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DIELS–ALDER CYCLOADDITIONS OF 1,4-DIAZA-1,3-BUTADIENES: A MNDO INVESTIGATION

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Abstract - MNDO calculations have been performed on several disubstituted 1,4-diaza-1,3-butadienes. The results obtained have been used to analyze both normal and inverse electron demand Diels-Alder reactions according to the frontier molecular orbital treatment.

Introduction

In a project devoted to the synthesis of 2-substituted pyrazines, we became interested in the Diels-Alder reaction of 1,4-diaza-1,3-dienes. To our knowledge only a select number of these systems has been shown to partecipate as 4 π component in [4+2] cycloaddition reactions. Diiminosuccinotrile[1] and diazabenzofurans[2] afford Diels–Alder products on reaction with electron rich olefins; dehydroindigo reacts with styrene, acrylonitrile, vinylaryls, methylacrylate, methylpropiolate under forcing conditions[3] ; N-aryl-1,4-diaza-1,3-butadienes give Diels-Alder products on reaction with reactive dienophiles[4]; substituted o-benzoquinones diimines react with diarylchetenes[5]. The [2+2] cycloaddition reaction to afford β-lactams or azetidines is often a competing reaction. The examples reported above are however related to functionalized chemical structures which are hardly convertible to the simpler skeleton of 2-substituted pyrazines.

In order to learn more about the possibility of synthezising simple pyrazines through [4+2] cycloadditions and to investigate the ease and predictability of this kind of approach we have performed semiempirical calculations on model compounds[6] and we have analyzed the results according to the frontier molecular orbital treatment, therefore assuming that the reactions take place in such a way as to maintain maximum bonding through the course of the reaction. Even if this approach has been the subject of some criticism in recent years, mainly due to its degree of "versatility", nevertheless it can be a useful tool to orient the choice of the reagents avoiding time consuming preparations of improper compounds, provided the theoretical indications fit the experimental data already available

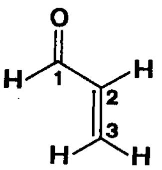
Results and discussion

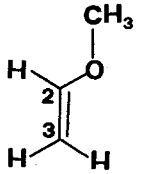
Both normal (HOMO diene controlled) and inverse electron demand (LUMO diene controlled) Diels-Alder reactions have been considered. Lower energy geometries, frontier orbitals energies and coefficients for acrolein, vinylether (choosen as model compounds for electron-deficient and electron-rich dienophiles) and various substituted 1,4-diaza-1,3-butadienes (Table 2, 3) have been estimated with the MNDO method as implemented in the AMPAC set[7] of computer programs. We have focused our attention to disubstituted 1,4- and 2,3-

1,4-diaza-1,3-butadienes 2-12 and to the o-benzoquinone diimine 13 both to limit the number of structures to be analyzed and to deal with symmetrical compounds which are easier to synthezise. To estimate the reactivity of the 1,4-diazadienes, butadiene 1 has been taken as reference compound. As it is rather a poor diene, a decrease of the HOMO for diazadienes as compared with that of butadiene can be reasonably associated to an unadequate reactivity in normal Diels-Alder reactions.

The results for acrolein and methylvinylether are reported in the Table 1. For 1,4-diaza-1,3-butadienes only cisoid planar (or quasi-planar) conformations are reported as no reaction occurs if the diene cannot adopt a cisoid conformation: in a preliminar conformational study it has been, however, verified that the energy differences respect to the more stable skew and transoid conformations are reasonably small (2-7.5 Kcal/mole for the a series and 0.2-1.2 Kcal/mole for b series).

