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# Local Softness as a Regioselectivity Indicator in [4+2] Cycloaddition Reactions

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As part of our continuing interest in the connection between chemical reactivity and the HSAB principle, both globally and locally, we explored via 3-21 G calculations on local and global softness the statement made by Gazquez and Mendez. Their statement, claiming that two chemical species should react through atoms showing equal softness, has been precised to rationalize the regioselectivity of Normal Electron Demand Diels−Alder reactions between terminally monosubstituted 1,3-butadienes and monosubstituted ethenes. In the presence of this substitution pattern, a head-to-head mode of cyclization is largely experimentally observed, also known as "ortho rule". The closest values of the condensed local softness were found for the unsubstituted termini, thereby suggesting that these cycloadditions would proceed through an asynchronous pathway, as supported by transition state geometries reported by Houk et al.

## I. Introduction

As one of the most investigated pericyclic reactions, the Diels−Alder reaction also presents a frequency of utilization in the synthetic field far superior to other classes of organic reactions. The usefulness of the Diels−Alder reaction is due to its versatility and to its almost never failing regio- and stereoselectivity.

Mostly used is the so-called Normal Electron Demand Diels−Alder reaction (NED reaction) where the diene contains electron-donating groups and the alkene electron-withdrawing groups. Its counterpart, the Inverse Electron Demand Diels−Alder reaction (IED reaction), is favored by opposite properties of the substituents on diene and alkene.

From the early beginning of application of the Diels−Alder reaction, experimentalists were aware of the "directing forces" of the substituents. Upon cycloadduct formation from asymmetrically substituted dienes with asymmetrical dienophiles it rapidly became obvious that one of two possible regioisomers always predominated or was formed exclusively. Often this reaction product proved to be the contrathermodynamic product (see Figure 1).

An overview[1] on structural orientation appeared as early as 1962, with the formulation of empirical generalizations. Upon reaction of a monosubstituted olefin with a 1-substituted diene, predominance of ortho cycloadduct (head-to-head cycloaddition) is to be expected and reaction with a 2-substituted diene predominantly yields the para cycloadduct (head-to-tail cycloaddition) at the expense of the meta cycloaduct, just as in the previous case.

The "ortho rule" and "para rule" remained but a time mere statements. From the 1960s on, their persistency prompted studies attempting to understand them on a theoretical basis.

As the ortho (-endo) cycloadduct is much more crowded, as compared to the meta (-endo) cycloadduct, it may be considered as a kinetic product. The elucidation of the regiochemistry of the Diels−Alder reaction has been attempted in a number of ways through mechanistic approaches. In the parent reaction of *sec*-butadiene with ethylene, a transition state resulting from the bonding of the termini to exactly the same extent at every stage of the reaction, i.e. in a synchronous, concerted manner, has been assumed and recently confirmed by a theoretical study of the reaction in the gas phase.[3] When the cycloaddends however are carrying substituents, either a stepwise or a concerted, not necessarily synchronous, pathway is generally accepted, although the exact nature of the transition state seems to remain controversial as can be deduced from the personal account, *Passions and Punctilios 1935−1995*, by K. N. Houk.[4]

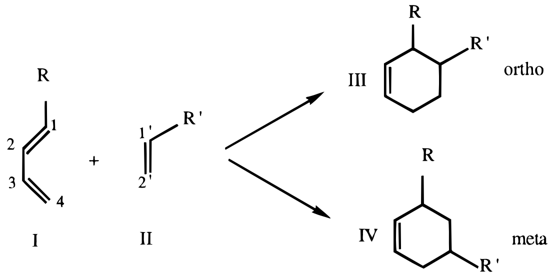

**Figure 1.** Formation of the ortho and meta regioisomers III and IV upon Diels−Alder reaction between I and II. The stereoselectivity of the cyclization—governed by the endo and cis rules and giving rise to diastereoisomerism—will be of no concern to us in this work.

Numerous qualitative and quantitative FMO studies[5−11] considering the HOMO−LUMO orbital interaction led to interpretations or predictions concerning the reaction rate and the regioselectivity of Diels−Alder reactions generally in agreement with experimental results.

It is firmly established that the energy difference between the HOMO LUMO of both $\pi$ systems determines the reaction rate, while regiocontrol is the result of the selective interaction between the termini pairs with the largest molecular orbital coefficients (for reviews see refs 12−18).

The NED Diels−Alder reaction is HOMO-diene−LUMO-dienophile-controlled: a smaller energy separation between the HOMO of the electron-rich diene and the LUMO of the electron-poor dienophile favors the process. So, coordination of a dienophile with Lewis acids shows significant rate and regioselectivity enhancement by lowering the difference between the MO energy levels. A LUMO-diene−HOMO-dienophile control is valid for IED Diels−Alder reactions. It is thus essential that

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cycloaddends should have complementary electronic character. In practice, when the cycloaddends are adequately matched, the rate and the regiochemistry have a synergetic effect on the production of but one regioisomer.[19]

In recent times, synthetically orientated research usually proposes interpretations of the observed experimental selectivities based on the FMO theory, although occasionally the validity of the simple FMO approach (where one term in the perturbation expansion is supposed to dominate all others) is questioned. A rigorous testing of the model has therefore been recommended.[20] Improvement of the model has been achieved by taking into account secondary orbital interactions.[21−24]

Actually, the prediction of the regiochemical outcome of a Diels−Alder reaction can start from the judicious choice of a two-center interaction (with or without implications on the transition state); the problem to be solved is to know which and why two termini are the leading centers in bonding. As early as 1958, Woodward and Katz, analyzing both one-step intermediates (the head-to-tail and the head-to-head intermediates) of the cyclodimerization of *s-cis*-acrolein (a NED reaction), pointed out that although more stabilized, the head-to-tail could only lead to the never-detected 3,4-dihydro-2*H*-pyran-3-carbaldehyde. Moreover, one-step intermediates could never account for the effect of substituents related to their location; these authors thus preferred the asynchronous two-step process, with a primary bonding between the unsubstituted termini to an open-chain intermediate, the 2,5-diradical of hexanedial; "secondary attractives forces" should operate in the subsequent cyclization step.[25]

About 20 years later, the faster bonding in the dimerization of acrolein between their terminal unsubstituted carbon atoms was recovered using SCF-perturbation theory.[26] Rapid bond closing between the unsubstituted carbons, instead of those close to the substituents, was demonstrated in the reaction of 1-butadienol and acrolein, yielding the ortho-endo adduct, by a MINDO study of the potential energy surface for the reaction which shows a considerable increase in the asymmetry of the process.[27]

