# A Diels Alder reaction

## *Historical review*

In 1950 Otto Diels and Kurt Alder have been awarded the Nobel prize for Chemistry. They described a very important reaction which is suitable for the formation of carbon-carbon bond in a six membered ring with high stereochemical control.

Otto Diels
1876-1954

Kurt Alder
1902-1958

Since 1928 several new compounds have been synthesized with the use of Diels-Alder (DA) reaction. This reaction provides an easier way for cyclization than other ring closure procedures of open-chain compounds.

O. Diels and K. Alder, Ann. 460, 98 (1928); Ber. 62, 2081, 2087 (1929)

J. A. Norton, Chem. Revs. 31, 319 (1942)

K. Alder in Newet Methods of Preparative Organic Chemistry, English Ed. (Interscience, New York, 1948), p 381

M. C. Koetzel, Organic Reactions 4, 1 (1948)

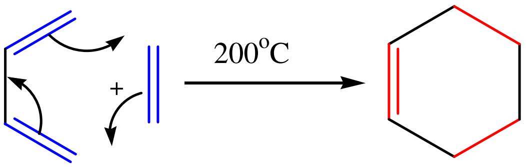
H. L. Holmes, Organic Reactions 4, 60 (1948)

L. W. Butz, Organic Reactions 5,136 (1949)

Madronero, Rev. cienc. apl. (Madrid) 12, 397 (1958); C.A. 53, 6984 (1959)

## Typical DA reactions

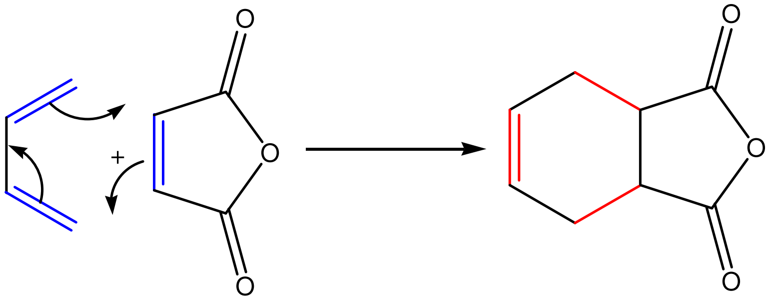
The simplest example of intermolecular DA reactions is not too effectiv. (1.1)



**Dien** **Dienophil** **Adduct: the cycloalkene**
(cyclohexene)

**1.1**

The reaction can be quantitative for the substituted compound shown bellow (1.2)



**Dien** **Dienophil** *orto*-thalic acid anhydride

**100%**

**1.2**

***Solomons 604***

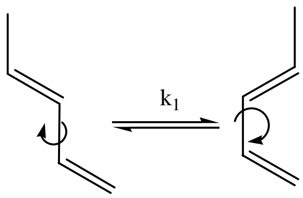
## The conception of 2+4 cycloaddition

The cycloaddition occurs between an molecule with double or triple bond (dienophil) and a diene with two conjugated double bonds. During the reaction a six membered ring is formed with the rearrangement of the π-bonds to σ-bonds.

## *Stereoselectivity of the reaction*

The conformation of the dienophil (**a**,**b**) is important. The rate of the reaction is influenced by the rate of the conformational exchange of the diene. Cyclic dienes with exocylic double bond(s) can not react (**c**) due to sterical reasons, but one with endocyclic double bonds shows high reactivity (**d**). This observation indicates that for an open chain compound a *pre*equilibrium is necessary. In the case of s-*trans* conformer (**a** and **c**) the two terminal carbone atoms are separated so far in space that the overlap between diene and dienmophile atoms would be negligible.

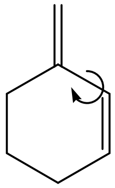
**Open chain rotamers**



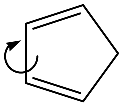
**a** **b**

s-*trans* conformation s-*cis* conformation

**Cyclic structures**



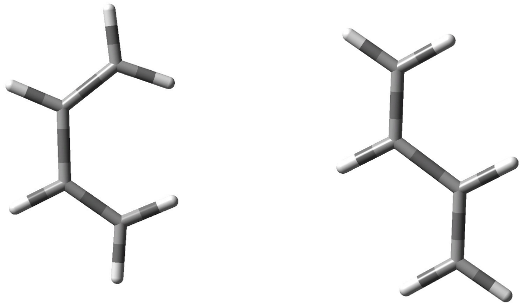
**c**



**d**

s-*trans* conformation s-*cis* conformation

**1.3**

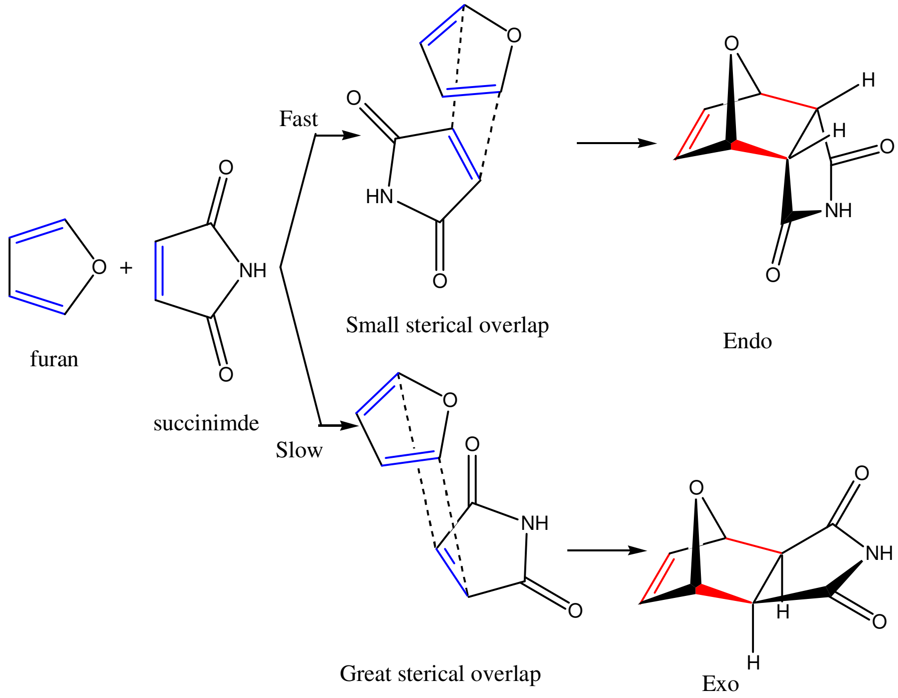


**E= -154.05945645 -154,05394323** (RHF/3-21G)

**ΔE=3.5 kcal/mol**

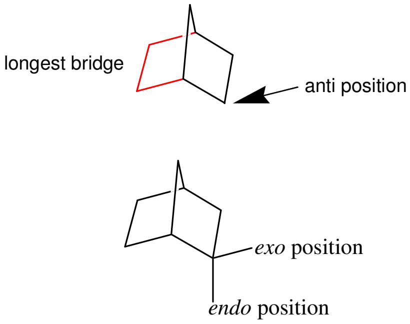
## *Configuration of the products*

The position of the diene relative to the dienophile in the transiton state, will determine the configuration of the final product. If the products consist of two rings their relative orientations could either be *endo* or *exo*. DA reaction of cyclopentadien analogue (furan) and the specified dienophile (succinimide) is shown below.



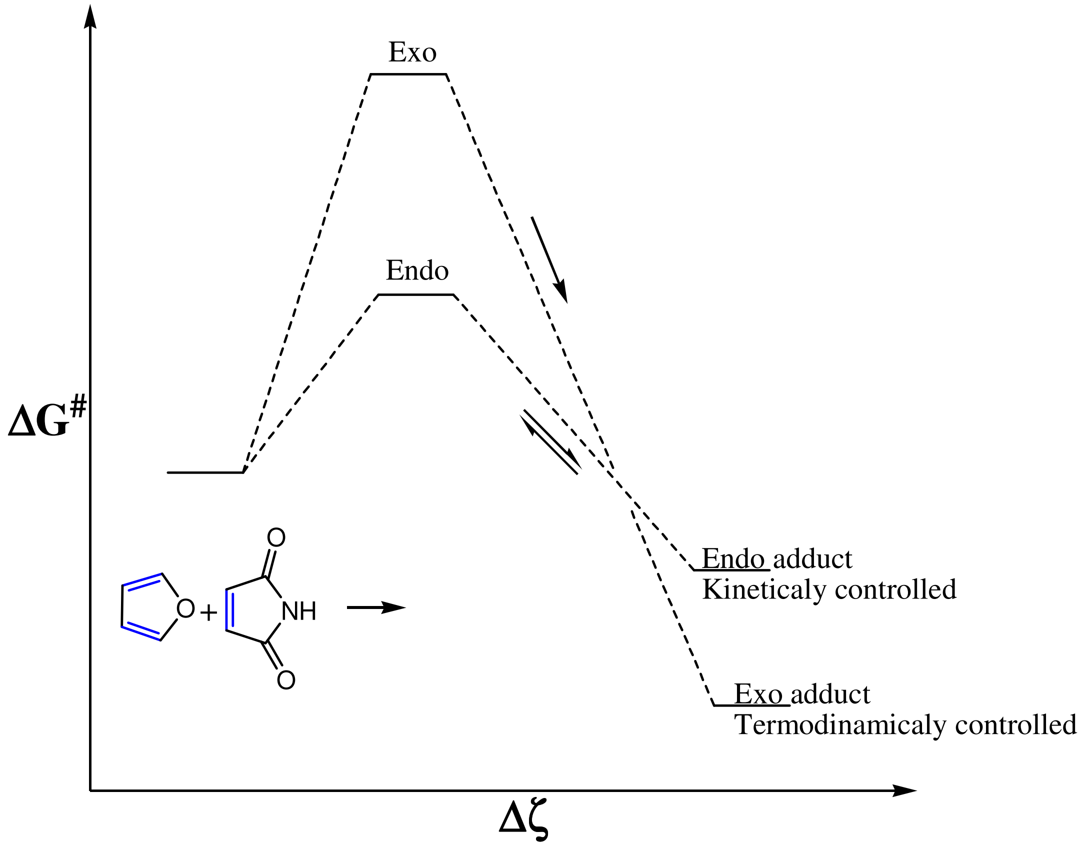
1.4

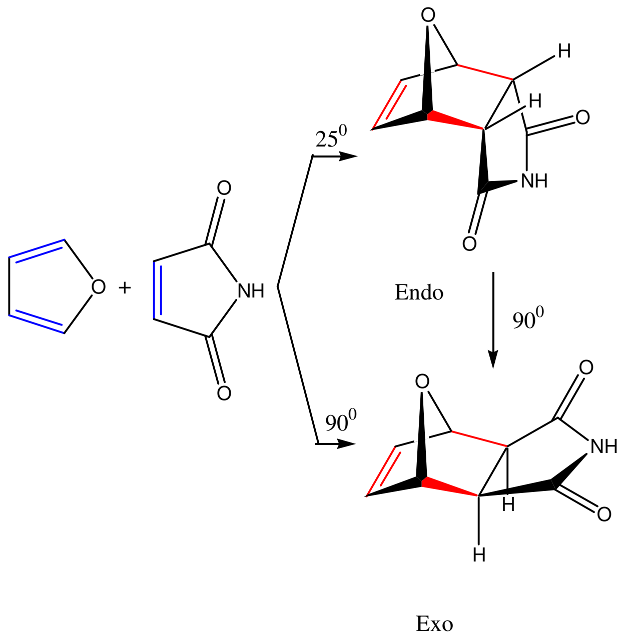
The DA reaction goes primarily in an *endo* rather than an *exo* fashion when the product formation is kinetically controlled. Note that, *endo* and *exo* are terms describing the stereochemistry of bridged rings such as bicycle[2.2.1]heptane. Selecting the longest bridge, the group that is in *anti* position relative to it is said to be the *exo*, while that on the same side is called the *endo* position.)



## *Energetics of endo and exo configurations*

At lower temperature, due to the lower barrier height, the formation of the product with *endo* conformation is allowed (Kinetic control). At higher temperature, both of the barriers with significantly different energies can be "overcome", but the *endo* „mechanism" will be reversible (Thermodynamic control), thus the more stable exo product is expected to be formed in a larger quantity.



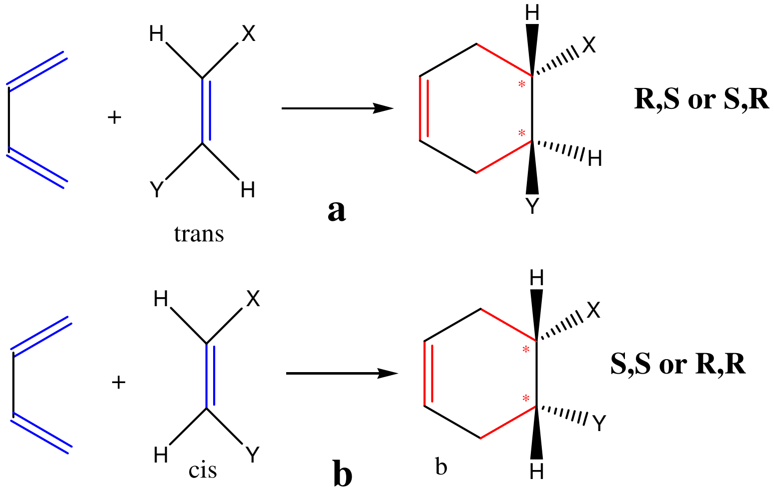


1.6

Note that the "*Endo* to *Exo"* direct conversion is a virtual reaction, but it may occur due to a "*retro*-DA" reaction or due to thermodynamic control.

