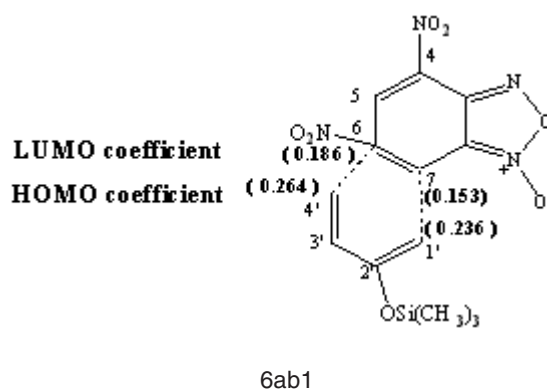


Fig. 5: orbitalairy interaction between the HOMO coefficient of the diene 2b₁ with LUMO coefficient of the dienophile 5a.

Table 3: Thermodynamic results for some reaction calculated at the DFT/B3LYP level of theory. (Kcal.mol⁻¹)

	Product of reaction	$\Delta_r E$	$\Delta_r H$	$\Delta_r G$
Reaction 1	3a1	-23.4	19.3	-15.6
	3b1	-26.7	23.4	-17.1
	6aa1	-17.4	27.2	-20.1
	6ab1	-29.4	31.4	-25.3
	6ba1	-18.9	21.5	-15.6
	6bb1	-16.3	22.3	-17.3
	6ca1	-12.5	18.9	-10.4
	6cb1	-13.1	14.7	-12.3
Reaction 2	3'a1	-13.9	16.3	-10.4
	3'b1	-21.1	15.2	-12.3
	6'aa1	-15.3	21.3	-19.5
	6'ab1	-20.2	25.7	-23.2
	6'ba1	-13.7	17.3	-12.4
	6'bb1	-14.8	10.4	-13.6
	6'ca1	-9.7	12.3	-8.4
	6'cb1	-11.5	15.2	-10.1

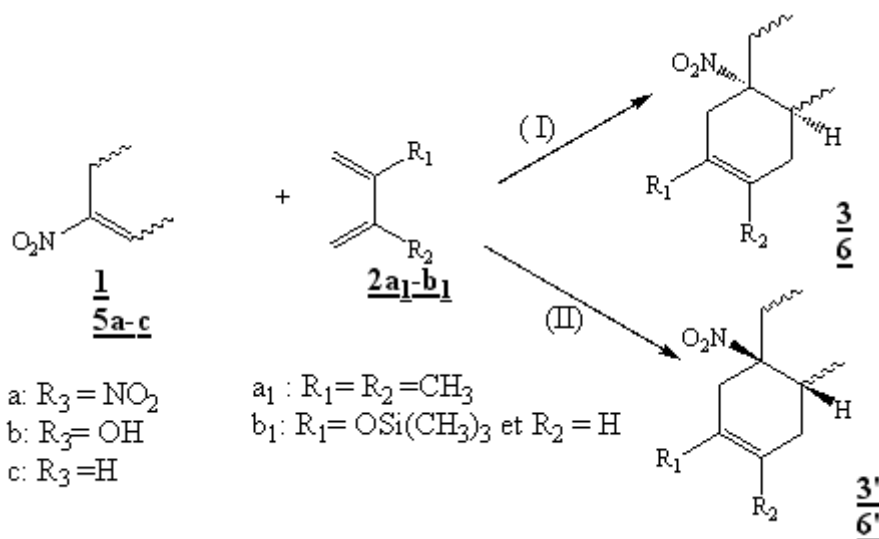


Fig. 6: DFT study of normal electrons demand Diels-Alder reaction between the diene 2a1-b1 with some heterocyclic molecules such as the 4-aza-6-nitrobenzofuroxane 1 and 6-nitrobenzofuroxane 5a-c.

CONCLUSION

We study the Diels-Alder reaction between a diene 2 like 2,3-dimethylbutadiene and 2-trimethylsilyloxybuta-1,3-diene with 6-nitrobenzofuroxane 5a-c, which is specially interesting for scientist in experimental workshop. Therefore the diene is activated by different substituents and the 6-nitrobenzofuroxane 5

substitute by $-\text{NO}_2$, $-\text{OH}$ and $-\text{H}$. We also study the influence by R_1 and R_2 in the Diels-Alder reactions. Our theoretical results show, that the reactions (I) give always the main product which is the endo products. The reaction between the diene 2-trimethylsilyloxybuta-1,3-diene 2b₁ and DNBF 5a gives most results than DNBF 5a with the diene 2,3-dimethylbutadiene 2a₁.

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