Recenty, in a few papers[28,29] devoted to pericyclic reactions, especially the Diels−Alder reaction, studies were performed by means of Density Functional Theory (DFT) which gained widespread use in present day quantum chemistry.[30]

It could be expected that the concepts of DFT[30] should provide a successful interpretation of both the regiochemistry and the mechanism of the Diels−Alder reactions. Indeed within the context of DFT, many useful and important classical chemical concepts, such as electronegativity,[31] hardness, and softness,[32] have been identified. Some DFT-based local properties such as the Fukui function,[33] the condensed and noncondensed local softnesses,[34] and the local hardness[35−39] already provided reliable predictions and interpretations of the regioselectivity of $\alpha,\beta$ unsaturated aldehydes and ketones,[40] substituted benzynes and hexarynes,[41] and monosubstituted benzenes,[42] in nucleophilic and electrophilic reactions, respectivily. Recently, the regioselectivity in the fullerene chemistry has been adequately rationalized by means of condensed local softness.[43]

On the other hand, local hardness, in one or another approximate form, was used in studies on intermolecular reactivity sequences: reactivity of monosubstituted benzenes,[39] acidity of substituted acetic acids,[44] simple hydrides,[45] model systems for zeolites,[46] and alkyl alcohols.[47] Within the FMO approach, the two atoms with higher softness should interact first.[48−49]

Very recently Gázquez and Méndez[50] emitted nevertheless a slightly modified point of view that could lead to an answer to the question of the first binding termini in Diels−Alder cycloadditions. They stated that "the interaction between two molecules A and B will not necessarily occur through the softer atoms but through those whose Fukui functions are approximately equal" as opposed to "the interaction between A and B is favored when it occurs through those atoms whose softnesses are approximately equal".

The aim of the present study is to use some of the above-mentioned DFT-based descriptors to interpret the orientation phenomena in some Diels−Alder reactions on the basis of both of the quoted Gázquez−Méndez's statements. We will thereby apply the hard and soft acid and base principle (HSAB) in a *local* sense. We will try to rationalize the predominance of ortho regioisomers in the cycloaddition of 1-substituted dienes and asymmetrical dienophiles, in view of the fact that regioselectivity cannot be explained by electronic effects, as replacement of an electron-donating substituent by an electron-attracting one does not alter the regioselectivity as discussed by Anh and co-workers.[17] Furthermore, these authors tentatively assumed that the first bond would link the softest centers, i.e. the two atoms giving the greatest overlap stabilization. Quantum chemistry is now at a level at which this proposal can be tested explicitely.

## II. Theory and Computational Details

**1. Local Softness as a Molecular Descriptor Emerging from DFT.** In density functional theory the fundamental differential expression for the change in energy from one ground state to another is[30]

$$dE = \mu\, dN + \int \rho(\underline{r})\, \delta\nu(\underline{r})\, d\underline{r} \qquad (1)$$

where $\mu$ is the electronic chemical potential defined as

$$\mu = (\partial \mathrm{E}/\partial N)_{\nu(\underline{r})} \qquad (2)$$

$\rho(\underline{r})$ is the electronic density and $\nu(\underline{r})$ the external potential.

Whereas $\mu$ can be considered as a response function to the d$N$ perturbations, $\rho(\underline{r})$ can be regarded as a response function to a $\delta\nu(\underline{r})$ perturbation as

$$\rho(\underline{r}) = (\delta E/\delta \nu(\underline{r}))_N \qquad (3)$$

The first partial derivative of $\mu$ with respect to N, the total number of electron, yields the global hardness

$$\eta = \frac{1}{2}\left(\frac{\partial \mu}{\partial N}\right)_{\nu(\underline{r})} \qquad (4)$$

which is given, using (2) and in a finite difference approximation, as

$$\eta = {}^{1}/_{2}(I - A) \qquad (5)$$

Inversely proportional to it is the global softness, in the same approximation given as

$$S = 1/(I - A) \qquad (6)$$

$I$ and $A$ are respectively the ionization energy and electron affinity of the $N$-electron system, the energies of the $N, N-1$, and $N+1$ systems being again evaluated at constant geometry.

The first-order derivative of $\rho(\underline{r})$ with respect to $N$, as defined by Parr and Yang,[33] is the Fukui function $f(\underline{r})$:

$$f(\underline{r}) = (\partial \rho(\underline{r})/\partial N)_{\nu(\underline{r})} \qquad (7)$$

which indicates how the incoming or outgoing number of electrons is redistributed in the various regions of the molecule.

The condensed forms of this function, for a nucleophilic and electrophilic attack respectively, on atom *k*, are as proposed by Yang and Mortier[35]

$$f_k^+ = q_k(N+1) - q_k(N) \tag{8a}$$

$$f_k^- = q_k(N) - q_k(N-1) \tag{8b}$$

Here $q_k(N)$ represents the electronic population on atom k, for the $N$ electron system considered. As local softness is related to the Fukui function via $s(\underline{r}) = Sf(\underline{r})$ the condensed local softness is related to the condensed Fukui function[34] through

$$s_k^+ = S[q_k(N+1) - q_k(N)] = Sf_k^+ \tag{9a}$$

$$s_k^- = S[q_k(N) - q_k(N-1)] = Sf_k^- \tag{9b}$$

$s_k^+$ and $s_k^-$ indicate how global softness, a global property, is redistributed among various atoms of the molecule by the condensed Fukui function. These quantities introduced in literature not so long ago afford explicit testing of a local HSAB principle because at various levels of approximation the softness of a given atom in a molecule can now be calculated.[51,52]

In the next section it is seen which criteria should be obeyed in order to fulfill this local HSAB principle.

## 2. The Local HSAB Principle

Gázquez and Méndez[50] recently analyzed the HSAB principle from an "atoms in molecule" viewpoint and arrived at a local HSAB principle starting from the change in their grand potential $\Omega$[53]

$$\Omega_i = E_i - \mu_i(N_i - N_i^0) \tag{10}$$

They concluded that, if an interaction between two molecules A and B takes place via atom k of A and atom l of B, the most favorable situation occurs when

$$(\Delta\Omega_{Ak})_{min} \approx (\Delta\Omega_{B1})_{min} \tag{11}$$

leading to the demand that

$$f_{Ak} \approx f_{B1} \tag{12}$$

where $f_{Ak}$ and $f_{B1}$ are the condensed Fukui functions on atom k of A and atom l of B, respectively.