## *Further details of reaction stereoselectivity*

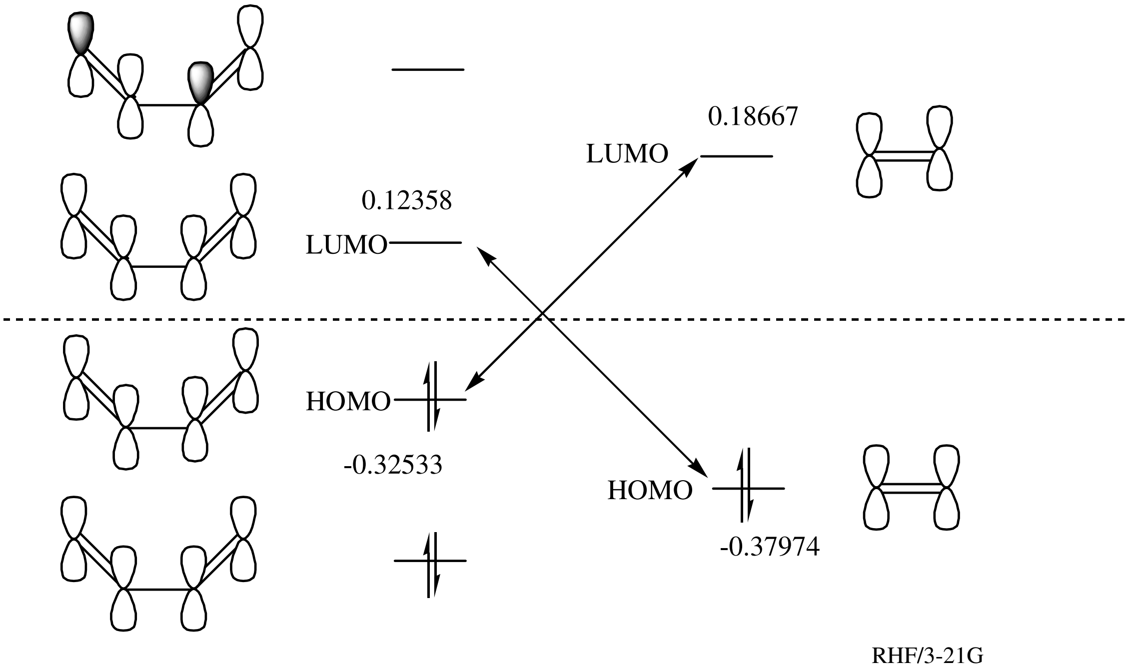
The reaction is highly stereospecific, namely the reaction is a *syn* addition resulting in a product where the configuration of the dienophile is retained. Because of the one-step reaction mechanim the *cis-trans* conformers are retained during the reaction. Thus, configuration of products depend on the configuration of the dienophile (**a**,**b**) (1.8).



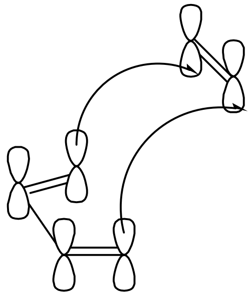
1.8

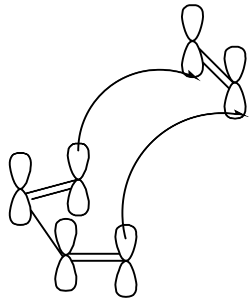
## *MO-theory of DA reactions*

Stereospecifity of DA reaction could be described with the local symmetry of the molecular orbitals involved. The HOMO of ethylene and the LUMO of butadiene, or the LUMO of ethylene and the HOMO of butadiene have matching (similar) MO symmetries. This means that in a DA reaction the two electrons can flow both ways. On the one hand, the diene (ethene) is an electron donor and the dienophile is the electron acceptor. On the other hand the diene is the electron acceptor with a dienophile being an electron donor. (During the reaction the two π-electron pairs are converted into two σ-bonds.) When the (buta-1,3-diene s-*cis*) is the electron acceptor group (1.9) the orbital energy gap is $\Delta E = \text{LUMO}_{\text{diene}} - \text{HOMO}_{\text{dienophile}}$= 0.50332 Hartree (~316 kcal/mol). For the other orbital gap a rather similar value was computed: 0.512 Hartree (~321 kcal/mol).



1.9

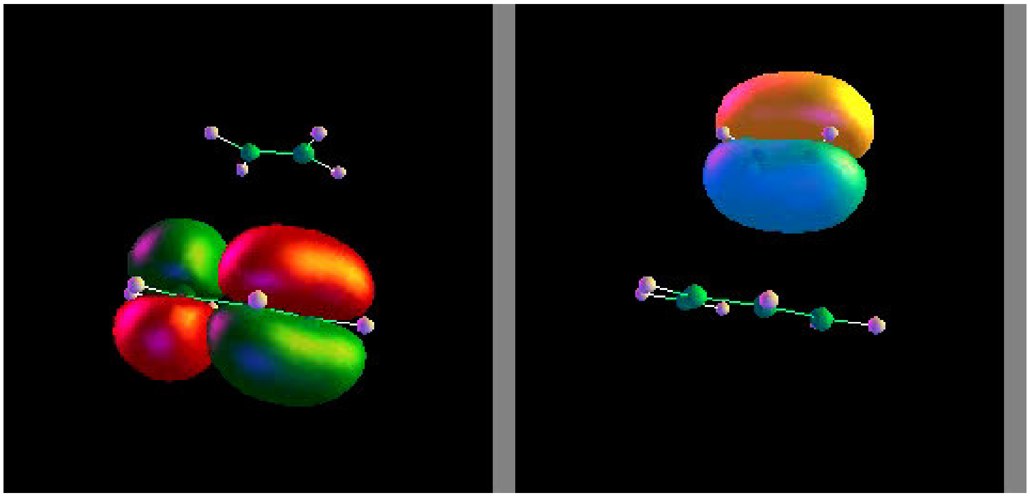




1.10

## *Deformation of HOMO and LUMO molecular orbitals during the reaction of ethylene and butadiene*

Movie on the left shows the deformations of HOMO of butadién, and the one on the right shows the LUMO of etilen.

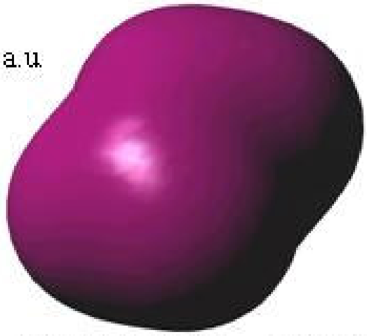


# Ethene ($C_2H_4$)

$\mu$= **0 Debye**

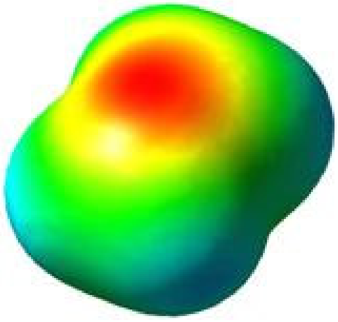
**TD**

$\rho$= 0.0004 a.u

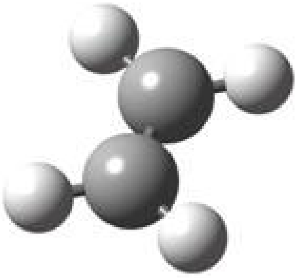


**EPS**

-0.02 ≤ töltés.≤ 0.02



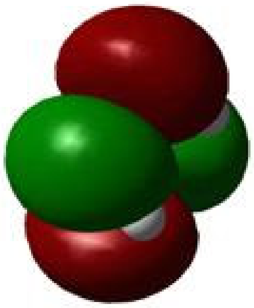
**E(RHF/3-21G)**= -77.60098817 Hartree

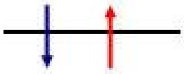


------ **π2 ***

**MO 9** (0.18663 )

**(LUMO)**



 **π1**

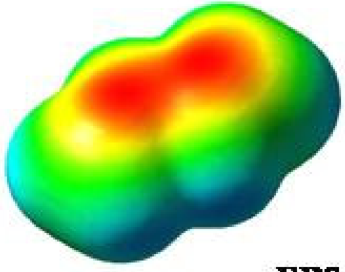
**MO 8** (-0.37970)

**(HOMO)**

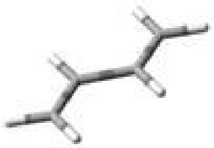
**TD:=total electron density** ($\rho$)

# Buta-1,3-diene ($C_4H_6$) $\mu$= 0 Debye

**TD**
ρ= 0.0004 a.u

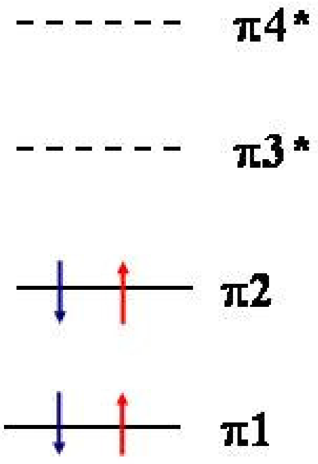


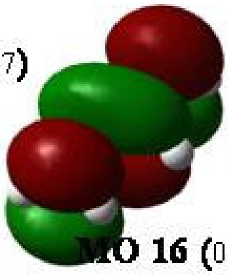
**EPS**
-0.44 ≤ töltés ≤ 0.44



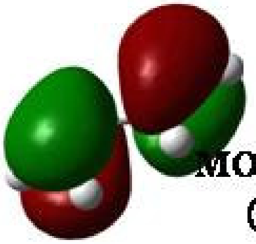
**E(RHF/3-21G)**= -154.05945647 Hartree

**MO 17** (0.27057)





**MO 16** (0.13177)
**(LUMO)**



**MO 15** (-0.32510)
**(HOMO)**

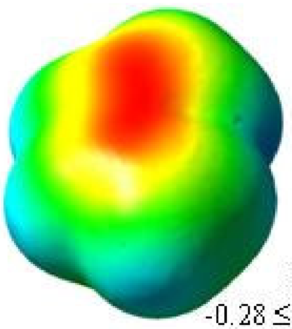
**MO 14** (-0.44795)

# **Buta-1,3-diene** ($C_4H_6$) $\mu$= **0.341 Debye**

**TD**

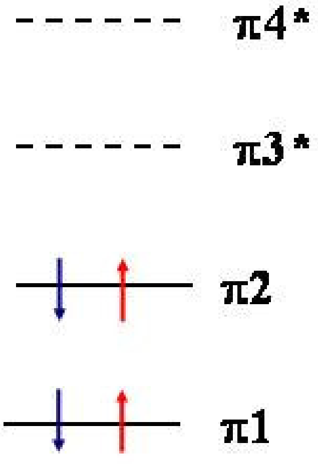
ρ= 0.0004 a.u

**E(RHF/3-21G)**= -154.05394323 Hartree



**EPS**

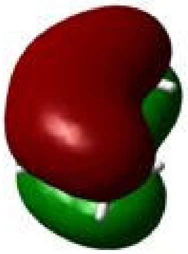
-0.28 ≤ töltés ≤ 0.28



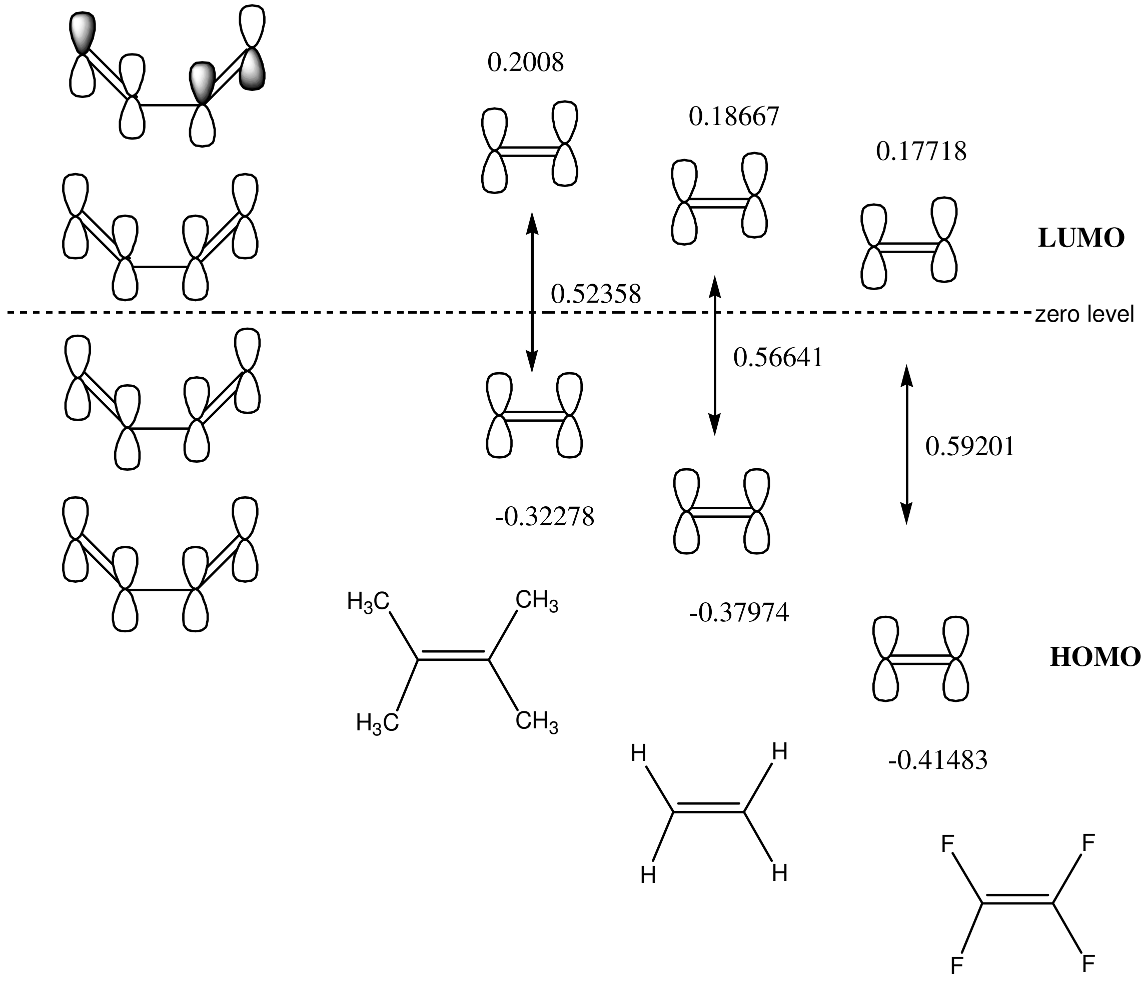
**MO 18** (0.27048)