Table 1. MNDO HOMO, LUMO energies (eV) and coefficients for acrolein and methylvinylether

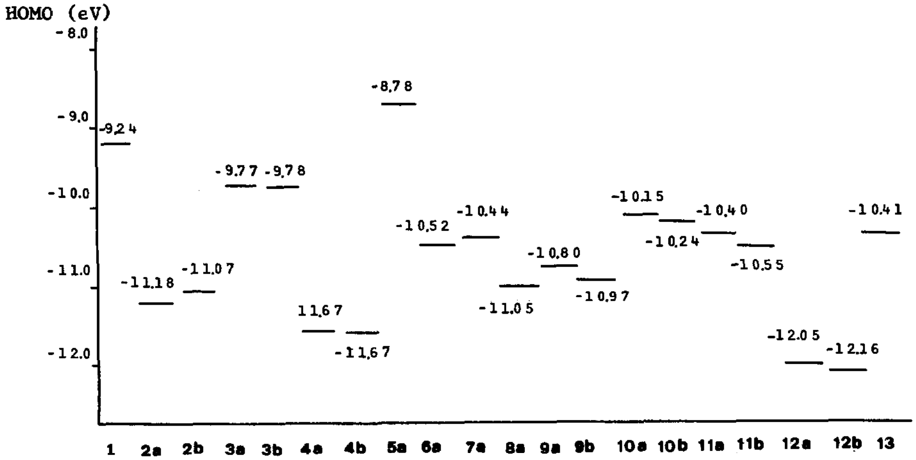




	Acrolein		Methylvinylether	
	HOMO	LUMO	HOMO	LUMO
Energy	-10.69	-0.08	-9.38	1.20
Coefficient				
C_1	-0.05	-0.46		
C_2	0.68	-0.47	-0.54	0.69
C_3	0.66	0.64	-0.68	-0.69
O	-0.30	0.40	0.43	0.14

The MNDO results show that replacing two carbon atoms with nitrogen into the conjugated system of butadiene confers electrophilic character to the system as shown by the HOMO which is lower in energy than that of butadiene (Figure 1). This observation suggests a lower reactivity of 2a and 2b, compared to butadiene 1, towards electron-deficient dienophiles. Furthermore the HOMO is composed by the s, p_x, and p_y atomic orbitals of the heavy atoms and would disfavour a HOMO-LUMO bonding interaction. Addition of substituents to the diazadiene system affects both the shape and the energy of frontier molecular orbitals depending on the nature of the substituent itself and on its location.

Figure 1. HOMO energies (eV) for compounds 1-13.



1,4-disubstituted-1,4-diaza-1,3-butadienes.

Addition of groups that contain an heteroatom with an unshared pair of electrons as exemplified by -OH (3a,b) produces a butadiene-like HOMO (even if extended to p_z orbitals of heteroatoms) and a $\simeq$ 1.3 eV rise of the HOMO as compared to that of the parent 1,4-diaza-1,3-butadiene. Nevertheless the HOMO-LUMO energetic gap, as compared with that for butadiene is still unfavorauble to the reaction with conventional dienophiles.

Addition of electron-withdrawing, conjugating groups as -CN and SO_2R (4a, 4b, 8a) accentuates the electron deficient nature of the diazadiene and consequently raises the magnitude of the $HOMO_{diazadiene}$ - $LUMO_{dienophile}$ energy separation related to a normal cycloaddition.

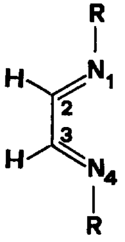
Also the addition of electron-donating groups as alkyls (methyl- and isopropyl) (6a, 7a) does not raise sufficiently the HOMO.

Addition of phenyl groups (5a) increases to such extent the nucleophilic character of the diazadiene system to suggest the use of conventional electron-deficient dienophiles.

2,3-Disubstituted-1,4-diaza-1,3-butadienes.