Since however, at another stage of this analysis, they found that the condition $\boldsymbol{S}_A = \boldsymbol{S}_B$ guarantees minimalization of $\Delta\Omega_{Ak}$ with respect to $\boldsymbol{S}_A$, at fixed $(\mu_B - \mu_A)$ and $\boldsymbol{S}_B$ (and analogous for $\Delta\Omega_{B1}$), it was concluded that the interaction sites may be characterized by the condition

$$\boldsymbol{s}_{Ak} \approx \boldsymbol{s}_{Bl} \tag{13}$$

It should be mentioned here that this equation is in fact a particular case of the general expression in which $\boldsymbol{S}_A$ may or may not be equal to $\boldsymbol{S}_B$ and $f_{Ak}$ may or may not be equal to $f_{B1}$ but $(\boldsymbol{S}_A f_{Ak}) = (\boldsymbol{S}_B f_{B1})$ and therefore

$$\boldsymbol{s}_{Ak} = \boldsymbol{s}_{B1} \tag{14}$$

As suggested by these authors, we below obtain (14) directly by simply assuming that A and B interact through their atoms k and l.

Adopting an "atoms in molecule" viewpoint, as was done in one of our previous papers[50] and in ref 53, the atoms can be considered as open subsystems leading to a consideration of the grand potential $\Omega_i$ (10) as natural quantity to describe these systems, in analogy with "macroscopic" thermodynamics. $N^0$ takes the meaning of the number of electrons in the isolated fragment (atom), $\mu_i$ its electronic chemical potential, and $E_i$ its energy.

Supposing now that the interaction between molecule A and B occurs between atoms k and l, one has, neglecting changes in external potential (their differential contribution might be expected to be relatively unimportant in considering regioselectivity problems) and adopting the "atoms in molecule viewpoint"

$$\Delta E_{Ak} = \mu_A \Delta N_{A,k} + \eta_{A,k}(\Delta N_{Ak})^2 \tag{15}$$

$$\Delta E_{B1} = \mu_B \Delta N_{B,1} + \eta_{B,1}(\Delta N_{B1})^2 \tag{16}$$

$\eta_{A,k}$ and $\eta_{B,1}$ represent the hardness of molecules A and B, respectively. The electron transfer between A and B is such that

$$\Delta N_{Ak} + \Delta N_{B1} = 0 \tag{17}$$

It should be noted that $\mu_A$ is the chemical potential of the isolated molecule A, equal throughout this system,[55] so that

$$\mu_A = \mu_{A,k} = \mu_{A,m} = ... \tag{18}$$

where k, m, etc. denote the atoms of molecule A.

Analogous reasoning can be forwarded for $\mu_B$, but of course not for $\eta_A$ and $\eta_B$ as hardness is not equalized.

One therefore obtains

$$\begin{aligned} \Delta E_{A,k} &= \mu_{A,k}\Delta N_{A,k} + \eta_{A,k}(\Delta N_{A,k})^2 \\ \Delta E_{B,1} &= \mu_{B,1}\Delta N_{B,1} + \eta_{B,1}(\Delta N_{B,1})^2 \end{aligned} \tag{19}$$

Upon interaction between A and B via k and l, equalization of their chemical potentials to a value $\mu_{AB}$ yields

$$\begin{aligned} \mu_{AB} &= \mu_A + 2\eta_{A,k}\Delta N_{A,k} \qquad \forall\, k \in A \\ \mu_{AB} &= \mu_B + 2\eta_{B,1}\Delta N_{B,1} \qquad \forall\, 1 \in B \end{aligned} \tag{20}$$

As now

$$\Delta N_{A,k} = \frac{\mu_B - \mu_A}{2(\eta_{A,k} + \eta_{B,1})}$$

one obtains

$$\Delta N_{A,k} = \frac{\mu_B - \mu_A}{s_{Ak} + s_{B1}} s_{Ak} s_{B1} \tag{21}$$

Considering now the change in $\Omega$ for atoms k on A and l on B

$$\begin{aligned} \Delta\Omega_{A,k} &= \Delta E_{A,k} - \Delta\mu_{A,k}(N_{A,k} - N_{A,k}^0) - \mu_{A,k}\Delta N_{A,k} \\ &= \mu_A \Delta N_{A,k} + \eta_{A,k}\Delta N_{A,k}^2 - \Delta\mu_A \Delta N_{A,k} - \mu_A \Delta N_{A,k} \\ &= \eta_{A,k}\Delta N_{A,k}^2 - \Delta\mu_A \Delta N_{A,k} \\ &= -\eta_{A,k}\Delta N_{A,k}^2 \end{aligned} \tag{22}$$

as

$$\Delta\mu_A = \Delta\mu_{A,k} = \mu_{AB} - \mu_A = 2\eta_{A.k}\Delta N_{A,k} \tag{23}$$

Via (21) one obtains

$$\Delta\Omega_{\mathrm{A,k}} = -\frac{1}{2}\frac{(\mu_{\mathrm{B}} - \mu_{\mathrm{A}})^2}{(s_{\mathrm{Ak}} + s_{\mathrm{B1}})^2} s_{\mathrm{Ak}} s_{\mathrm{B1}}{}^2$$

$$\Delta\Omega_{\mathrm{B,1}} = -\frac{1}{2}\frac{(\mu_{\mathrm{B}} - \mu_{\mathrm{A}})^2}{(s_{\mathrm{Ak}} + s_{\mathrm{B1}})^2} s_{\mathrm{B1}} s_{\mathrm{Ak}}{}^2 \qquad (24)$$

It is easily seen, combining (17), (18), (19), (24), and (25) that

$$\Delta E = \Delta E_{\mathrm{A,k}} + \Delta E_{\mathrm{B,1}} = \Delta\Omega_{\mathrm{A,k}} + \Delta\Omega_{\mathrm{B,1}} = \Delta\Omega \qquad (25)$$

so that the total energy change governing the reactivity in the elementary process in the gas phase equals the total change in grand potential, the latter quantity (vide supra) being more suited to describe the evolution of the open system type “atoms in molecule”.