**MO 16** (0.12358)
**(LUMO)**

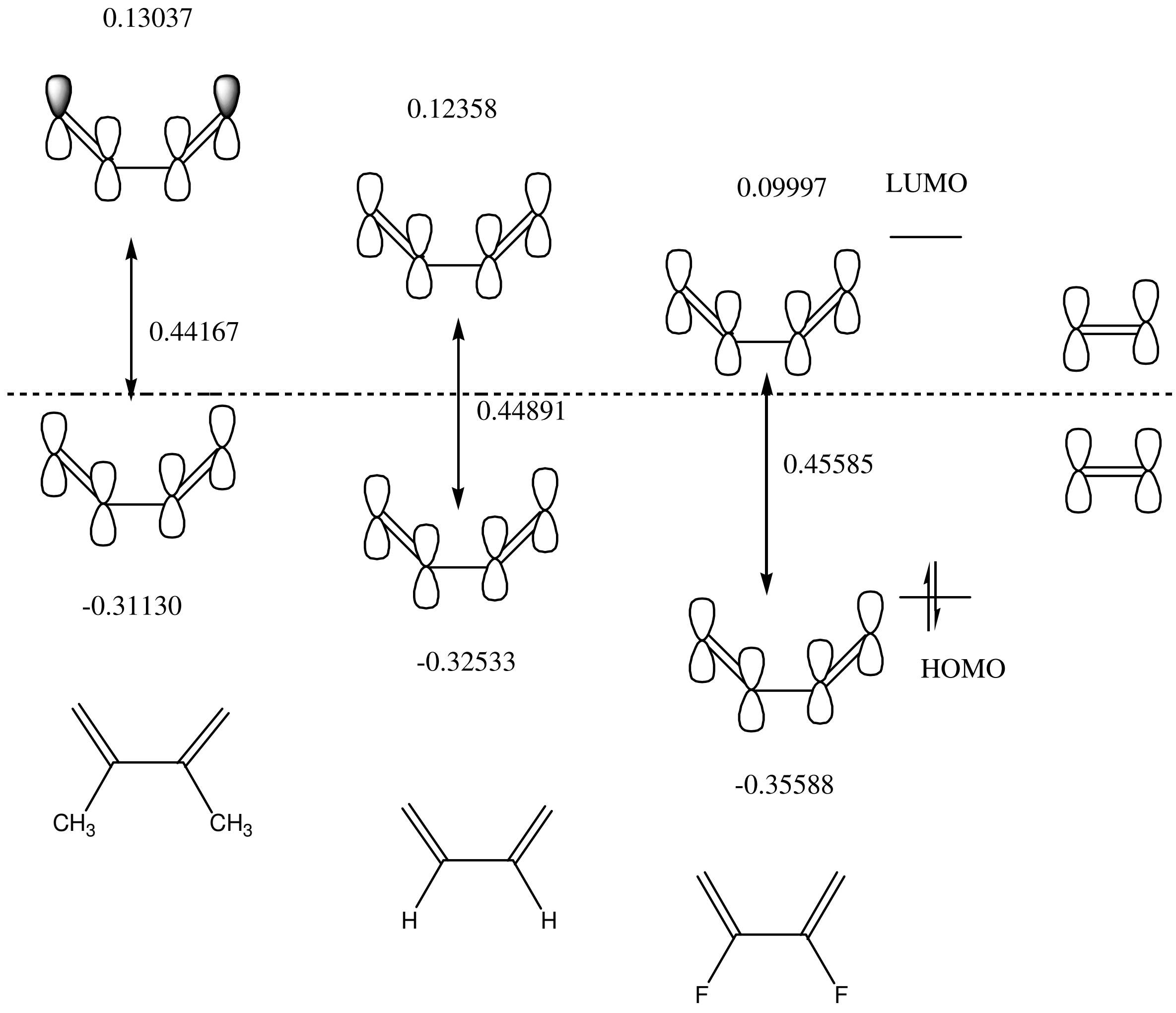
**MO 15** (-0.32533)
**(HOMO)**



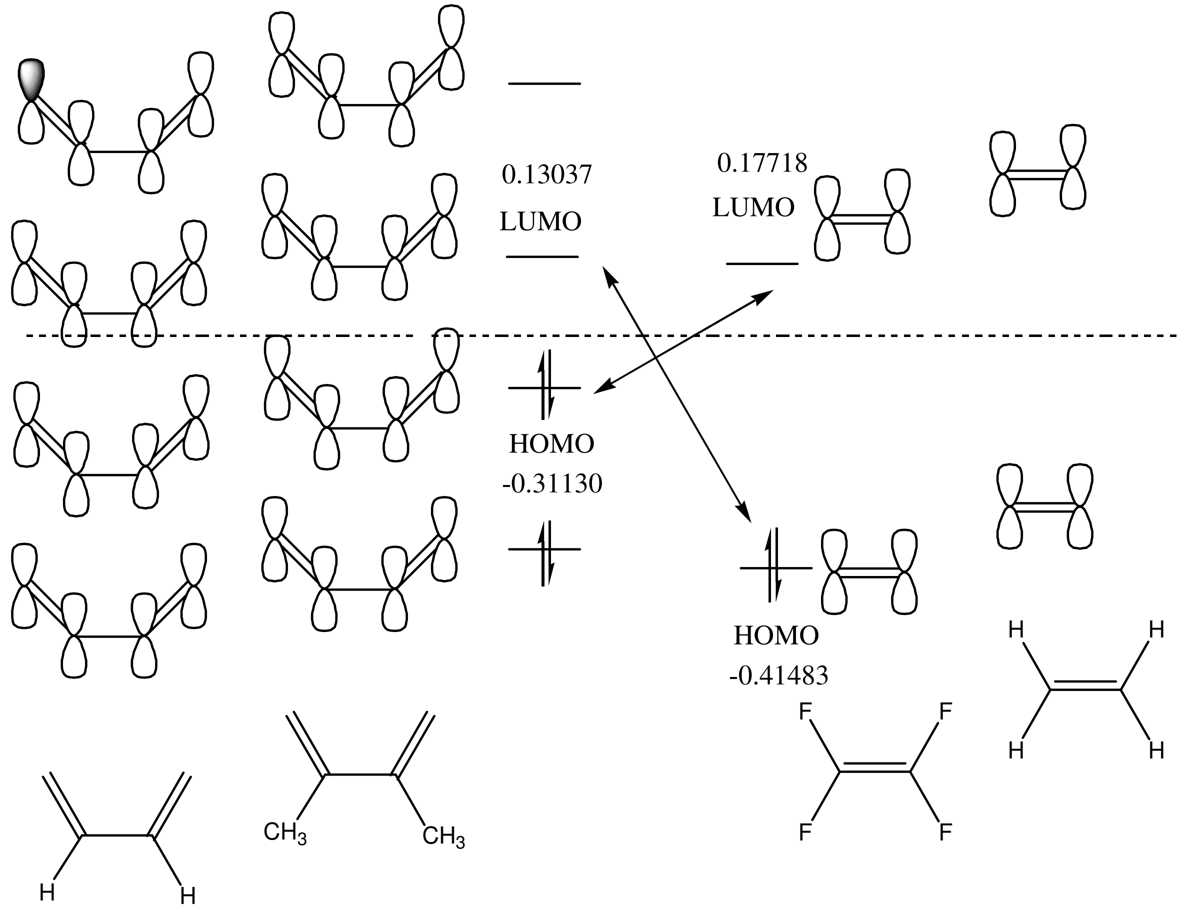
**MO 14** (-0.44447)



HOMO and LUMO energies in Hartree of the different dienophiles as computed at RHF/3-21G level of theory are shown (**Fig..**). Electron withdrawing groups, such as fluorine lower both the HOMO and the LUMO energy levels, relative to those of ethene. Furthermore, the energy difference between HOMO and LUMO, $\Delta E_{(LUMO\text{-}HOMO)}$, increases. On the other hand, functional groups pushing electrons to ethane (e.g. $-CH_3$) have both HOMO and LUMO energy levels increased. In addition, $\Delta E_{(LUMO\text{-}HOMO)}$ of the latter molecule decreases.

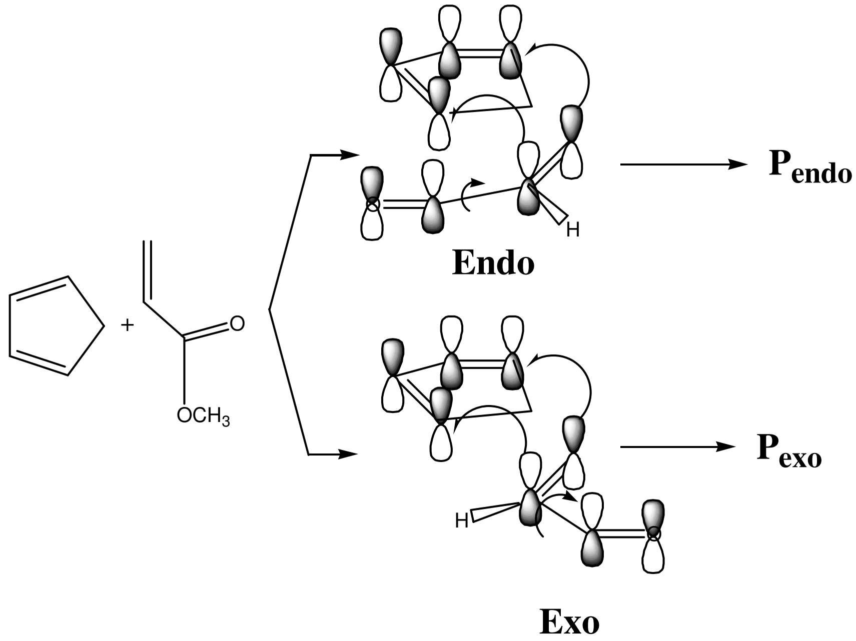


The influence of electron donating and electron withdrawing groups on the energies of the HOMO and LUMO has been discussed above. Therefore, increasing the HOMO of the diene (e.g. 2,3 dimethyl buta-1,3-diene s-cis) with electron donating groups and decreasing the LUMO of the dienophile (e.g. tetrafluoro ethene) with electron withdrawing substituents clearly facilitates DA reaction. In the case of the latter reaction the diene will be the electron donor and the dienophile the electron acceptor.



In the case of the latter reaction (2,3-dimethyl buta-1,3-diene s-cis plus tetrafluoro ethene) when the diene is be the electron donor and the dienophile is the electron acceptor the orbital energy level gap is: $\Delta E=\mathrm{LUMO}_{\mathrm{diene}} - \mathrm{HOMO}_{\mathrm{dienophile}}= 0.48848$ Hartree (~306 kcal/mol). The quasi equivalence of the two orbital energy level matching (Fig. 1.9) is clearly lost. The $\Delta E=\mathrm{LUMO}_{\mathrm{dienophule}} - \mathrm{HOMO}_{\mathrm{diene}}$ is ~342 kcal/mol. **DFT.** In conclusion we might say that the one-electron approach may only give an indication but not a full explanation of the energetics. Thus, more sophisticated theoretical approaches is necessary.

## Kinetic measurements



1.12

Relative orientation of the orbitals plays an important role in explaining the difference in activation energies and product formation. Monitoring the product concentration we can calculate the rat constant as function of temperature and therefore the difference in activation energy.

$$\Omega = \ln\frac{[P_{endo}]}{[P_{exo}]} = \ln\frac{k_{endo}}{k_{exo}} = \ln\left(\frac{A_{endo}}{A_{exo}} * \frac{e^{-E_A^{endo}/RT}}{e^{-E_A^{exo}/RT}}\right)$$

$$\Omega = \ln\frac{[P_{endo}]}{[P_{exo}]} = -\left[\frac{\Delta E_A}{R}\right] * \frac{1}{T} - \ln\frac{A_{endo}}{A_{exo}}$$

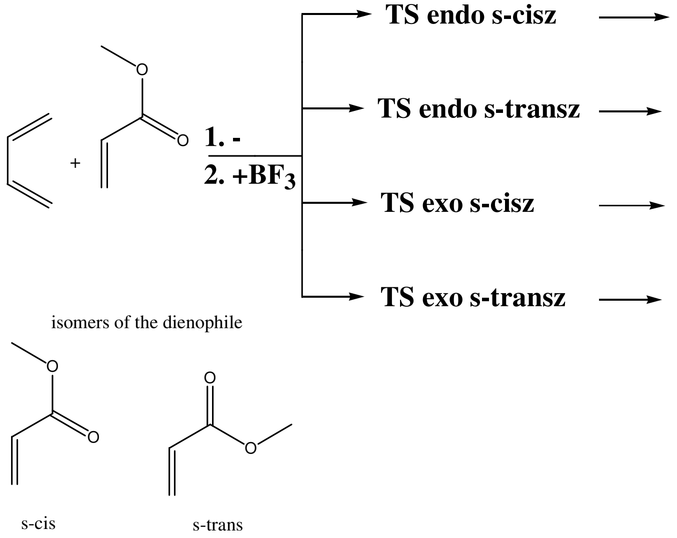
If we plot the log of concetration of product versus the reciprocal temperature we get a line ( y=mx+b ) and its steepness or tangent (m) is equal to $-\Delta E_A/R$ and b will be the y intercept, namely $\ln(A_{endo}/A_{exo})$ .

# Further examples in literature

## *1. Reaction between butadiene and metacrylate*

In this work 4 transition states of the reaction of butadien and metacrylate were investigated with and without $BF_3$ catalyses using three different basis sets.

The *endo/exo* selectivity of reaction depend on the orientation of metacrylate. This effect is greatly influenced by the inclusion of a Lewis-acid (e.g. $BF_3$) catalyst.



1.13

Each trasition states(TS) have different orientations. These are denoted due to the configuration of the product and the konformation of the metil-akrilat. The TS can be in endo or exo conformation.

J. I. Garcia,J. Mayoral, Luis Salvatella *Tetrahedron,* 1997 **53** 6057-6064

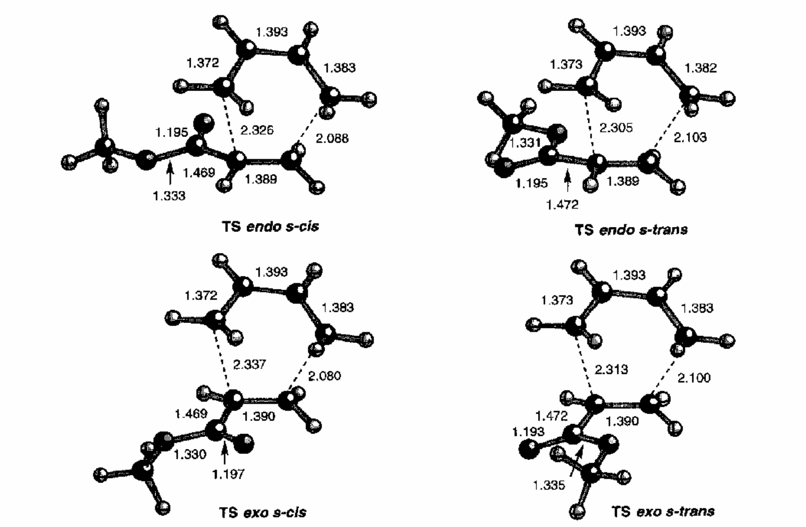


Figure 1.14. The possible four TS of non-catalyzed reaction with adequate atomic distances and bond lengths. The optimization was performed at RHF/6-31G* level of theory.