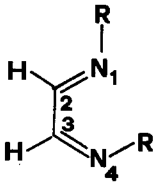
As for 1,4-disubstituted-1,4-diaza-1,3-butadienes, addition of groups that contain an heteroatom with an unshared pair of electrons (O, S, N) to the position 2,3 of the diazadiene system (9, 10, 11) lowers the electrophilic character of the diazadiene system and raises the energy of the HOMO compared with that of the parent 1,4-diazadiene; however its value is still lower than that of butadiene. The resonance predicts that all these groups should be electron donating though all are electron withdrawing by the field effect. In these models the low energy of the HOMO of the diazadiene should indicate that the resonance is more important than the field effect. An opposite effect is produced by addition of groups that lack an unshared pair of electrons, and are electron-withdrawing both by resonance and field effect as -CN (12). In this case a stabilizing effect is observed: the energy of HOMO is lower respect to both butadiene and 1,4-diaza-1,3-butadiene and the electrophilic character of the system is raised.

Table 2. MNDO HOMO, LUMO energies (eV) and coefficients for compounds 2 - 8[a].



a

2 R = H
3 R = OH
4 R = CN
5 R = C_6H_5
6 R = CH_3
7 R = $CH(CH_3)_2$
8 R = SO_2CH_3



b

HOMO	2a	2b	3a[b]	3b[b]	4a[c]	4b	5a[d]	6a[e]	7a[e]	8a[e]
Energy	-11.18	-11.07	-9.77	-9.78	-11.67	-11.67	-8.78	-10.52	-10.44	-11.05
Coefficient										
N_1	*	*	-0.42	0.42	-0.42	*	-0.22	*	*	*
C_2	*	*	-0.41	0.39	-0.34	*	-0.25	*	*	*
C_3	*	*	0.38	-0.39	0.34	*	0.24	*	*	*
N_4	*	*	0.42	-0.43	0.42	*	0.22	*	*	*

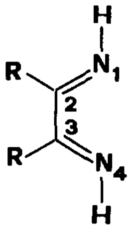
LUMO	2a	2b	3a[b]	3b[b]	4a[c]	4b[c]	5a[d]	6a	7a	8a
Energy	0.13	-0.01	0.03	0.02	-1.79	-1.84	-0.79	0.07	0.18	-2.11
Coefficient										
N_1	-0.53	-0.56	-0.52	0.53	-0.45	-0.47	0.32	-0.50	-0.51	*
C_2	0.47	0.53	0.44	-0.45	0.46	0.51	-0.36	0.47	0.47	*
C_3	0.47	0.41	0.45	-0.44	0.46	0.42	-0.36	0.47	0.47	*
N_4	-0.53	-0.48	-0.52	0.51	-0.45	-0.42	0.32	-0.50	-0.51	*

a) The molecules lie on the XY plane. The coefficients refer to the p_z orbitals.
b) The HOMO and LUMO extend on the oxygen p_z orbitals.
c) The HOMO and LUMO extend on the carbon and nitrogen p_z orbitals of the CN group.
d) The HOMO and LUMO extend on the p_z orbitals of aromatic carbons.
e) For 1,4-disubstituted-1,4-diaza-1,3-butadienes 5-8 only trans,trans-disubstituted isomers have been considered.
*) The molecular orbitals, which are not π type, are composed by the s, p_x, and p_y atomic orbitals of the heavy atoms (C, heteroatoms).

Almost in all instances, accentuated in the latter case, we also observe a stabilization of the LUMO which is lower in energy in comparison with that of the parent 1,4-diaza-1,3-butadiene. This result strongly suggests a participation of these systems, when the reaction is allowed by orbital symmetry, in inverse electron demand Diels-Alder reactions with electron-rich dienophiles. This prediction is indeed experimentally verified by the successful cycloaddition reaction of diiminosuccinonitrile with methylvinylethers.

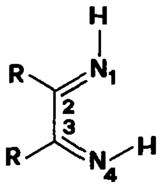
In this context we have also examined the o-benzoquinone diimine 13, which is however a tetra-substituted diazadiene (Table 4). The MNDO analysis suggests a more favourable inverse electron demand reaction in agreement with the observed experimental behaviour.