Minimalization of $\Delta\Omega_{\mathrm{A,k}}$ with respect to $s_{\mathrm{Ak}}$ at fixed $\mu_{\mathrm{B}} - \mu_{\mathrm{A}}$ and $_{\mathrm{sB1}}$ (cf. ref 52) yields

$$\begin{aligned}\frac{\mathrm{d}\Delta\Omega_{\mathrm{A,k}}}{\mathrm{d}s_{\mathrm{Ak}}} &= \tau \frac{\mathrm{d}}{\mathrm{d}s_{\mathrm{Ak}}} \frac{s_{\mathrm{Ak}}}{(s_{\mathrm{Ak}} + s_{\mathrm{B1}})^2} \\ &= \tau \frac{1}{(s_{\mathrm{Ak}} + s_{\mathrm{B1}})^2} - \frac{2s_{\mathrm{Ak}}}{(s_{\mathrm{Ak}} + s_{\mathrm{B1}})^3} \\ &= \tau \frac{(s_{\mathrm{Ak}} + s_{\mathrm{B1}} - 2s_{\mathrm{Ak}})}{(s_{\mathrm{Ak}} + s_{\mathrm{B1}})^3} \\ &= \tau \frac{(s_{\mathrm{B1}} - s_{\mathrm{Ak}})}{(s_{\mathrm{Ak}} + s_{\mathrm{B1}})^3} \qquad (26)\end{aligned}$$

where $\tau$ is equal to $-{}^1/_2(\mu_{\mathrm{B}} - \mu_{\mathrm{A}})^2 s_{\mathrm{B1}}{}^2$, yielding the demand

$$s_{\mathrm{Ak}} = s_{\mathrm{B1}} \qquad (27)$$

In fact the interaction energy expression (16) only considers the charge transfer; the second term, corresponding to a reshuffling of the charge distribution was shown by Gázquez and Méndez to yield similar conclusions.[56]

Analogous minimalization of $\Delta\Omega_{\mathrm{B1}}$, with respect to $s_{\mathrm{B1}}$ at fixed $(\mu_{\mathrm{B}} - \mu_{\mathrm{A}})$ and $s_{\mathrm{Ak}}$ leads to the same requirement.

In this way the change in grand potential $\Delta\Omega_{\mathrm{A,k}}$ at the minimum may be written as

$$\Delta\Omega_{\mathrm{A,k}} = -\frac{1}{2}\frac{(\mu_{\mathrm{B}} - \mu_{\mathrm{A}})^2}{4s_{\mathrm{Ak}}^2} s_{\mathrm{Ak}}^3 = -{}^1/_8(\mu_{\mathrm{B}} - \mu_{\mathrm{A}})^2 s_{\mathrm{Ak}} \qquad (28)$$

and the total change in energy is

$$\begin{aligned}\Delta E_{\mathrm{A,k}} + \Delta E_{\mathrm{B,1}} &= (\mu_{\mathrm{A,k}} - \mu_{\mathrm{B,1}})\Delta N_{\mathrm{A,k}} + (\eta_{\mathrm{A,k}} + \eta_{\mathrm{B,1}})\Delta N_{\mathrm{A,k}}{}^2 \\ &= -(\mu_{\mathrm{A}} - \mu_{\mathrm{B}})^2 \frac{s_{\mathrm{Ak}} s_{\mathrm{B1}}}{s_{\mathrm{Ak}} + s_{\mathrm{B1}}} \\ &\quad + (\eta_{\mathrm{Ak}} + \eta_{\mathrm{B1}}) \frac{s_{\mathrm{Ak}}^2\, s_{\mathrm{B1}}^2}{(s_{\mathrm{Ak}} + s_{\mathrm{B1}})^2}(\mu_{\mathrm{B}} - \mu_{\mathrm{A}})^2\end{aligned}$$

Using $\eta_{Ak} = 1/(2s_{\mathrm{Ak}})$ and $\eta_{\mathrm{B1}} = 1/(2s_{\mathrm{B1}})$ one obtains

$$\Delta E_{\mathrm{A,k}} + \Delta E_{\mathrm{B,1}} = -{}^1/_2(\mu_{\mathrm{A}} - \mu_{\mathrm{B}})^2 \frac{s_{\mathrm{Ak}} s_{\mathrm{B1}}}{s_{\mathrm{Ak}} + s_{\mathrm{B1}}} \qquad (29)$$

indicating that for a given electronic chemical potential difference and fulfilling the demand (27), the energy lowering is proportional (first) to the square of the chemical potential difference and (second) to the (equal) local softness of the interacting termini.

## 3. Computational Details

The Diels−Alder reactions examined in this work are of the NED type, i.e, as emphazised above, diene (donor) HOMO−dienophile (acceptor) LUMO controlled reactions. As a consequence, the electrophilic dienophile and the diene, playing the role of the nucleophile, are associated to Fukui function related quantities as indicated in (8a) and (9a), in (8b) and (9b), respectively.

The systems considered were (cf Figure 1) for the dienes, R = −Me, −OMe, −COOH, −CN, $-NH_2$, $-NMe_2$, $-NEt_2$, and −OEt, for the dienophiles, R′ = −COOH, −COOMe, −CN, −CHO, $-NO_2$, and −COMe, ensuring that in most cases a reaction with Normal Electron Demand can be expected.

All (*E*)-butadiene derivatives were considered in their s-cis conformation, as required for a pericyclic reaction. Furthermore, in the cases where the substituent contains a carbonyl group (C=O) the conformer with s-cis $C_1{=}C_2$ and C=O double bonds was taken; it proved, after optimization of all possible structures, to be the most stable one.

All neutral molecule geometries were optimized at the 3-21 level.[57] The cationic and anionic systems, needed in the evaluation of $s^{\pm}$, were kept at the geometry of the neutral system in order to fulfill the demand of constant external potential (7).

Condensed Fukui functions were calculated via (8a) and (8b) using Mulliken’s population analysis[58] and converted into local softness values via (9a) and (9b), the softness being evaluated via (6).

All calculations were carried out with a 3-21 basis set at the HF level using the GAMESS[59] and GAUSSIAN92[60] programs on the CRAY Y-MP/916 computer of the Free Universities of Brussels combined with the UNICHEM software package on a SILICON GRAPHICS ONYX Graphical Work Station.[61]

A word of caution should be included here. The use of single determinantal wave functions is of course an approximate procedure in evaluating the condensed Fukui functions. The problem of the influence of electron correlation has been studied in depth in recent publications of ours,[52,62] where it was seen that as opposed to absolute values, Hartree−Fock type trends are reproduced at higher levels.

At the single determinantal level the relatively small 3-21G basis set has been shown to yield an optimal quality cost ratio in a basis set investigation.[63] Presently, a study is undertaken in order to check the influence of correlation on the total softness values via I and A[64] (see also ref 65).