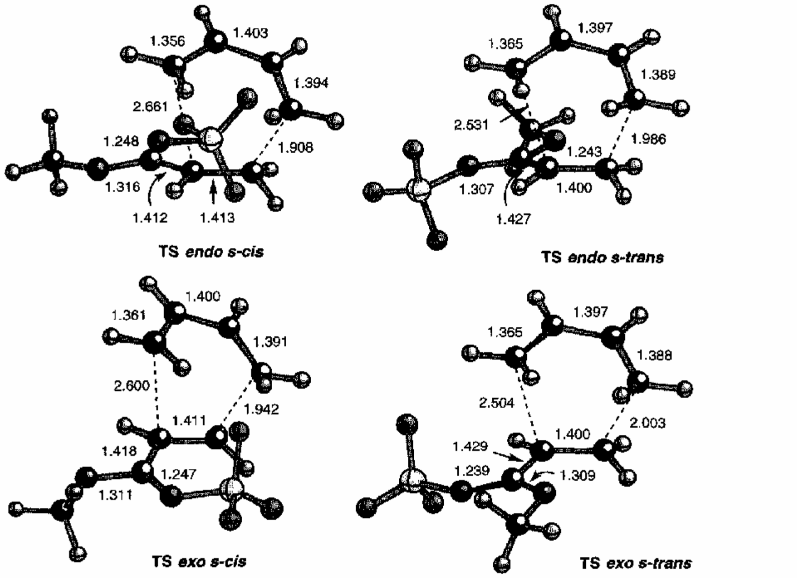


Figure 1.15. The four possible TS with $BF_3$ catalyzed reaction with corresponding bond lengths and distances at RHF/6-31G* level of theory.

## 1.1.4 Results

Without catalyst at every level of theory *s-cis* conformation was preferred in agreement with the experimental results.

With $BF_3$ catalyst the s-*trans* transition state has lower energy and became more stable similar to the experimental data.

| **Structure** | **RHF/6-31G*// RHF/6-31G*** | | **RHF/6-311++G**// RHF/6-31G*** | | **B3Lyp/6-311+G(2d,p)// RHF/6-31G*** | |
|---|---|---|---|---|---|---|
| butadien, s-trans | -154.919653 | | -154.962249 | | -156.044455 | |
| methyl acrylate, s-cis | -304.680672 | **0.00** | -304.765124 | 0.00 | -306.569448 | 0.00 |
| methyl acrylate, s-trans | -304.679773 | 0.56 | -304.764425 | 0.44 | -306.568407 | 0.65 |
| methyl acrylate–$BF_3$,s-cis | -627.887629 | 1.77 | -628.059948 | 1.98 | -631.260826 | 1.71 |
| methyl acrylate–$BF_3$,s-trans | -627.890442 | **0.00** | -628.063104 | 0.00 | -631.258104 | 0.00 |
| TS endo s-cis | -459.534063 | 0.16 | -459.655482 | 0.31 | -462.577738 | 0.38 |
| TS endo s-trans | -459.532078 | 1.41 | -459.653568 | 1.51 | -462.57571 | 1.65 |
| TS exo s-cis | -459.534322 | **0.00** | -459.655975 | 0.00 | -462.578342 | 0.00 |
| TS exo s-trans | -459.532143 | 1.36 | -459.653901 | 1.30 | -462.576053 | 1.44 |
| TS endo s-cis-$BF_3$ | -782.749754 | 2.84 | -782.959815 | 2.51 | -787.274886 | 2.23 |
| TS endo s-trans-$BF_3$ | -782.754290 | **0.00** | -782.963810 | 0.00 | -787.278442 | 0.00 |
| TS exo s-cis-$BF_3$ | -782.751645 | 1.66 | -782.960503 | 2.07 | -787.277135 | 0.82 |
| TS exo s-trans-$BF_3$ | -782.751519 | 1.74 | -782.961505 | 1.54 | -787.277118 | 0.83 |

Table 1.The calculated total (Hartree) and relative (kcal/mol) energy of reactants and the Transiton states at different levels.

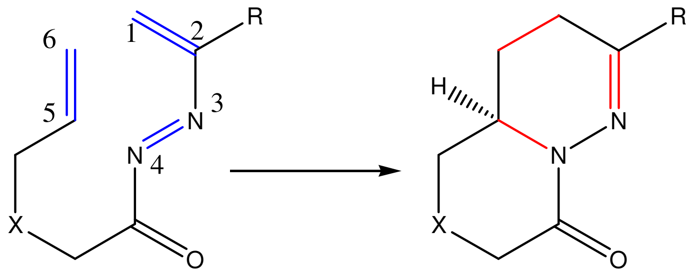
| **Structure** | **E+ZPE** | $\Delta E$ | **H** | $\Delta H^a$ | **G** | $\Delta G$ |
|---|---|---|---|---|---|---|
| butadiene, s-trans | -154.823670 | | -154.822725 | | -154.854498 | |
| methyl acrylate, s-cis | -304.571100 | 0.00 | -304.570156 | 0.00 | -304.607467 | 0.00 |
| methyl acrylate, s-trans | -304.570173 | 0.58 | -304.569228 | 0.58 | -304.606568 | 0.56 |
| methyl acrylate–$BF_3$,s-cis | -627.758613 | 1.69 | -627.757669 | 1.69 | -627.806305 | 1.83 |
| methyl acrylate–$BF_3$,s-trans | -627.761304 | 0.00 | -627.760360 | 0.00 | -627.809218 | 0.00 |
| TS endo s-cis | -459.335662 | 0.12 | -459.334718 | 0.12 | -459.380847 | 0.42 |
| TS endo s-trans | -459.333634 | 1.39 | -459.332690 | 1.39 | -459.378795 | 1.66 |
| TS exo s-cis | -459.335850 | 0.00 | -459.332756 | 0.00 | -459.381285 | 0.00 |
| TS exo s-trans | -459.333700 | 1.35 | -459.332756 | 1.35 | -459.379073 | 1.32 |
| TS endo s-cis-$BF_3$ | -782.536080 | 2.61 | -782.535136 | 2.61 | -782.591698 | 2.14 |
| TS endo s-trans-$BF_3$ | -782.540241 | 0.00 | -782.539297 | 0.00 | -782.595653 | 0.00 |
| TS exo s-cis-$BF_3$ | -782.537602 | 1.66 | -782.536658 | 1.66 | -782.593470 | 1.79 |
| TS exo s-trans-$BF_3$ | -782.537649 | 1.63 | -782.536705 | 1.63 | -782.593713 | 0.92 |

Table 2. Nullpont (ZPE) és hő (T=298. 15 K) energia korrekció (hartree) a reaktánsokra és az átmeneti elemekre katalizált és nem katalizált reakcióban RHF/6-31G* szinten. (A számolt energia: kcal mol-l).

## 2. Intramolecular hetero-cycloadditions of Azoalkens

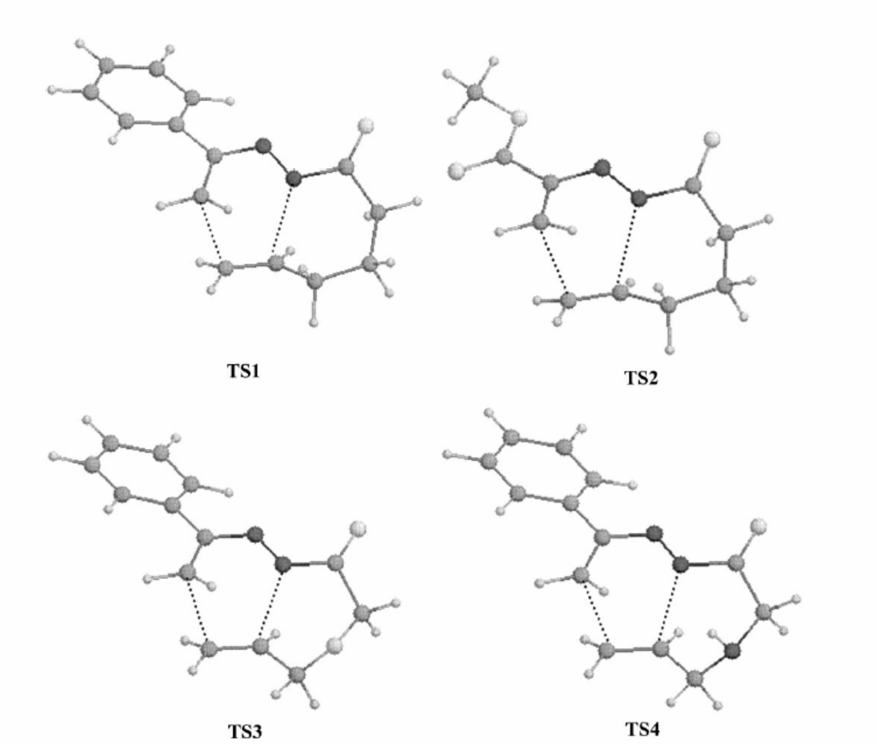
Investigation of intramolecular hetero-DA cycloaddition of Azoalken derivatives with (IMDAC) *ab-initio* method substituting different X, R funtion groups. The reaction is kineticaly controlled and a transition state is possible

It was investigated the effects of X and R groups to the assincronity and the activation energy of transition states.



**1; X=CH$_2$, R=C$_6$H$_5$**
**2; X=CH$_2$, R=COOEt**
**3; X=O, R=C$_6$H$_5$**
**4; X=NH, R C$_6$H$_5$**

1.16 Starting compounds and products of reaction.



1.17 ábra Intermediers of reaction optimised at B3LYP/6-31G* base set.

| | TS1 | | TS2 | | TS3 | | TS4 | |
|---|---|---|---|---|---|---|---|---|
| | HF/3-21G | B3LYP/6-31G* | HF/3-21G | B3LYP/6-31G* | HF/3-21G | B3LYP/6-31G* | HF/3-21G | B3LYP/6-31G* |
| C1-C6 | 2.188 | 2.297 | 2.186 | 2.274 | 2.234 | 2.341 | 2.231 | 2.33 |
| N4-C5 | 2.192 | 2.377 | 2.271 | 2.412 | 2.204 | 2.345 | 2.227 | 2.37 |
| C1-C2 | 1.364 | 1.382 | 1.366 | 1.379 | 1.369 | 1.383 | 1.37 | 1.385 |
| C2-N3 | 1.413 | 1.379 | 1.35 | 1.375 | 1.352 | 1.376 | 1.351 | 1.374 |
| N3-N4 | 1.309 | 1.284 | 1.283 | 1.282 | 1.288 | 1.285 | 1.287 | 1.285 |
| C1-C6-C5-N4 | 29.849 | 28.656 | 211.348 | 26.87 | 29.869 | 25.712 | 25.181 | 23.43 |
| Dr | 0.004 | 0.079 | 0.085 | 0.138 | 0.03 | 0.003 | 0.004 | 0.04 |

3.táblázat Geometric parametersof TS1, TS2, TS3 and TS4 strutures at RHF/3-21G and B3LYP/6-31G* levels. Assincronity is measured by differnce of C1-C6 and N4-C5 bondlenght

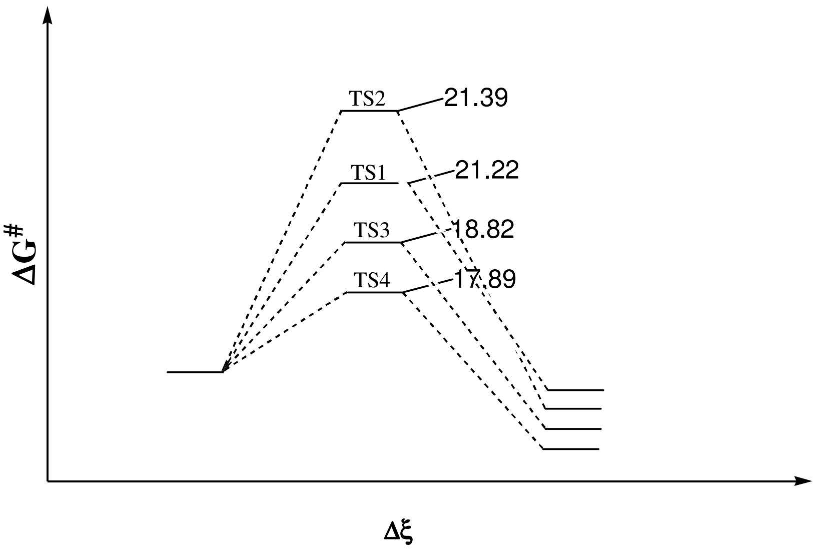
C.N. Alves, O.A.S. Romero, A.B.F. da Silva *Journal of Molecular Structure (Theochem)* 2001 **535** 165-169

| | HF/3-21G | B3LYP/6-31G* |
|---|---|---|
| R1 | -719.09 | -727.758 |
| R2 | -716.196 | -724.575 |
| R3 | -754.69 | -763.642 |
| R4 | -734.972 | -743.779 |
| TS1 | -719.048 | -727.733 |
| TS2 | -716.154 | -724.55 |
| TS3 | -754.65 | -763.621 |
| TS4 | -734.934 | -743.759 |
| $\Delta E_{TS1}$ | 26.31 | 15.34 |
| $\Delta E_{TS2}$ | 26.05 | 16.05 |
| $\Delta E_{TS3}$ | 24.97 | 13.39 |
| $\Delta E_{TS4}$ | 23.85 | 12.65 |

Results of calculations at B3LYP/6-31G*

| | ΔH# | ΔHS# | ΔG# |
|---|---|---|---|
| $\Delta E_{TS1}$ | 16.17 | 216.93 | 21.22 |
| $\Delta E_{TS2}$ | 16.84 | 215.26 | 21.39 |
| $\Delta E_{TS3}$ | 13.92 | 216.43 | 18.82 |
| $\Delta E_{TS4}$ | 13.35 | 215.23 | 17.89 |

Stability order is TS4, TS3,TS1, TS2 with agreement of experimental results.