Table 3. MNDO HOMO, LUMO energies and coefficients for compounds 9 - 12[a].



a

9 R = OH
10 R = SH
11 R = NH_2
12 R = CN



b

	HOMO							
	$9a^b$	$9b^b$	$10a^b$	$10b^b$	$11a^c$	$11b^d$	$12a^e$	$12b^e$
Energy	-10.80	-10.97	-10.15	-10.24	-10.40	-10.55	-12.05	-12.16
Coefficient								
N_1	0.64	-0.56	-0.43	-0.30	0.52	0.55	0.52	-0.44
C_2	0.39	-0.31	-0.19	-0.11	0.26	0.25	0.38	-0.29
C_3	-0.20	0.28	0.05	0.14	-0.20	-0.19	-0.38	0.43
N_4	-0.40	0.52	0.14	0.36	-0.39	-0.37	-0.53	0.58

	LUMO							
	$9a^b$	$9b^b$	$10a^b$	$10b^b$	11a	11b	$12a^e$	$12b^e$
Energy	0.06	-0.06	-0.32	-0.43	0.19	0.04	-1.13	-1.32
Coefficient								
N_1	0.45	0.49	-0.48	-0.53	-0.49	0.50	0.51	0.56
C_2	-0.39	-0.47	0.40	0.49	0.45	-0.50	-0.41	-0.49
C_3	-0.55	-0.48	0.52	0.43	0.49	-0.45	-0.41	-0.34
N_4	0.54	0.49	-0.55	-0.49	-0.51	0.48	0.51	0.45

a) The molecules lie on the XY plane. The coefficients refer to the p_z atomic orbitals.
b) The HOMO and LUMO extend on the p_z orbitals of oxygen and sulfur.
c) The HOMO extend on the p_z orbitals of the nitrogen atoms of the $-NH_2$ groups. Contribution from p_y atomic orbitals of N_1 (0.14), N_4 (0.10) and of the nitrogen atoms of the $-NH_2$ groups (0.18 and 0.14) are also observed.
d) The HOMO extend on the p_z orbitals of the nitrogen atoms of the $-NH_2$ groups. Contribution from p_y atomic orbitals of N_1 (0.10), p_y orbitals of the nitrogen atoms of the $-NH_2$ groups (0.14) and s orbitals of the nitrogen atoms of the $-NH_2$ groups (0.16) are also observed.
e) The HOMO and LUMO extend on the p_z orbitals of the carbon and nitrogen atoms of the -CN groups.

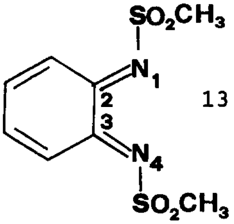
Conclusion

The MNDO investigation reported above shows the electrophilic character of the diazadiene system: this feature is accentuated by addition of groups which can behave as electron-withdrawing substituents (-CN, $-SO_2R$) apparently with a scarce influence of the position of the substituents.

The addition of electron-donating substituents both by resonance (OH-, SH-, NH_2-) and by field effect (alkyls) raises the nucleophilic character of the system, but the energy of the HOMO is still lower compared to that of butadiene.

Only the addition of the delocalized system of the phenyl group to the 1,4 positions increases the nucleophilic character of the diazadiene to such extent as to allow a normal Diels–Alder reaction. However as the majority of the substituents of interest can be accomodated into the first two categories mentioned above, the most general use of 1,4-diaza-1,3-butadienes appears to be related to inverse electron demand Diels–Alder reactions.

Table 4. MNDO HOMO, LUMO energies and coefficients for compound 13[a].



13

	HOMO[b]	LUMO[b]
Energy	-10.41	-2.31
Coefficient		
N_1	0.26	-0.40
C_2		0.36
C_3		0.36
C_4	0.26	0.40

[a] The molecule lie in the XY plane. The coefficient refer to p_z orbitals

[b] The HOMO and LUMO are extended to the p_z orbitals of carbons of the ring.

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