## III. Results and Discussions

Let us consider the cycloaddition between diene I and dienophile II leading to two possible disubstituted cyclohexenes, the so-called ortho regiomer III and meta regioisomer IV, as shown in Figure 1.

Table 1a lists the values of the condensed Fukui function and condensed local softness of both terminal carbon atoms 1 and 4 of diene I and Table 1b lists those for both carbon atoms 1′ and 2′ of the dienophile.

For *N*,*N*-diethyl-1,3-butadien-1-amine the observed negative value for the Fukui function could seem abnormal. It means that carbon atom 1 is gaining electrons when going from the *N*-electron system to the (*N*−1)-electron system, with a negative value for $f_{1'}^{-}$ ($f_{1'}^{-} = -0.104$) as a result. This effect is less important ($f_{1'}^{-} = -0.046$) for *N*,*N*-dimethyl-1,3-butadien-1-

**TABLE 1: Condensed Fukui Functions $f_k^+$, $f_k^-$, Global Softness, and Condensed Local Softnesses $s_k^+$, $s_k^-$ ($k = 1, 1', 4, 2'$) for the Monosubstituted Dienes (a) and Dienophiles (b) (Values in au)**

a. Dienes

| R | $S$ | $f_1^+$ | $f_1^-$ | $f_4^+$ | $f_4^-$ | $s_1^+$ | $s_1^-$ | $s_4^+$ | $s_4^-$ |
|---|---|---|---|---|---|---|---|---|---|
| $CH_3$ | 2.711 | 0.098 | 0.102 | 0.114 | 0.104 | 0.266 | 0.277 | 0.309 | 0.282 |
| $OCH_3$ | 2.574 | 0.141 | 0.075 | 0.114 | 0.078 | 0.363 | 0.193 | 0.293 | 0.201 |
| $CO_2H$ | 2.737 | 0.099 | 0.043 | 0.082 | 0.048 | 0.271 | 0.118 | 0.224 | 0.131 |
| $NH_2$ | 2.903 | 0.139 | 0.015 | 0.122 | 0.088 | 0.404 | 0.044 | 0.354 | 0.256 |
| $NMe_2$ | 2.972 | 0.139 | −0.046 | 0.108 | 0.065 | 0.413 | −0.137 | 0.321 | 0.193 |
| $NEt_2$ | 2.868 | 0.138 | −0.104 | 0.098 | 0.036 | 0.396 | −0.298 | 0.281 | 0.103 |
| OEt | 2.599 | 0.142 | 0.068 | 0.113 | 0.076 | 0.369 | 0.177 | 0.294 | 0.198 |
| CN | 2.929 | 0.142 | 0.121 | 0.090 | 0.109 | 0.416 | 0.354 | 0.264 | 0.319 |

b. Dienophiles

| R′ | $S$ | $f_{1'}^+$ | $f_{1'}^-$ | $f_{2'}^+$ | $f_{2'}^-$ | $s_{1'}^+$ | $s_{1'}^-$ | $s_{2'}^+$ | $s_{2'}^-$ |
|---|---|---|---|---|---|---|---|---|---|
| $CO_2H$ | 2.426 | 0.069 | 0.030 | 0.126 | 0.062 | 0.167 | 0.073 | 0.306 | 0.150 |
| $CO_2CH_3$ | 2.478 | 0.067 | 0.031 | 0.121 | 0.056 | 0.166 | 0.077 | 0.300 | 0.139 |
| CN | 2.058 | 0.144 | −0.007 | 0.132 | 0.068 | 0.296 | −0.014 | 0.278 | 0.140 |
| CHO | 2.680 | 0.011 | 0.009 | 0.115 | 0.103 | 0.030 | 0.024 | 0.309 | 0.276 |
| $NO_2$ | 2.801 | −0.019 | −0.026 | 0.104 | 0.092 | −0.053 | −0.073 | 0.291 | 0.258 |
| $COCH_3$ | 2.723 | 0.014 | 0.037 | 0.120 | 0.069 | 0.038 | 0.101 | 0.327 | 0.188 |

**TABLE 2: Energy Difference between the Two Possible HOMO/LUMO Combinations of the Dienes and Dienophiles in Table 1 (Values in au)**

| R | R′ | $E_{\mathrm{lumo}}^{\mathrm{dienophile}} - E_{\mathrm{homo}}^{\mathrm{diene}}$ | $E_{\mathrm{lumo}}^{\mathrm{diene}} - E_{\mathrm{homo}}^{\mathrm{dienophile}}$ | R | R′ | $E_{\mathrm{lumo}}^{\mathrm{dienophile}} - E_{\mathrm{homo}}^{\mathrm{diene}}$ | $E_{\mathrm{lumo}}^{\mathrm{diene}} - E_{\mathrm{homo}}^{\mathrm{dienophile}}$ |
|---|---|---|---|---|---|---|---|
| $CH_3$ | $CO_2H$ | 0.420 | 0.531 | $NH_2$ | $CO_2H$ | 0.375 | 0.557 |
| $CH_3$ | $CO_2CH_3$ | 0.426 | 0.526 | $NH_2$ | $CO_2CH_3$ | 0.381 | 0.552 |
| $CH_3$ | CN | 0.418 | 0.527 | $NH_2$ | CN | 0.374 | 0.553 |
| $CH_3$ | CHO | 0.410 | 0.528 | $NH_2$ | CHO | 0.365 | 0.554 |
| $CH_3$ | $NO_2$ | 0.361 | 0.557 | $NH_2$ | $NO_2$ | 0.316 | 0.583 |
| $CH_3$ | $COCH_3$ | 0.420 | 0.517 | $NH_2$ | $COCH_3$ | 0.376 | 0.543 |
| $OCH_3$ | $CO_2H$ | 0.418 | 0.554 | $NMe_2$ | $CO_2H$ | 0.376 | 0.563 |
| $OCH_3$ | $CO_2CH_3$ | 0.423 | 0.549 | $NMe_2$ | $CO_2CH_3$ | 0.382 | 0.558 |
| $OCH_3$ | CN | 0.416 | 0.550 | $NMe_2$ | CN | 0.375 | 0.559 |
| $OCH_3$ | CHO | 0.408 | 0.552 | $NMe_2$ | CHO | 0.365 | 0.560 |
| $OCH_3$ | $NO_2$ | 0.359 | 0.580 | $NMe_2$ | $NO_2$ | 0.317 | 0.589 |
| $OCH_3$ | $COCH_3$ | 0.418 | 0.541 | $NMe_2$ | $COCH_3$ | 0.376 | 0.550 |
| $CO_2H$ | $CO_2H$ | 0.452 | 0.474 | $NEt_2$ | $CO_2H$ | 0.432 | 0.525 |
| $CO_2H$ | $CO_2CH_3$ | 0.458 | 0.469 | $NEt_2$ | $CO_2CH_3$ | 0.437 | 0.520 |
| $CO_2H$ | CN | 0.451 | 0.470 | $NEt_2$ | CN | 0.430 | 0.521 |
| $CO_2H$ | CHO | 0.442 | 0.471 | $NEt_2$ | CHO | 0.421 | 0.522 |
| $CO_2H$ | $NO_2$ | 0.393 | 0.500 | $NEt_2$ | $NO_2$ | 0.373 | 0.551 |
| $CO_2H$ | $COCH_3$ | 0.453 | 0.461 | $NEt_2$ | $COCH_3$ | 0.432 | 0.511 |
| CN | $CO_2H$ | 0.454 | 0.469 | OEt | $CO_2H$ | 0.416 | 0.555 |
| CN | $CO_2CH_3$ | 0.460 | 0.464 | OEt | $CO_2CH_3$ | 0.422 | 0.550 |
| CN | CN | 0.453 | 0.465 | OEt | CN | 0.415 | 0.551 |
| CN | CHO | 0.444 | 0.466 | OEt | CHO | 0.406 | 0.552 |
| CN | $NO_2$ | 0.395 | 0.495 | OEt | $NO_2$ | 0.357 | 0.581 |
| CN | $COCH_3$ | 0.455 | 0.455 | OEt | $COCH_3$ | 0.417 | 0.542 |