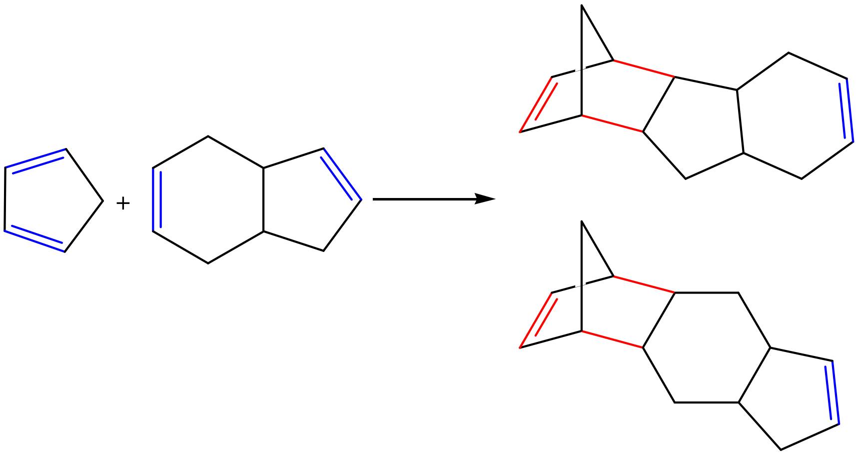


**Results**

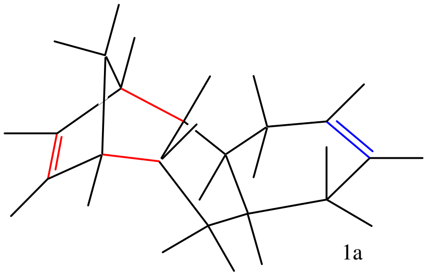
- Compared with experimental results, the calculations at RHF/3-21G base set are not enough in agreement with Houk. The minimal level is RHF/3-21G*
- Based on calculation at B3LYP/6-31G* level the TS4, TS3, TS1, TS2 stability order was achieved. This results and the free energy diffences shows qualitative similarity with experimental data

# 3. Diels-Alder reaction of cyclopentadien and bicyclononadieds

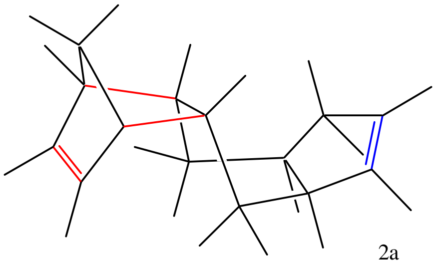
During the following reaction 8 different types of product are possible, depend on whether the cyclo-pentadien attack on thedouble bond of 5 or 6 membered ring and depend on the end or exo conformation of product.



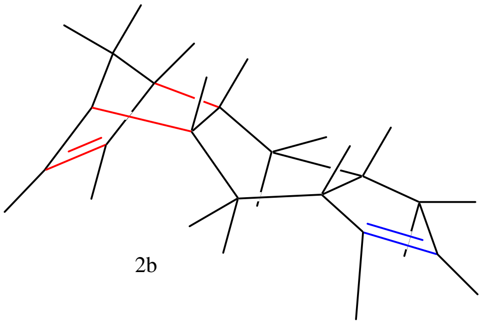
Based on experimental data three main product possible. The three main product is labelled with 1a, 2a, 2b. The possible products are endo derivatives and the 1a and 2a have exo- the 2b has endo conformation.



1a



2a

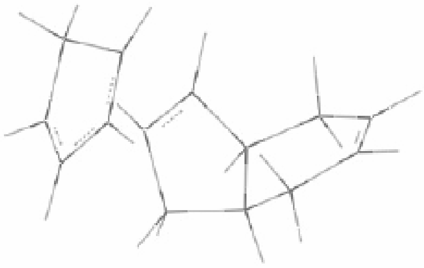


2b

The three main product. The corresponding NMR shifts are collected in the following table.

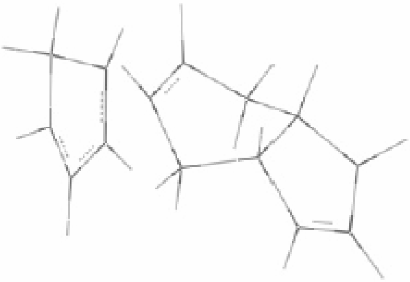
|  | 1a |  |  | 2a |  |  | 2b |  |  |
|---|---|---|---|---|---|---|---|---|---|
| Atom | $\delta^{13}$C(ppm) | $\delta^{1}$H(ppm) |  | $\delta^{13}$C(ppm) | $\delta^{1}$H(ppm) |  | $\delta^{13}$C(ppm) | $\delta^{1}$H(ppm) |  |
| 1 | 45.5 | 2.73 |  | 39.1 | 2.24 | 2.58 | 40.3 | 1.87 | 2.59 |
| 2 | 136 | 6.13 |  | 128.9 | 5.6 |  | 128.4 | 5.55 |  |
| 3 | 136.8 | 6.14 |  | 135.6 | 5.44 |  | 134.2 | 5.46 |  |
| 3a | 44.2 | 2.73 |  | 44 | 2.93 |  | 46.4 | 2.66 |  |
| 4 | 51.6 | 2.34 |  | 28 | 0.93 | 1.52 | 30.3 | 0.49 | 1.6 |
| 4a | 37.8 | 1.47 |  | 34.4 | 1.92 |  | 39.2 | 2.01 |  |
| 5 | 26.6 | 1.96 | 2.16 | 46.6 | 2.66 |  | 45.8 | 2.73 |  |
| 6 | 124.5 | 5.56 |  | 135.1 | 6.06 |  | 135.2 | 6.05 |  |
| 7 | 125.9 | 5.64 |  | 135.5 | 6.06 |  | 135.3 | 6.05 |  |
| 8 | 28.3 | 1.48 | 1.73 | 46.6 | 2.62 |  | 46.5 | 2.6 |  |
| 8a | 39.7 | 2.09 |  | 33.2 | 1.99 |  | 39 | 1.95 |  |
| 9 | 35.2 | 1.01 | 1.42 | 30.5 | 1 | 1.34 | 32 | 0.63 | 1.51 |
| 9a | 45.1 | 2.76 |  | 32.3 | 2.51 |  | 35.3 | 2.26 |  |
| 10 | 54.2 | 1.46 | 1.66 | 49.1 | 1.21 | 1.39 | 49.5 | 1.28 | 1.46 |

The computations at B3LYP/6-31G(d) were performed to map the PES. Four possible reaction path were investigated and the TSs and energy barriers are colleted in the picture above



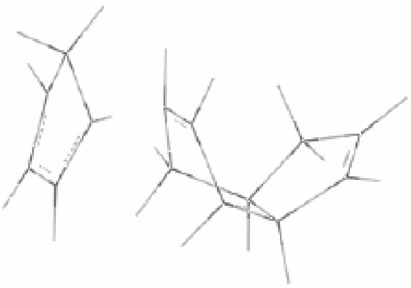
**TS1a**

$\Delta E_a = 114.6$ kJ/mol
$\Delta r = 0.041$



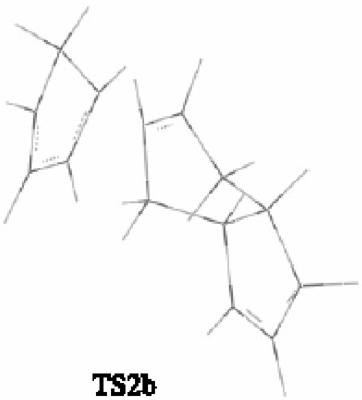
**TS1b**

$\Delta E_a = 131.2$ kJ/mol
$\Delta r = 0.05$



**TS2a**

$\Delta E_a = 109.0$ kJ/mol
$\Delta r = -0.015$



**TS2b**

$\Delta E_a = 108.2$ kJ/mol
$\Delta r = -0.021$

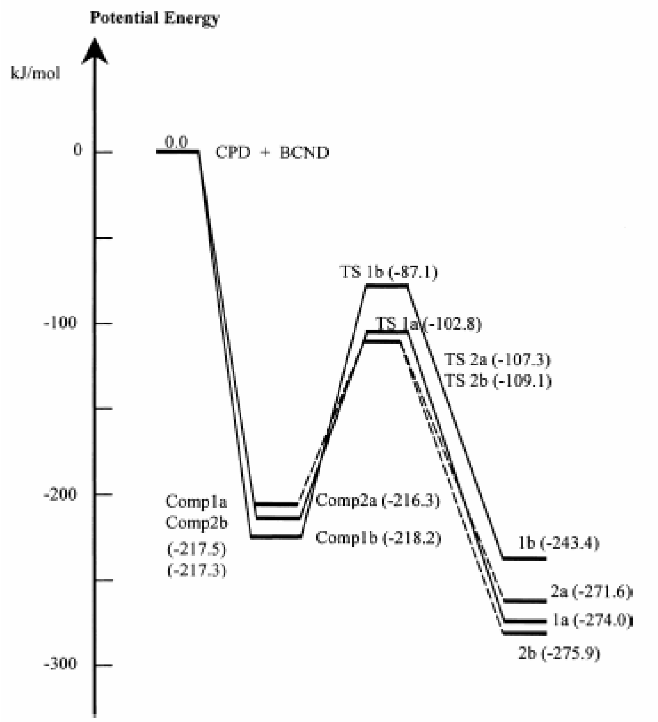
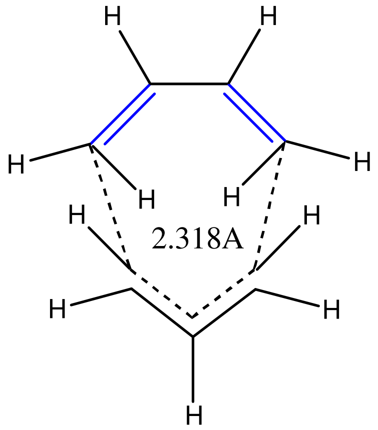


**Figure 3.** The relative energies of the reactant complexes ('comp'), transition states ('TS') and products with respect to the isolated CPD and BCND reactants calculated at the B3LYP/6-31G(d) level.

As the diagramm shows the lack of 1b product is understable and the stability order of three main product derived from calculation and experiment are same.

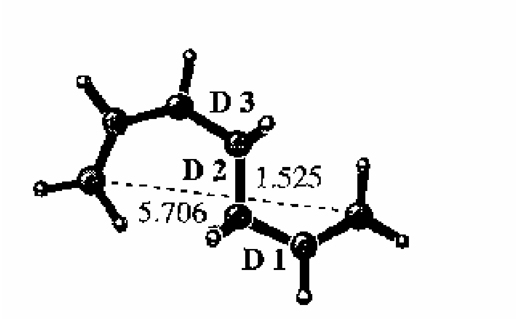
## A butadién és allil kation ionos Diels-Alder reakciójának teoretikus vizsgálata

Beatriz de Pasquale-Teresa and K.N.Houk The Ionic Diels Alder Reaction of Allyl Cation and Butadiene: Theoretical investigation: *Tetrahedron Letters* 1996 **37** 1759-1762



SP1

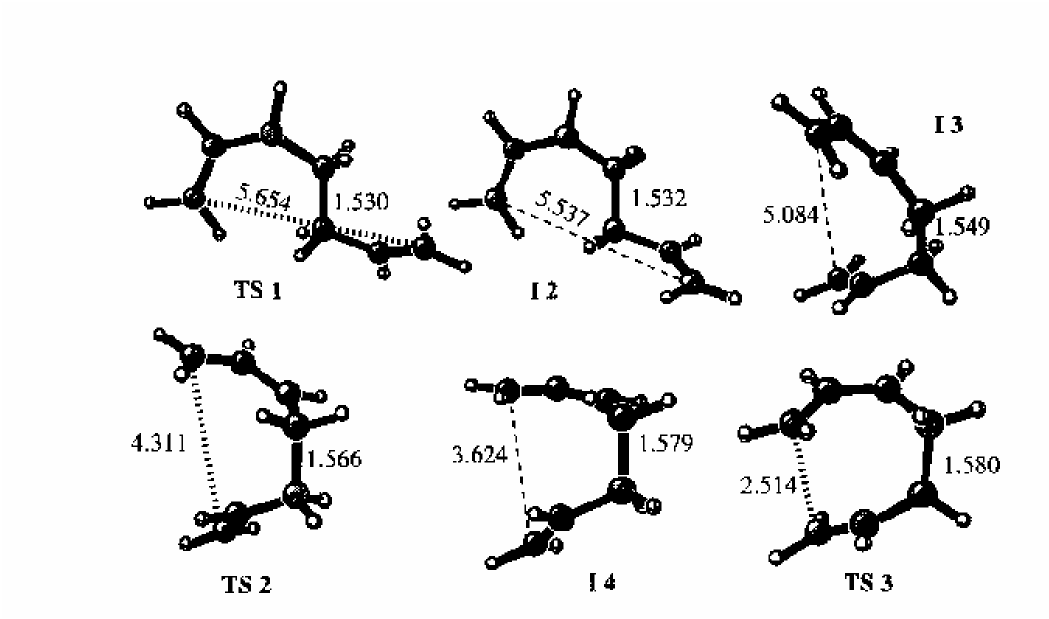
Butadién reakciója az allil kationnal, ionos Diels Alder reakció során *ab-initio* reakciókövetéssel. A feltételezés szerint az allilkation lehet olyan polarizált hogy a reakció során az asszinkronitás elérheti azt a pontot, hogy reakció töblépéses lehet. A fenti ábra a teoretikus potenciális energia felszín egy stacionárius pontjához (SP1) tartozó szerkezetet ábrázolja. A számolt reakciókoordináta megfelel a kötés kialakulás távolságának. A további vizsgálatok további minimumokhoz és nyeregpontokhoz vezettek a felületen.



**I 1**

Az ábra az egyes számú intermedier (I1) példáján keresztül definiálja a megfelelő torziós szögeket (D1, D2, D3), és kötéstávolságokat (R1, R2).

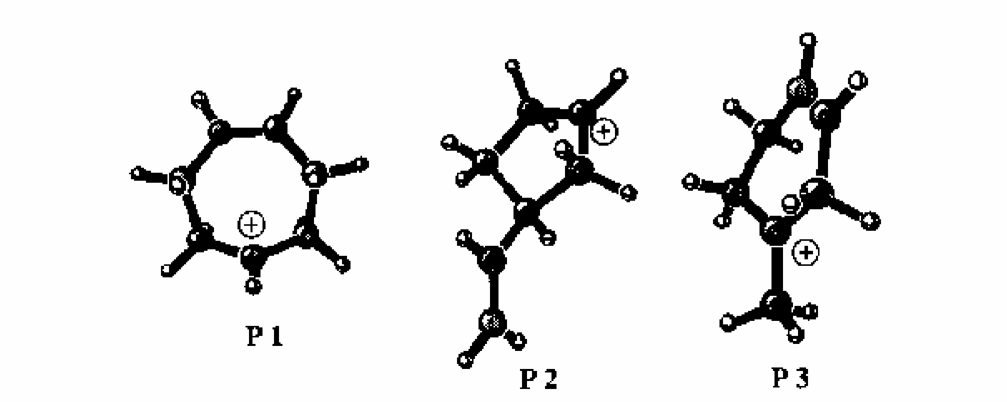
Az egyes minimum helyekhez tartozó konformerek (I) és a hozzájuk tartozó átmeneti állapotok (TS) a lenti ábrán láthatóak.



A különböző bázisokon számolt energiák, a reakció koordináták értékei és a torziós szögek a az alábbi táblázatban lettek összefoglalva.

| Structure | RHF/6-31G* | MP2/6-31G*//RHF/6-31G* | R1 | R2 | D1 | D2 | D3 |
|---|---|---|---|---|---|---|---|
| SP1 | -13.8 | -43.3 | 2.318 | 2.318 | 89.4 | -82.9 | 77.1 |
| I1 | -30.6 | -38.3 | 1.525 | 5.706 | 0 | 180 | 0 |
| TS1 | -29.7 | -37.5 | 1.53 | 5.654 | 46.3 | 176.6 | 3.3 |
| I2 | -32.2 | -39.6 | 1.532 | 5.537 | 115 | 178.5 | 0.5 |
| I3 | -36.4 | -43.3 | 1.549 | 5.084 | 116.8 | -59.8 | 133.2 |
| TS2 | -36.2 | -43.9 | 1.566 | 4.311 | 116.9 | -73.2 | 109.3 |
| I4 | -36.4 | -45.8 | 1.579 | 3.634 | 113.1 | -82.8 | 92.3 |
| TS3 | -34.3 | -53.4 | 1.58 | 2.519 | 103.2 | -76.2 | 65.9 |
| P1 | -44.5 | -61.1 | 1.603 | 1.603 |  | -72 |  |
| P2 | -41.4 | -53.2 |  |  |  |  |  |
| P3 | -61.5 | -73.4 |  |  |  |  |  |

A számítások alapján három terméket (P) találtak, melyek közül kettő stabil (**P1 és P3**) még a harmadik (**P2**) temék tovább alakul a P3 termékké.



## Further example of usage of *ab-initio* methodts in literature

- **J. I. Garcia,J. Mayoral, Luis Salvatella** An Ab Initio Study on the Confirmational and Endo/exo Preferences of Acrylates in DieIs-Alder Reactions *Tetrahedron,* 1997 **53** 6057-6064
- **Beatriz de Pasquale-Teresa and K.N.Houk** The Ionic Diels Alder Reaction of Allyl Cation and Butadiene: Theoretical investigation: *Tetrahedron Letters* 1996 **37** 1759-1762
- **C.N. Alves, O.A.S. Romero, A.B.F. da Silva** A theoretical study of the intramolecular hetero Diels-Alder cycloaddition reactions of azoalkenes *Journal of Molecular Structure (Theochem)* 2001 **535** 165-169
- **Monique Biesemans, Hassan Dalil, Loc Thanh Nguyen, Bart Haelterman, Ghislain Decadt, Francis Verpoort, Rudolph Willem and Paul Geerlings,** Regio- and stereoisomeric composition of the product mixture in the Diels–Alder reaction of dicyclopentadiene with bicyclononadiene: a NMR and DFT quantum chemical investigation *Tetrahedron* 2002 **58** 10447–10453
- Michel Couturier, Yves L. Dory, Daniel Fortin, Alain Rouillard, and Pierre Deslongchamps Ab initio and Semiempirical Corroboration of the Observed Stereoselectivity in the Transannular Diels-Alder Reaction Leading to Steroids *Tetrahedron* 1998 **54** 10089-101
- Michel Couturier, Yves L. Dory, Daniel Fortin, Alain Rouillard, and Pierre Deslongchamps Ab initio and Semiempirical Corroboration of the Observed Stereoselectivity in the Transannular Diels-Alder Reaction Leading to Steroids *Tetrahedron* 1998 **54** 10089-101
- Metin Zora A theoretical study of the cycloaddition between cyclopentadiene and allylideneammonium cation: an AM1 study *Journal of Molecular Structure (Theochem)* 2002 **619** 121–133
- Mei-Fun Cheng, Wai-Kee Li; A computational study of the Diels–Alder reactions involving acenes: reactivity and aromaticity *Chemical Physics Letters* 2003 **368** 630–638
- R. Vijaya, G. Narahari Sastry A theoretical study of intramolecular Diels–Alder reactions, diene–(CH2)n–dienophile (n Ľ 1, 2, 3 and 4) *Journal of Molecular Structure (Theochem)* 2002 **618** 201–208
- C. Delamere, C. Jakins, E. Lewars Reactions of oxiranylidene and dimethyloxiranylidene, and their generation by retro Diels–Alder-type reactions: a computational study *Journal of Molecular Structure (Theochem)* 2002 **593** 79–91

- Luis Salvatella 1, Ahmed Mokrane, Alain Cartier, Manuel F. Ruiz-Lopez, Combined AM1rMM3 computations on organic systems: the Diels–Alder reaction as a test case *Chemical Physics Letters* 1998 **296** 239–244

# Intermolecular cycloadditions

The more difficult case of an electrocyclic reaction involving cyclization by two or more reactant molecules cannot be treated in terms of simple molecular orbital diagrams, as mentioned earlier. It is therefore necessary in every case to use energy level correlation diagrams, and it is preferable to amplify and justify the explanation of the resulting selection rules by using state-correlation diagrams as well. To illustrate the procedure involved in treating intramolecular processes, let us first consider the simplest possible case, the (2 + 2) cycloaddition of two ethylenes to give cyclobutane (24). It is first of all necessary to put together the reactant molecule in a reactant complex (**A**) and the final molecular product (**B**). Let us assume a reasonable geometry of approach of the two ethylenes. Although other stereochemical approaches are feasible, it is most reasonable to assume that the two ethylenes approach each other perpendicularly with respect to the parallel nodal planes of their two π-systems (as shown in Fig 2). In this way the π–lobes will overlap most directly to form the new σ–bonds of the cyclic product. It is evident that two essential elements of symmetry are retained by the system as the cyclobutane is formed. These are the plane of symmetry $\sigma_1$ that bisects the two

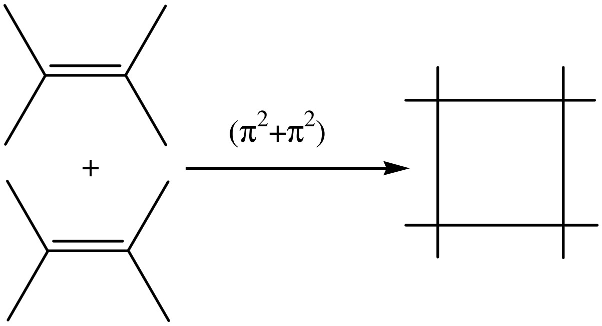


**Fig 1**

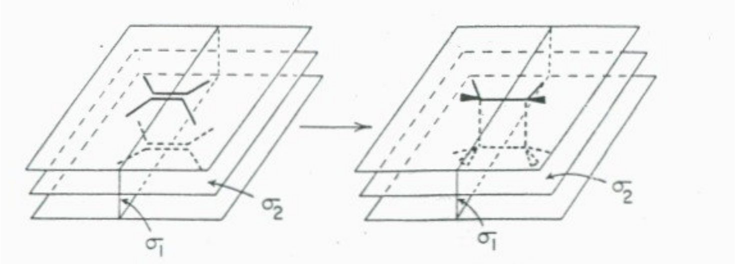


**Fig 2**

ethylenes, and the plane $\sigma_2$ that lies midway between the parallel nodal planes of the approaching $\pi$–systems. Each of these planes is a symmetry element of the product cvclobutane, and each bisects bonds being made or broken during the reaction.

Without necessarily considering the relative energies of the MOs involved, it is clear that as the four $\pi$–level of the two ethylenes interact to give cyclobutane, there will arise four corresponding $\sigma$–leves. It is reasonable to depict these levels as shown in Fig. 3. The question is: How do the $\pi$–MOs corresponding to these levels interact and what are their symmetries with respect to the two platnes $\sigma_1$, and $\sigma_{□}$? In looking at the reaction in the direction of cyclization, it is necessary to treat the two ethylenes as one system, since once overlap begins to occur they will in effect be one system. Only in this wav can the appropriate symtnetry elements be considered. It is simplest to project the above diagrams of reactants and products onto the plane that contains

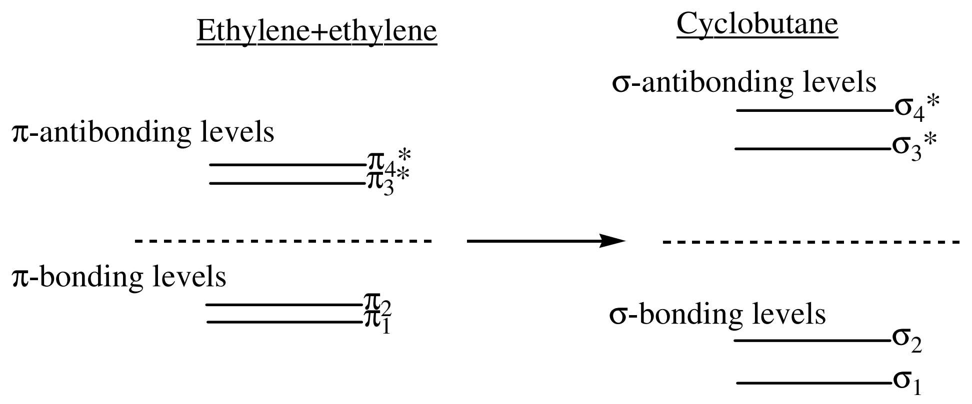
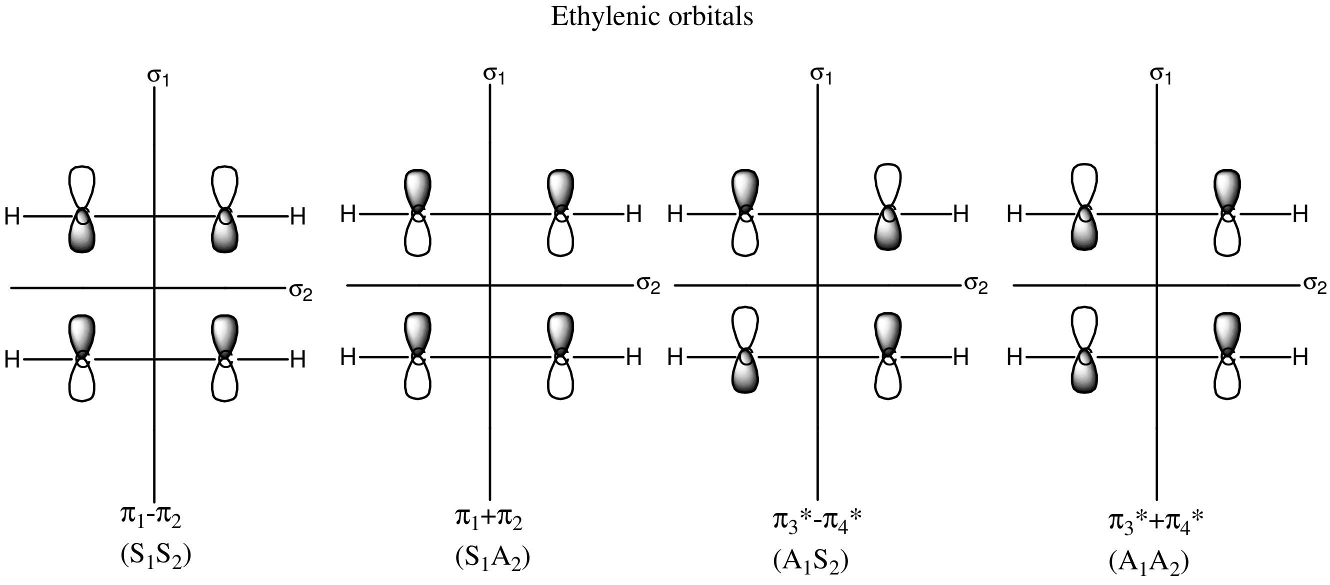


**Fig 3**



$\pi_1$-$\pi_2$ ($S_1S_2$)

$\pi_1$+$\pi_2$ ($S_1A_2$)

$\pi_3$*-$\pi_4$* ($A_1S_2$)

$\pi_3$*+$\pi_4$* ($A_1A_2$)

possible combinations of π-bonding MOs

possible combinations of π-antibonding MOs

**Fig. 4**

all four carbons and depict all possible combinations of the two sets of ethylenie π–orbitals. The planes $\sigma_1$ and σ□ then become the orthogonal lines shown in Fig. 4. It is seen that only four combinations are possible. These are the symmetric and antisymmetric combinations of each pair of either bonding or antibonding π–orbitals. Other combinations are not allowed, since they would lead to formation of product MOs that are unacceptable wave functions for the cyclobutane system.

In order to consider the symmetry conservation rule the symmetry of the molecular orbitals involved must be assigned. Althoug the product is a square, $D_{4h}$, the two ethylane molecules approachin each other can be assigned to the $C_{2v}$ point group. The two σ-planes will be used to characterize the symmetry of the orbitales involved, Namely +1, +1 as well as -1, -1 will be classified as “symmetric”, namely the first one (+1, +1) belongs to the $A_1$ and the second (-1, -1) to $A_2$ irreducibile representation. Furthermore, there is a +1,-1 and a -1,+1 combination result in the $B_1$ and the $B_2$ irreducibile representations.

| $C_{2v}$ | E | $C_2(z)$ | $\sigma_v(x,z)$ | $\sigma_v(yz)$ |
|---|---|---|---|---|
| $A_1$ | +1 | +1 | +1 | +1 |
| $A_2$ | +1 | +1 | -1 | -1 |
| $B_1$ | +1 | -1 | +1 | -1 |
| $B_2$ | +1 | -1 | -1 | +1 |

A and B are both one dimensional representations, „character” +1 stands for symmetric and -1 for antisymmetric „operation”

If these interactions are allowed to continue to form the final σ–type orbitals of cyclobutane, they can be represented as shown in **Fig. 5.** As before only the σ–envelopes in the regions of the newly formed bonds are shown, although the σ–orbitals of cyclobutane will be completely delocalized. The symmetries of the orbital combinations of the two ethylenes can now be assigned with respect to $\sigma_1$ and $\sigma_\square$. The first combination ($\pi_1 - \pi_\square$) is symmetric with respect to both $\sigma_1$ and $\sigma_\square$ and is designated as $(S^1S^2)$ or more simply (SS). The second combination ($\pi_1 + \pi_2$) is $(S^1A^2)$ or (SA), and so on. The cyclobutane σ–orbitals have corresponding symmetries, as indicated in parentheses in the diagram.