amine while for the primary amine derivative this abnormality seems inexistant ($f_{1'}^- = 0.015$).

This effect could be a consequence of the dual character of alkyl groups on the nitrogen atom, bonded to $C_1$. It is indeed known (cf. our studies on alkylamines[66] and alkyl alcohols[47]) that when placed close to electron-rich centers, these groups act as electron acceptors, whereas, when placed close to positively charged centers, their electron-donating character predominates.

The higher the polarizability of the alkyl groups, the higher their ability to stabilize positive charges, as seen here when passing from $NH_2$ (positive Fukui function) to $NMe_2$ and $NEt_2$. The situation of the nitro group on the dienophile, where $f_{1'}^+$ and $f_{1'}^-$ are very slightly negative, as is shown in Table 1b, is less clear cut.

In Table 2 we report the values of the energy differences for the two possible combinations of molecular orbitals, either the HOMO diene−LUMO dienophile or the LUMO diene−HOMO dienophile. The difference for the former combination being smaller for all couples considered, their cyclizations can be considered of the NED type, i.e. controlled by the HOMO of the diene and the LUMO of the dienophile, although in a few cases the difference is small.

The study of the regioselectivity of these cyclizations will consist in considering four possible interactions, those of $C_1$ with either $C_{1'}$ or $C_{2'}$ and those of $C_4$ with either $C_{1'}$ or $C_{2'}$ and in selecting the most favored one which will be the controlling pair.

In order to correlate the ideas of Gázquez and Méndez and the experimental regioselectivity we defined for each cyclization two quantities $\boldsymbol{S}_{\mathrm{ortho}}$ and $\boldsymbol{S}_{\mathrm{meta}}$ as indicated below

$$\boldsymbol{S}_{\mathrm{ortho}} = (s_1^- - s_{1'}^+)^2 + (s_4^- - s_{2'}^+)^2 \tag{30}$$

$$\boldsymbol{S}_{\mathrm{meta}} = (s_1^- - s_{2'}^+)^2 + (s_4^- - s_{1'}^+)^2 \tag{31}$$

Their values are shown in Table 3.

The local softnesses of the diene are of the $s_k^-$ type, those of the dienophile of the $s_k^+$ type, the diene being electron donor and the dienophile electron acceptor in a NED reaction.

**TABLE 3: Values of the $S_{ortho}$ and $S_{meta}$ Quantities Defined in (30) and (31) (in $10^{-2}$ au) for All Possible Diene−Dienophile Combinations (Figure 1)[a]**

| R | R′ | $S_{ortho}$ | $S_{meta}$ | exp | R | R′ | $S_{ortho}$ | $S_{meta}$ | exp |
|---|---|---|---|---|---|---|---|---|---|
| $CH_3$ | $CO_2H$ | 1.25 | 1.40 | 69, 70 | $NH_2$ | $CO_2H$ | 1.79 | 7.65 | |
| $CH_3$ | $CO_2CH_3$ | 1.25 | 1.40 | 24, 71 | $NH_2$ | $CO_2CH_3$ | 1.70 | 7.37 | |
| $CH_3$ | CN | 0.05 | 0.02 | 24, 72 | $CH_2$ | CN | 6.42 | 5.37 | |
| $CH_3$ | CHO | 6.17 | 6.47 | 24, 73 | $NH_2$ | CHO | 0.30 | 12.1 | |
| $CH_3$ | $NO_2$ | 10.8 | 11.3 | 73 | $CH_2$ | $NO_2$ | 1.06 | 15.7 | |
| $CH_3$ | $COCH_3$ | 5.88 | 6.20 | 24, 73 | $NH_2$ | $COCH_3$ | 0.51 | 12.7 | |
| $OCH_3$ | $CO_2H$ | 1.16 | 1.38 | 74 | $NMe_2$ | $CO_2H$ | 10.5 | 19.6 | |
| $OCH_3$ | $CO_2CH_3$ | 1.05 | 1.26 | 74 | $NMe_2$ | $CO_2CH_3$ | 10.3 | 19.1 | 81 |
| $OCH_3$ | CN | 1.57 | 1.53 | 74 | $NMe_2$ | CN | 19.4 | 17.7 | 81 |
| $OCH_3$ | CHO | 3.83 | 4.26 | 75, 77 | $NMe_2$ | CHO | 4.08 | 22.5 | |
| $OCH_3$ | $NO_2$ | 6.88 | 7.42 | 76 | $NMe_2$ | $NO_2$ | 1.66 | 24.4 | |
| $OCH_3$ | $COCH_3$ | 3.99 | 4.43 | 74 | $NMe_2$ | $COCH_3$ | 4.84 | 23.9 | |
| OEt | $CO_2H$ | 1.18 | 1.75 | 77 | $NEt_2$ | $CO_2H$ | 25.8 | 36.9 | 76 |
| OEt | $CO_2CH_3$ | 1.06 | 1.61 | 77 | $NEt_2$ | $CO_2CH_3$ | 25.4 | 36.2 | 76 |
| OEt | CN | 1.98 | 1.88 | 77 | $NEt_2$ | CN | 38.2 | 36.2 | 76 |
| OEt | CHO | 3.39 | 4.55 | 75, 77 | $NEt_2$ | CHO | 14.9 | 37.3 | 82, 83 |
| OEt | $NO_2$ | 6.17 | 7.60 | 76 | $NEt_2$ | $NO_2$ | 9.54 | 37.2 | 76 |
| OEt | $COCH_3$ | 3.59 | 4.79 | 77 | $NEt_2$ | $COCH_3$ | 16.3 | 39.5 | 76, 84 |
| $CO_2H$ | $CO_2H$ | 3.29 | 3.66 | 78, 79 | CN | $CO_2H$ | 3.52 | 2.54 | 76, 84 |
| $CO_2H$ | $CO_2CH_3$ | 3.07 | 3.44 | 80 | CN | $CO_2CH_3$ | 3.59 | 2.65 | |
| $CO_2H$ | CN | 5.16 | 5.09 | 73, 76 | CN | CN | 0.56 | 0.74 | 76 |
| $CO_2H$ | CHO | 3.90 | 4.67 | 73, 76 | CN | CHO | 10.6 | 8.61 | 76 |
| $CO_2H$ | $NO_2$ | 5.48 | 6.42 | 73, 76 | CN | $NO_2$ | 16.7 | 14.3 | 76 |
| $CO_2H$ | $COCH_3$ | 4.45 | 5.24 | 73, 76 | CN | $COCH_3$ | 10.0 | 7.98 | 76 |

[a] The experimental reference (exp) in which (invariably ortho) preference is found is given where available.

**TABLE 4: Comparison of the Four Quadratic Terms in (30) and (31) (in $10^{-2}$ au) for All Combinations between Dienes and Dienophiles (Figure 1)**

| R | R′ | $(s_1^- - s_{1'}^+)^2$ | $(s_4^- - s_{2'}^+)^2$ | $(s_1^- - s_{2'}^+)^2$ | $(s_4^- - s_{1'}^+)^2$ | R | R′ | $(s_1^- - s_{1'}^+)^2$ | $(s_4^- - s_{2'}^+)^2$ | $(s_1^- - s_{2'}^+)^2$ | $(s_4^- - s_{1'}^+)^2$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| $CH_3$ | $CO_2H$ | 1.19 | 0.06 | 0.08 | 1.31 | $NH_2$ | $CO_2H$ | 1.53 | 0.25 | 6.87 | 0.77 |
| $CH_3$ | $CO_2CH_3$ | 1.22 | 0.03 | 0.05 | 1.34 | $NH_2$ | $CO_2CH_3$ | 1.50 | 0.20 | 6.57 | 0.80 |
| $CH_3$ | CN | 0.04 | 0.01 | 0.00 | 0.02 | $NH_2$ | CN | 6.39 | 0.03 | 5.20 | 0.17 |
| $CH_3$ | CHO | 6.10 | 0.07 | 0.10 | 6.37 | $NH_2$ | CHO | 0.02 | 0.28 | 7.00 | 5.11 |
| $CH_3$ | $NO_2$ | 10.9 | 0.01 | 0.02 | 11.2 | $NH_2$ | $NO_2$ | 0.94 | 0.13 | 6.14 | 9.53 |
| $CH_3$ | $COCH_3$ | 5.68 | 0.20 | 0.25 | 5.94 | $NH_2$ | $COCH_3$ | 0.00 | 0.51 | 8.02 | 4.72 |
| $OCH_3$ | $CO_2H$ | 0.07 | 1.10 | 1.27 | 0.11 | $NMe_2$ | $CO_2H$ | 9.25 | 1.27 | 19.6 | 0.07 |
| $OCH_3$ | $CO_2CH_3$ | 0.07 | 0.98 | 1.14 | 0.12 | $NMe_2$ | $CO_2CH_3$ | 9.16 | 1.14 | 19.0 | 0.07 |
| $OCH_3$ | CN | 1.07 | 0.50 | 0.62 | 0.91 | $NMe_2$ | CN | 18.7 | 0.62 | 16.7 | 1.06 |
| $OCH_3$ | CHO | 2.68 | 1.15 | 1.32 | 2.93 | $NMe_2$ | CHO | 2.76 | 1.32 | 19.8 | 2.68 |
| $OCH_3$ | $NO_2$ | 6.07 | 0.82 | 0.96 | 6.45 | $NMe_2$ | $NO_2$ | 0.70 | 0.96 | 18.3 | 6.07 |
| $OCH_3$ | $COCH_3$ | 2.40 | 1.58 | 1.79 | 2.65 | $NMe_2$ | $COCH_3$ | 3.06 | 1.78 | 21.5 | 2.40 |
| OEt | $CO_2H$ | 0.01 | 1.17 | 1.66 | 0.09 | $NEt_2$ | $CO_2H$ | 21.7 | 4.10 | 36.5 | 0.41 |
| OEt | $CO_2CH_3$ | 0.01 | 1.04 | 1.51 | 0.10 | $NEt_2$ | $CO_2CH_3$ | 21.5 | 3.86 | 35.8 | 0.39 |
| OEt | CN | 1.43 | 0.55 | 0.90 | 0.98 | $NEt_2$ | CN | 35.4 | 2.84 | 32.5 | 3.73 |
| OEt | CHO | 2.17 | 1.22 | 1.73 | 2.82 | $NEt_2$ | CHO | 10.7 | 4.20 | 36.8 | 0.54 |
| OEt | $NO_2$ | 5.29 | 0.88 | 1.31 | 6.29 | $NEt_2$ | $NO_2$ | 6.01 | 3.53 | 34.8 | 2.45 |
| OEt | $COCH_3$ | 1.92 | 1.67 | 2.25 | 2.54 | $NEt_2$ | $COCH_3$ | 11.3 | 5.01 | 39.1 | 0.43 |
| $CO_2H$ | $CO_2H$ | 0.25 | 3.04 | 3.53 | 0.13 | CN | $CO_2H$ | 3.50 | 0.02 | 0.24 | 2.31 |
| $CO_2H$ | $CO_2CH_3$ | 0.23 | 2.84 | 3.32 | 0.12 | CN | $CO_2CH_3$ | 3.55 | 0.04 | 0.30 | 2.35 |
| $CO_2H$ | CN | 3.19 | 1.97 | 2.37 | 2.72 | CN | CN | 0.34 | 0.23 | 0.68 | 0.05 |
| $CO_2H$ | CHO | 0.78 | 3.13 | 3.63 | 1.04 | CN | CHO | 10.5 | 0.01 | 0.21 | 8.40 |
| $CO_2H$ | $NO_2$ | 2.92 | 2.56 | 3.01 | 3.41 | CN | $NO_2$ | 16.6 | 0.08 | 0.40 | 13.9 |
| $CO_2H$ | $COCH_3$ | 0.63 | 3.82 | 4.37 | 0.87 | CN | $COCH_3$ | 10.0 | 0.01 | 0.08 | 7.90 |