Cyclobutane MOs

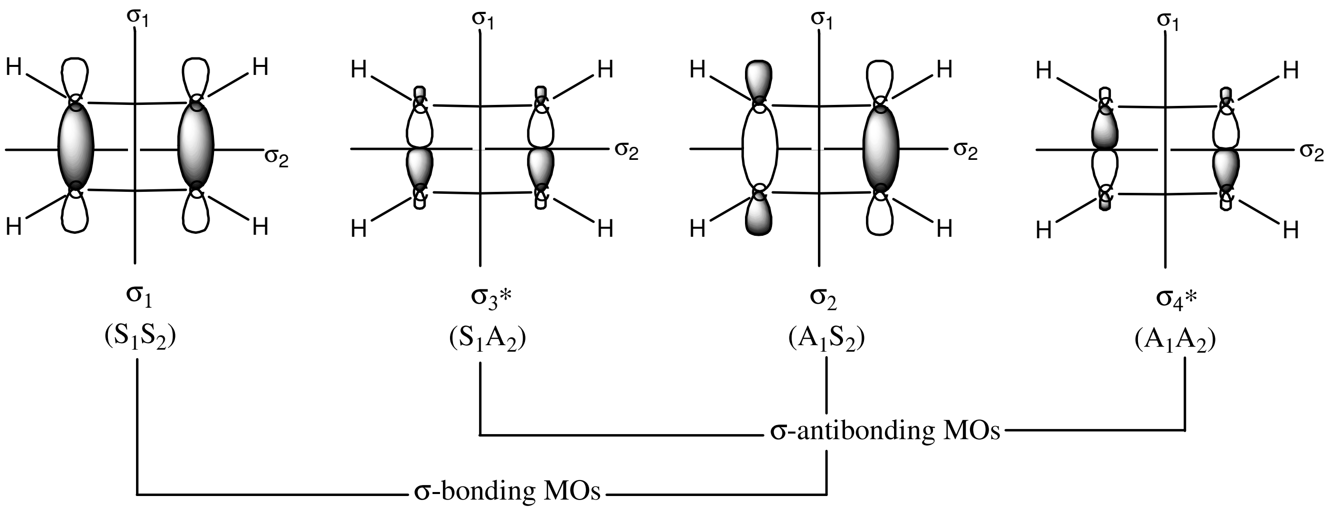


**Fig 5**

It can be seen from the two orbital diagrams Figs. 4 and 5 that the original π–bonding orbitals of the ethylenic systems combine to give the (SS) and (SA) orbitals of the interacting system, but the final σ–bonding orbitals of cyclobutane are (SS) and (AS). This is shown more clearly in schematic form (Fig 6), where the two π–levels are initially shown as degenerate, as are the two π*-levels. The σ–levels are ranked according to their increasing numbers of nodes. The main point is that the bonding orbitals of the reactant system do not correlate directly with the bonding orbitals of the product, thus level-crossings must occur between bonding and antibonding levels durring reaction. Although the $\pi_{ss}$ combination decreases in energy along the reaction coordinate. the psa combination increases markedly as the reaction proceeds as it tries to correlate with an antibonding level in the product. The reaction is therefore thermally forbidden, since to conserve orbital symmetry the ground-state reactants are trying to form a doubly excited product and the reaction has a large symmetry-imposed barrier. However, if one of the ethylenic π–electrons is excited to a π*-level, the reaction will then be allowed since the reactant system now correlates directly with a singly excited state of the product, as shown in Fig. 7. (This point will be shown more clearly later by means of a state-correlation diagram (Fig 14).)

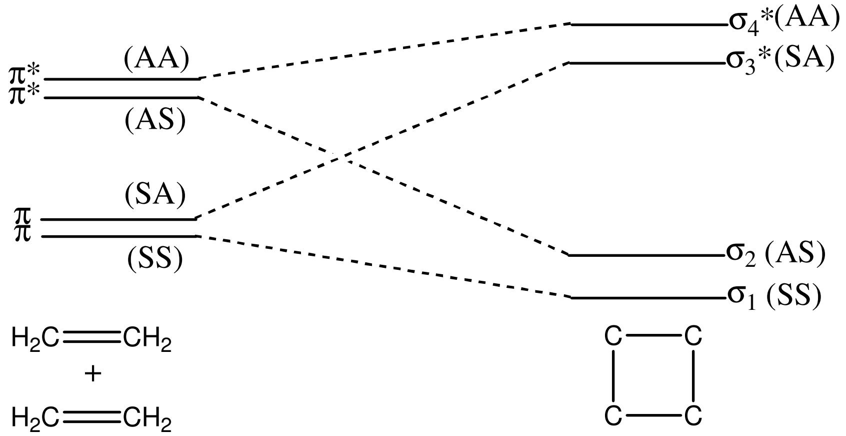


**Fig 6**

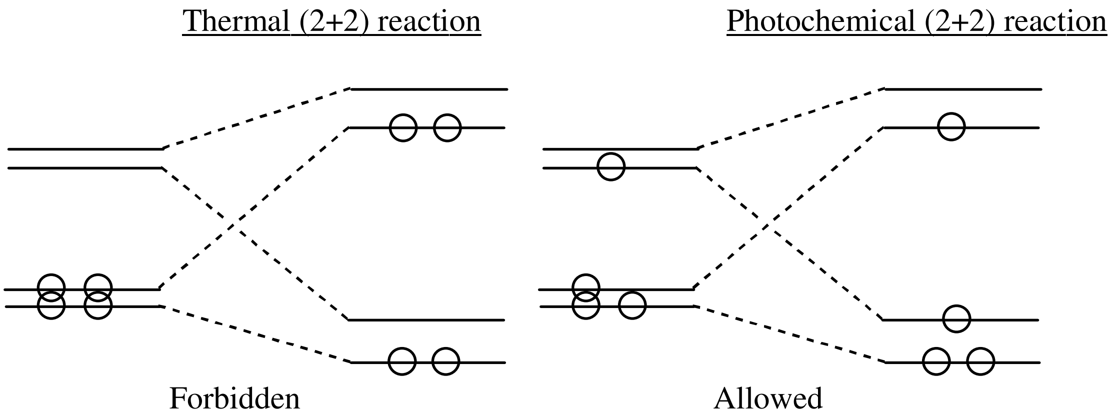


**Fig 7**

We next consider the reaction of ethylene and butadiene to form cyclohexene. This prototypical Diels−Alder reaction is called a (π4 + π2), or simply a (4 + 2) cycloaddition. The transition state for this addition is reasonably considered to have the diene and dienophile in parallel planes with the reacting termini as close together as possible. Thus reactants and products are arranged as shown in Fig. 8 Now there is only one element of symmetry that is common to the reactant "molecule" (the interacting diene and dienophile) and the product. This is the plane of symmetry $\sigma_1$ that bisects both the interacting ethylene and butadiene, and also bisects the newly formed cyclohexene double bond.

We now try to relate the six reactant levels, which are all π−type (four from butadiene, two from ethylene) to the resultant four σ−type and two π−type levels of the product cyclohexene. These are depicted in

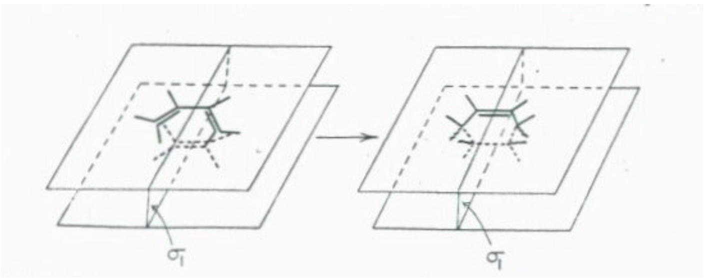


**Fig 8**

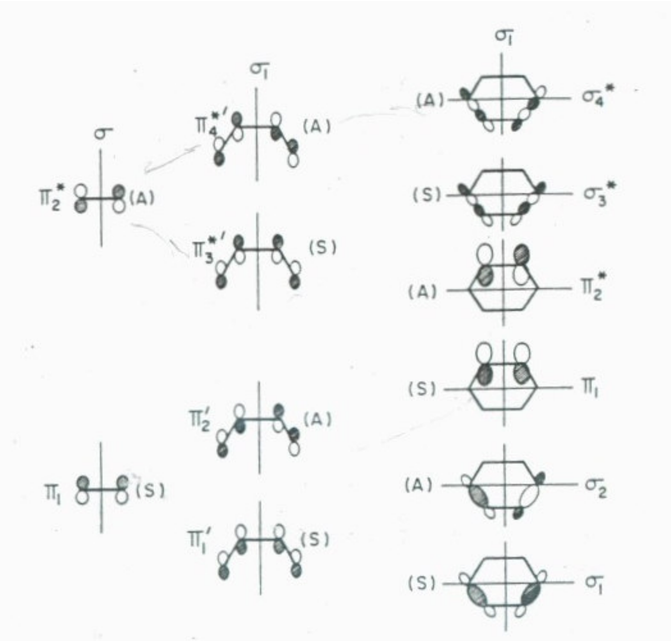


**Fig 9**

Fig. 9 There is no problem in representing the two sets of reactant MOs., which are shown side-by-side for convenience, and their symmetries with respect to the plane σ. Similarly there is no problem in describing the p and π* orbitals of the product, which are taken to be like the HMO orbitals of ethylene. To deal with the σ–type orbitals in the product, clearly there must be two σ–orbitals and two σ*-orbitals. These will be delocalized over both newly formed σ–bonding regions and can only be reasonably represented in those regions as shown. It is also reasonable to rank the more symmetrical s (or σ*) orbital as being lower in energy than the less symmetrical one, since it has fewer nodes. The symmetries of the cyclohexene orbitals with respect to s are also shown.

An energy level correlation diagram (Fig. 10) can now be constructed. Although the particular ordering and spacings shown for the various energy levels is reasonable, this is not essential to the discussion.

Again, it is only the separation into either bonding or antibonding levels that is important.

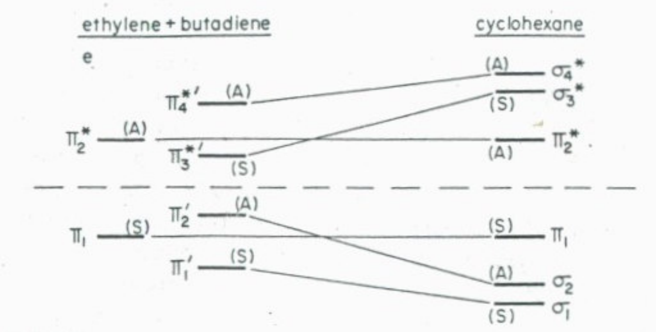
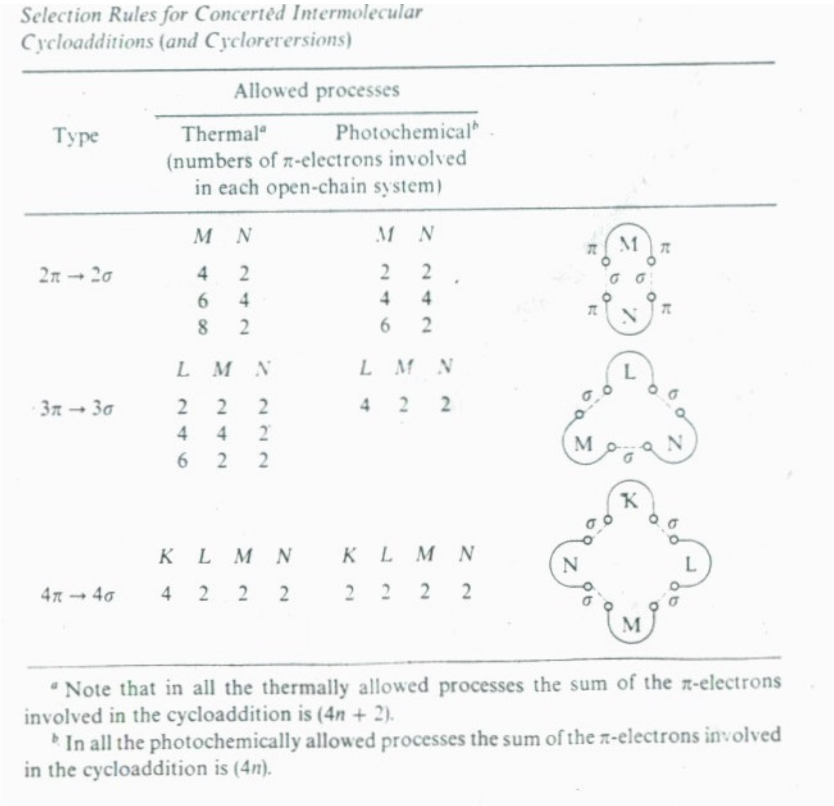


**Fig 10.**

Again, levels of like symmetry that are closest in energy are connected. Since there are equal numbers of bonding levels of a particular symmetry in both reactants and product, there are no correlations between bonding and antibonding levels. Thus there is no symmetryimposed barrier and the (4 + 2) reaction is thermally allowed. The most accessible excited state of the reactants would involve promotion of an electron from π2' to p3*' of butadiene. This would then give a direct correlation with a much higher and different type (s –s* ) of excited state of the product, thus the (4 + - 2) cycloaddition is photochemically forbidden. (Again it is not clear why other possible excited state processes should not be allowed. However, it will be shown later by means of state-correlation diagrams that there is a symmetryimposed barrier to all reasonable photochemical processes and that the reaction is forbidden in this mode.)

To summarize, and compare the above types of intermolecular cycloaddition. it is seen that the (π2 + π2) process should be thermally very diffcult because orbital symmetry conservation requires a correlation between a bonding level in the reactants and an antibonding level in the product. Thus the energy of the system increases along the reaction coordinate and the reaction is said to be symmetry forbidden. Excitation of an electron in one of the reactants causes the energy, change along the reaction coordinate to be decreased, and the reaction becomes more favorable photochemically and is said to be symmetry allowed. On the other hand, the (p4 + π2) cycloaddition involves no such correlations of honding levels in the reactant and antibonding correlations of bonding levels in the reactant and antibonding levels in the product, hence the energy does not increase along the reaction coordinate. Thus the thermal (p4 + π2) reaction is said to be symmetry allowed. However, excitation of an electron in the reactants causes the energy change along the reaction coordinate to be increased, and the photochemical (p4 + π2) reaction is said to be forbidden.

Similar considerations can be applied to other types of intermolecular cycloaddition reactions, which may involve two or more reactant molecules. Using this type of approach, Woodward and Hoffmann have extended the selection rules to cover the general ypes of intermolecular cycloaddition. These rules are given in Table VII. 3. The basis of these rules is exactly as described for the two simple cases above: If orbital symmetry conservation requires one or more correlations between bonding levels in the initial state and antibonding levels in the final state, the reaction will be energetically unfavorable in a thermal sense, but favorable photochemically. If no such correlation



*Selection Rules for Concerted Intermolecular Cycloadditions (and Cycloreversions)*

| | Allowed processes | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Type | Thermal[a] (numbers of π-electrons involved in each open-chain system) | | | | Photochemical[b] | | | |
| | | | M | N | | | M | N |
| 2π → 2σ | | | 4 | 2 | | | 2 | 2 |
| | | | 6 | 4 | | | 4 | 4 |
| | | | 8 | 2 | | | 6 | 2 |
| | | L | M | N | | L | M | N |
| 3π → 3σ | | 2 | 2 | 2 | | 4 | 2 | 2 |
| | | 4 | 4 | 2 | | | | |
| | | 6 | 2 | 2 | | | | |
| | K | L | M | N | K | L | M | N |
| 4π → 4σ | 4 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |

[a] Note that in all the thermally allowed processes the sum of the π-electrons involved in the cycloaddition is $(4n + 2)$.

[b] In all the photochemically allowed processes the sum of the π-electrons involved in the cycloaddition is $(4n)$.

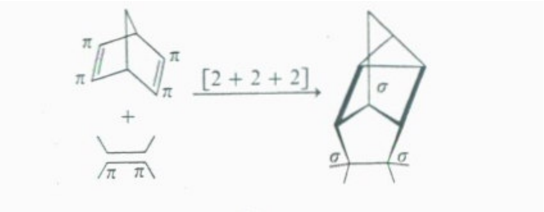
Note that in all the thermally allowed processes the sum of the π–electrons involved in the cycloaddition is (4n + 2).

In all the photochemically allowed processes the sum of the π–electrons involved in the cycloaddition is (4n)

exist, the reaction will be favorable thermally, but difficult photochemically.

These selection rules are in excellent accord with experiment for the many known cases of thermal and photochemical cycloadditions and cycloreversions. A few general illustrations of the success of these rules are as follows.

The (2 + 2) cycloaddition of two ethylenic systems is a widely observed photochemical reaction, whereas the reaction does not readily take place thermally. The reverse reaction, such as the pyrolysis of cyclobutane, is known, but there is evidence that it is a stepwise process involving a radical intermediate. On the other hand, thermal Diels-Alder or (4 + 2) cycloaddition reactions are extremely widespread and there is overwhelming evidence that these are concerted processes. Photochemical Diels-Alder reactions are much less common and there is less evidence available on whether these are stepwise or concerted. The (4 + 4) cycloaddition is a well-known reaction, but has only been observed photochemically. Thermal [6 + 4] cycloadditions were unknown until formulation of the principle of conservation of orbital symmetry and the selection rules stimulated a search for such processes; they are now well-known reactions. Cycloadditions involving more than two molecules are less well known since entropy factors do not favor such processes, but the thermal reaction of three acetylene molecules to give benzene is an example of a (2 + 2 + 2) cycloaddition. Similar processes are known where two of the three π–systems are incorporated into the same molecule, in a nonconjugated arrangement, such as in (25). Many specific examples of cycloaddition and cycloreversion reactions are given in Woodward and Hoffmann's original monograph on the subject of conservation of orbital symmetry. It is suffitcient to say that the success of their selection rules both in explaining known results and in predicting new ones has been truly remarkable.



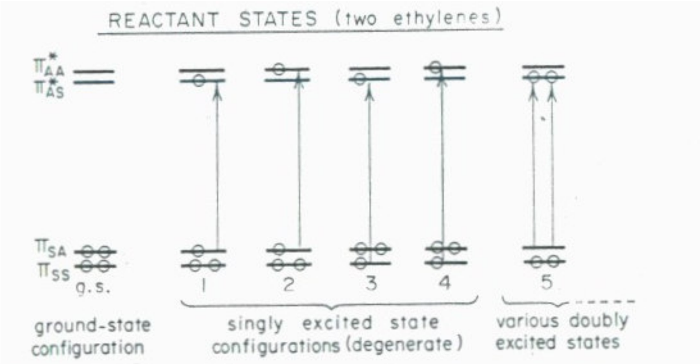
(25)

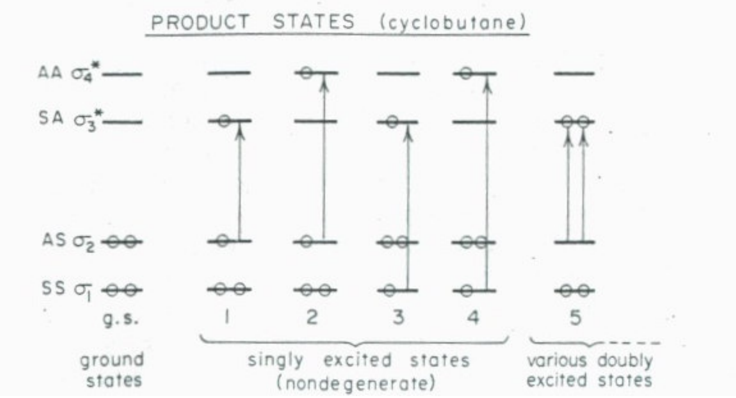
It has been pointed out that for intramolecular cycloadditions it is necessary to consider state-correlation diagrams to provide a fully satisfactory evplanation of the differences in stereochemical preference exhibited by thermal as against photochemical modes of a given reaction. This is also true for intermolecular cycloadditions, since we have already seen that it is not always evident from energy level correlation diagrams why an allowed thermal process should necessarily be photochemically forbidden, or vice versa. Construction of state diagrams for the (2 + 2) and (4 + 2) cycloadditions just considered will illustrate more clearly why this difference occurs between the thermal and photo-chemical reactions.

## State-correlation diagrams for intermolecular cycloadditions and cycloreversions

We proceed in the same way as before by considering the various possible excited states of the reactants and products, and their total state symmetries as well as the symmetry characteristics of the individual electronic components. For the (2 + 2) cycloaddition of two ethylenes, the ground-state configuration of the reactant system and those of its various electronically excited states are shown in Fig. VII 26. The corresponding ground-state and excited state configurations of the product are given in Fig. VII 27.

The symmetries corresponding to the individual levels have already been determined for the energy level correlation diagram in Fig. VII. 21.





A table of reactant and product-state symmetries (with respect to elements σ1 and σ2, respectively) can now be drawn.up (Table VII. 4), based on the various electronic configurations.

In order to conserve orbital symmetry, both states and levels of like symmetry correlate, as showin in the state diagram in Fig. VII.28. It can be seen that thermally, the ground-state reaction (p)2(p)2----(σ1)2(σ2)2 has a high symmetry-imposed barrier, since (SS)2(SA)2 in the reactants correlates with (SS)2(SA)2 in the products, which is the highly excited state configuration (σ1)2(s3*)2. Therefore, the (2 +2) reaction is thermally forbidden. Photochemically one of the degenerate reactant excited states (SS)2(SA)1(AS)1 correlates directly with the lowest of the cyclobutane excited states

(SS)2(AS)1(SA)1 with no barrier due to, orbital symmetry conservation. Therefore, the reaction is allowed photochemically. The other excited states [(2)-(4)] only correlate with more highly excited states (not shown in the diagram).

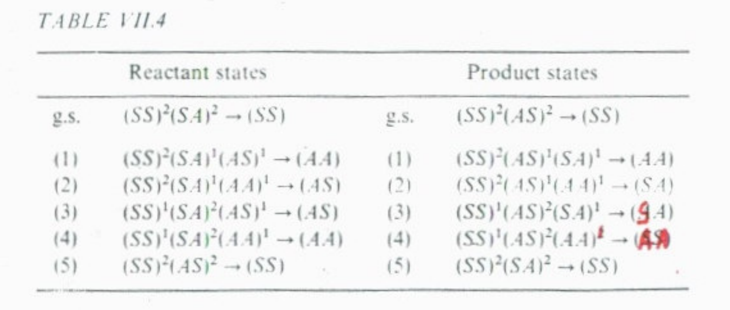
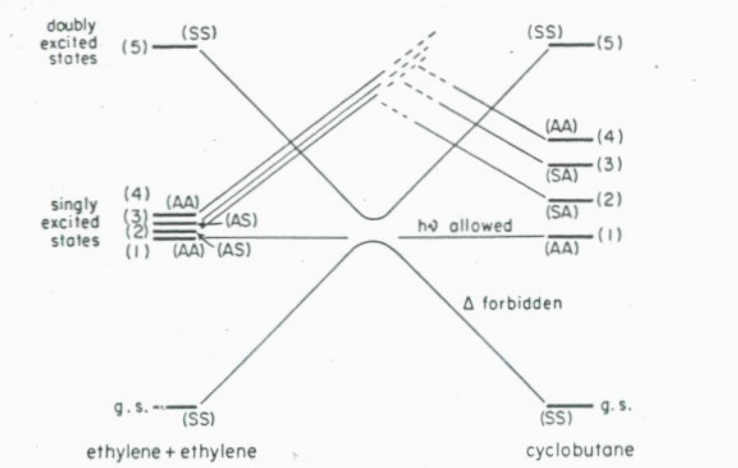


TABLE VII.4

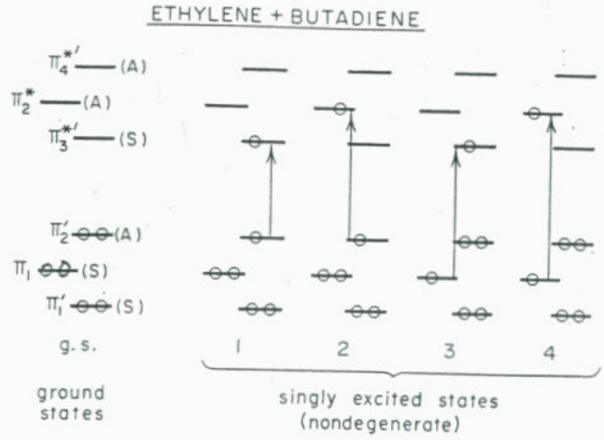
| | Reactant states | | Product states |
|---|---|---|---|
| g.s. | $(SS)^2(SA)^2 \rightarrow (SS)$ | g.s. | $(SS)^2(AS)^2 \rightarrow (SS)$ |
| (1) | $(SS)^2(SA)^1(AS)^1 \rightarrow (AA)$ | (1) | $(SS)^2(AS)^1(SA)^1 \rightarrow (AA)$ |
| (2) | $(SS)^2(SA)^1(AA)^1 \rightarrow (AS)$ | (2) | $(SS)^2(AS)^1(AA)^1 \rightarrow (SA)$ |
| (3) | $(SS)^1(SA)^2(AS)^1 \rightarrow (AS)$ | (3) | $(SS)^1(AS)^2(SA)^1 \rightarrow (SA)$ |
| (4) | $(SS)^1(SA)^2(AA)^1 \rightarrow (AA)$ | (4) | $(SS)^1(AS)^2(AA)^1 \rightarrow (AS)$ |
| (5) | $(SS)^2(AS)^2 \rightarrow (SS)$ | (5) | $(SS)^2(SA)^2 \rightarrow (SS)$ |



Turning to the (4 + 2) cycloaddition, the ground and various singly excited state configurations are shown in Fig. VII. 29. The corresponding reactant and product symmetries are given in Table VII.5.

The state-correlation diagram can be constructed as before, conserving orbital symmetry with respect to both states and individual levels and keeping in mind the noncrossing rule. This is shown in Fig. VII 30. Unlike the case of the (2 + 2) reaction, there is now a direct correlation between reactant [(S)2(S)2(A)2] and product [(S)2(A)2(S)2] ground states, and the reaction is thermally allowed. Turning to the various excited state processes, the lowest excited state in the reactants (S)2(S)2(A)1(S)1 correlates directly with a much higher (doubly) excited state of the products (S)2(A)1(S)2(S)1. This process has a large barrier and will be difficult photochemieally. It appears at first that either of the two (S) --- (S) interconversions, which have no symmetryimposed barrier, would allow the reaction to take place photochemically. However, consideration of the energy level diagrams for (ethylene and butadiene) shows that neither of these processes is feasible, since each necessitates excitation from a bonding orbital in one reactant molecule to an antibonding orbital in the other. Thus (4 + 2) reaction is still photochemically forbidden.

Alternatively, in the reverse direction, these processes would involve starting from a (π−σ*) or (σ−p*) state of cyclobutane to give an ethylene product with one or three electrons and a butadiene with five or three.



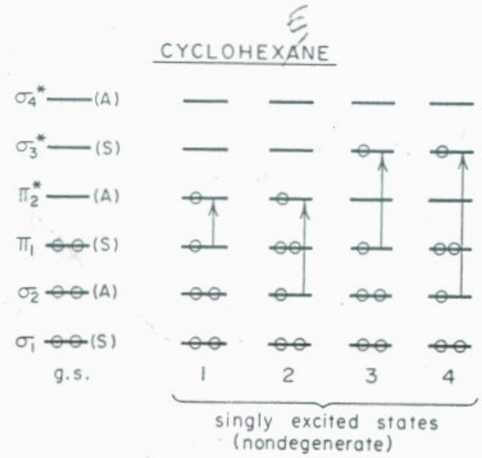
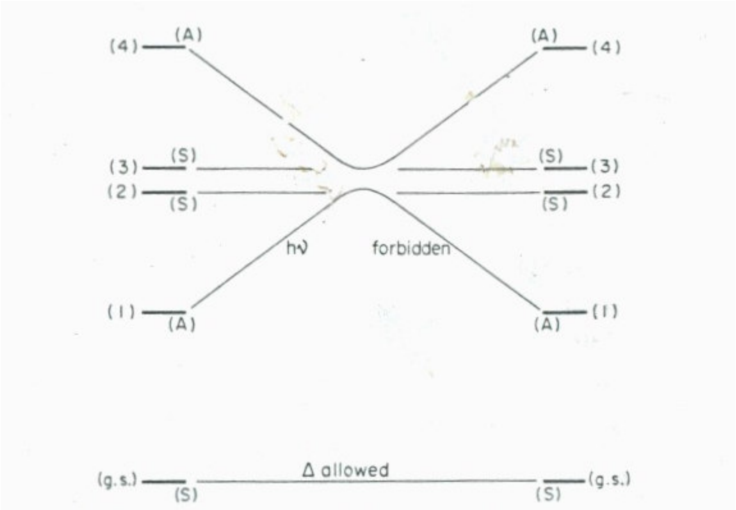


*TABLE VII.5*

| | Reactant states | | Product states |
|---|---|---|---|
| (g.s.) | $(S)^2(S)^2(A)^2 \rightarrow (S)$ | (g.s.) | $(S)^2(A)^2(S)^2 \rightarrow (S)$ |
| (1) | $(S)^2(S)^2(A)^1(S)^1 \rightarrow (A)$ | (1) | $(S)^2(A)^2(S)^1(A)^1 \rightarrow (A)$ |
| (2) | $(S)^2(S)^2(A)^1(A)^1 \rightarrow (S)$ | (2) | $(S)^2(A)^1(S)^2(A)^1 \rightarrow (S)$ |
| (3) | $(S)^2(S)^1(A)^2(S)^1 \rightarrow (S)$ | (3) | $(S)^2(A)^2(S)^1(S)^1 \rightarrow (S)$ |
| (4) | $(S)^2(S)^1(A)^2(A)^1 \rightarrow (A)$ | (4) | $(S)^2(A)^1(S)^2(S)^1 \rightarrow (A)$ |


(4)
(A)
(A)
(4)
(3)
(S)
(S)
(3)
(2)
(S)
(S)
(2)
hν
forbidden
(1)
(A)
(A)
(1)
Δ allowed
(g.s.)
(S)
(S)
(g.s.)