The formulation by Gázquez and Méndez, claiming that interaction between centers of close values of the Fukui function is favored, can now be visualized in the case of Diels−Alder cyclizations: the smaller values in $\boldsymbol{S}_{ortho}$ as compared to $\boldsymbol{S}_{meta}$ will correspond to predominance of the ortho cycloadduct formation.

Note that this idea is based on the simultaneous fulfillment of a local HSAB principle at both termini. Note also that in $\boldsymbol{S}_{ortho}$ and $\boldsymbol{S}_{meta}$ the total softness of neither diene nor the dienophile can be separated, indicating that the use of comparable expressions for $\boldsymbol{S}_{ortho}$ and $\boldsymbol{S}_{meta}$, only involving Fukui functions, is not advisable. In practice however, in our cases $S_{diene}$ and $S_{dienophile}$ are quite close in almost all cases. The results for the inequalities for the Fukui function analogues to (30) and (31), $\boldsymbol{F}_{ortho}$ and $\boldsymbol{F}_{meta}$, are therefore almost identical to those obtained for $\boldsymbol{S}_{ortho}$ and $\boldsymbol{S}_{meta}$.

Table 3 shows that as far as Diels−Alder reactions with normal electron demand are concerned, $\boldsymbol{S}_{ortho}$ is always smaller than $\boldsymbol{S}_{meta}$, except in the cases where a *CN* substituent is present either in the diene or in the dienophile. Two reasons could be put forward for this apparent failure. The electronic characteristics of the CN group, known to demand for a highly correlated treatment as was for example evidenced in our group properties study[67] where the CN group was systematically an outlier. On the other hand, the considerations on $\boldsymbol{S}_{ortho}$ and $\boldsymbol{S}_{meta}$ are based on the idea that this reaction occurs in a synchronous way, both couples of reactive termini playing an identical role. As concertedness is not a synonym to synchronicity,[12,68] we looked for the smallest quadratic form out of $(s_1^- - s_{1'}^+)^2$, $(s_4^- - s_{2'}^+)^2$, $(s_1^- - s_{2'}^+)^2$, $(s_4^- - s_{1'}^+)^2$ in each of both expressions (30) and (31) (Table 4).

In almost all cases, even when the reagents carry a cyanide function, the quantity $(s_4^- - s_{2'}^+)^2$, corresponding to the 4−2′ interaction, is the smallest. In fact this result does not appear to be surprising since these two termini are, contrary to the two others, more remote from the substituent and thereby less influenced by its electronic effect.

This result might suggest an asynchronous mechanism in which the ortho attack may be favored by an interaction between the two unsubstituted carbon atoms proceeding faster than between the two substituted ones. This point is strengthened by the results of transition-state calculations, for cases with R and R′ ≠ H, where asymmetric transition states were found, with a $C_4-C_{2'}$ distance invariably shorter than $C_1-C_{1'}$.[68] So this local softness study not only illustrates the very appropriate vision of Gázquez and Méndez concerning the reactivity, but also enables us to draw a conclusion about the cyclization mechanism: the formation of the $\sigma$-bond between both unsubstituted termini of the cycloaddends proceeds faster. This shows again the correlation between mechanism and regiochemistry.

Combining the demand for the smallest of the quadratic forms with that of $S_{\text{ortho}}$ or $S_{\text{meta}}$, one retrieves the regioselectivity except in the cases of $CH_3$ on butadiene (1,3-pentadiene) and CN on ethene (acrylonitrile).

Finally, according to the small differences between the two quantities $E_{\text{lumo}}^{\text{dienophile}} - E_{\text{homo}}^{\text{diene}}$ and $E_{\text{lumo}}^{\text{diene}} - E_{\text{homo}}^{\text{dienophile}}$ in the case of 1-cyano-1,3-butadiene, we also considered the two reagents reacting as radicals and so considered $s_k^0$ values on all terminal atoms in order to calculate the quantities $S_{\text{ortho}}$ and $S_{\text{meta}}$. The values obtained did not show to be conclusive, proving that the problem in the *CN* compounds should only be related to the correlation treatment level.

As a whole, our study provides an isolated molecule property-based answer to the long-pending hypothesis formulated by Anh and co-workers,[17] mentioned in the introduction and saying that "it is likely that the first bond would link the softest centers, i.e. the atoms giving the greatest overlap stabilization". The ab initio calculated local softness values support this point of view, forwarded 20 years ago, in an univoqual way.

## IV. Conclusions

In this study, the local HSAB principle has been applied to rationalize the regioselectivity in a series of normal electron demand Diels−Alder reactions. On the basis of the Gázquez-Méndez conclusion that interaction between two molecules not necessarily occurs through their softest atoms but rather through those of nearly equal softnesses, two quantities $S_{\text{ortho}}$ and $S_{\text{meta}}$ corresponding to a favored ortho and a meta attack, respectively, have been calculated. The comparison between their values indicates in nearly all cases a smaller $S_{\text{ortho}}$ value. This result very clearly supports the idea that the regioselectivity in cycloaddition reactions is governed by the condensed local softnesses on the four interacting terminal atoms and that it cannot be interpreted in terms of electronic effects (electron-donating or electron-withdrawing character of the substituent). A local HSAB principle clearly governs the reaction process. Also the asynchronous character of the mechanism can be accounted for on the basis of condensed local softness. The almost equal values of the local softness on the unsubstituted atoms in diene and dienophile suggest that bond formation between these two termini proceeds faster than between the two other termini.

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