

Initial Hardness Response and Hardness Profiles in the Study of Woodward–Hoffmann Rules for Electrocyclizations

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Abstract: The fundamental principles of pericyclic reactions are governed by the Woodward–Hoffmann rules, which state that these reactions can only take place if the symmetries of the reactants' molecular orbitals and the products' molecular orbitals are the same. As such, these rules rely on the nodal structure of either the wave function or the frontier molecular orbitals, so it is unclear how these rules can be recovered in the density functional reactivity theory (or “conceptual DFT”), where the basic quantity is the strictly positive electron density. A third, nonsymmetry based approach to predict the outcome of pericyclic reactions is due to Zimmerman which uses the concept of the aromatic transition states: allowed reactions possess aromatic transition states, while forbidden reactions possess antiaromatic transition states. Based on our recent work on cycloadditions, we investigate the initial response of the chemical hardness, a central DFT based reactivity index, along the reaction profiles of a series of electrocyclizations. For a number of cases, we also compute complete initial reaction coordinate (IRC) paths and hardness profiles. We find that the hardness response is always higher for the allowed modes than for the forbidden modes. This suggests that the initial hardness response along the IRC is the key for casting the Woodward–Hoffmann rules into conceptual DFT.

1. Introduction

The well-known Woodward–Hoffmann rules¹ provide the basis of our current understanding of pericyclic reactions—reactions involving a cyclic rearrangement of electrons. Examples of pericyclic reactions include cycloadditions, electrocyclizations, sigmatropic rearrangements, and chelotropic reactions.² Three different approaches to interpreting

the pericyclic reactivity trends are common in the literature; two out of three use symmetry arguments based on signs of either the frontier molecular orbitals or the total wave function of the system.^{1,3} A third method, introduced by Zimmerman,⁴ for the prediction of the outcome of these reactions uses the concept of the (anti)aromaticity of the transition state. In this approach, reactions with aromatic transition states are asserted to be allowed, while those with an antiaromatic transition state are considered forbidden. Depending on the number of nodes in the π system at the transition state of a given mode (e.g., conrotatory vs disrotatory, suprafacial vs antarafacial approach) in the pericyclic reaction, systems can be classified as either Hückel (zero or even number of nodes) or Möbius (odd number of

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nodes) systems. Hückel and Möbius systems are aromatic for $(4n + 2)$ and $4n$ π electrons and antiaromatic for $4n$ and $(4n + 2)$ π electrons, respectively.⁵

It has been argued that density functional theory (DFT)⁶ provides an excellent framework for the formulation of a general theory of chemical reactivity.⁷ This involves the introduction of a series of chemical concepts via the so-called response functions of the energy of the system with respect to either the number of electrons, the external potential (for an isolated atomic or molecular system, this is the potential due to the nuclei), or both. Their use in connection with a series of chemical principles rooted theoretically in DFT, often within a perturbative perspective on chemical interactions, was shown to provide powerful machinery in problems of reactivity and stability; this area of research has been termed “conceptual DFT”.⁷ However, none of these concepts or principles are connected to the phase of the wave function and the question thus arises as to how the Woodward–Hoffmann rules can be recovered from the conceptual DFT. The DFT itself uses the electron density, a quantity which is always larger than or equal to zero, of the system as the basic source of information of all atomic and molecular properties. Conceptual DFT based reactivity descriptors (especially the hardness) have been used in the past to analyze the Woodward–Hoffmann rules.⁸ Recently, we have found that the concept of initial hardness response (i.e., the change of the hardness of the reagents along the initial stage of a model reaction coordinate of the pericyclic reaction) can be used to explain the Woodward–Hoffmann rules in the case of two prototypical cycloaddition reactions, i.e. the $[4 + 2]$ Diels–Alder reaction of 1,3-butadiene with ethylene and the $[2 + 2]$ cycloaddition of two ethylene molecules.⁹ This finding connects with the proposed linear relationship between hardness and aromaticity.^{10,11} It was concluded that the initial hardness response could be considered to be a predictor of the activation hardness, which encapsulates information about the aromaticity of the transition state, which in turn provides a rationale for the Woodward–Hoffmann rules.⁹ In addition, we have used a related quantity, the “dual descriptor”¹² in the rationalization of these rules for cycloadditions, electrocyclizations, and sigmatropic shift reactions.¹³

In this contribution, we will investigate in detail the use of the initial hardness response descriptor in the study of electrocyclization reactions, for which we will also construct energy and hardness profiles. In these pericyclic reactions, the π system will undergo an intramolecular rearrangement, leading to the formation of a σ bond and a ring. Depending on the number of π electrons involved in this process, the process will follow a conrotatory or a disrotatory pathway, resulting in a different stereochemical outcome. In the cyclization of linear polyenes, the conrotatory mode corresponds to a Möbius-like ring closure, which corresponds to an aromatic system when it involves $4n$ π electrons. The disrotatory movement, yielding a Hückel-like ring closure, is aromatic when $(4n + 2)$ π electrons are involved.⁴

We have focused our attention on five examples of electrocyclizations, depicted in Figure 1. This paper can be divided into two parts. In the first part, the hardness response

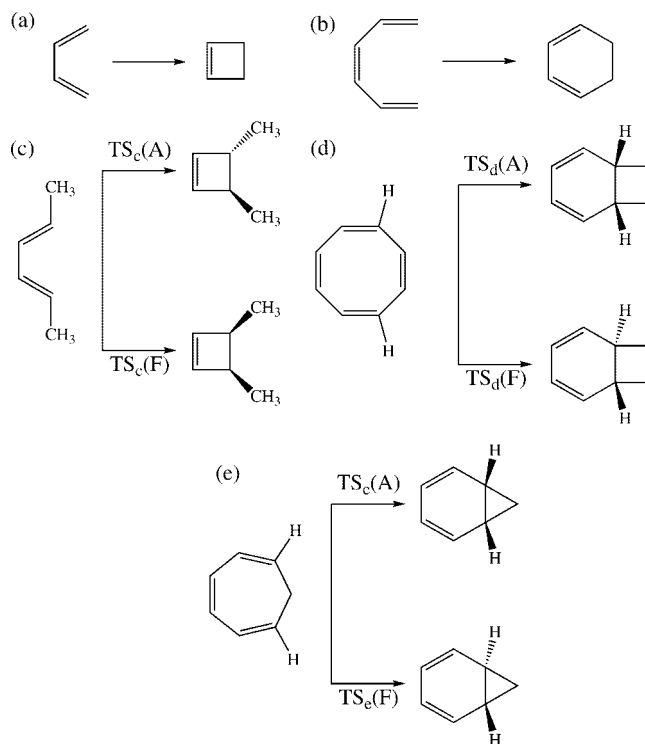


Figure 1. Summary of the different electrocyclizations investigated in this work.

for the thermal and photochemical electrocyclization reactions of 1,3-butadiene and 1,3,5-hexatriene (reactions a and b in Figure 1) have been studied along the initial stages of model *conrotatory* and *disrotatory* reaction coordinates. Next, we have investigated the *allowed* and *forbidden* cyclizations for a series of larger systems, 2,4-hexadiene, cyclooctatetraene, and cycloheptatriene in their ground states to obtain more insights into the complete reaction and hardness profiles of these reactions (reactions c, d, and e in Figure 1).

2. Theoretical Background and Computational Details

The chemical hardness η ^{14,15} is a central quantity for use in the study of reactivity and stability, through the hard and soft acids and bases principle^{14,16} and the principle of maximum hardness.^{14c,17,18} Parr and Pearson have introduced the chemical hardness as the second derivative of the energy of the system with respect to the number of electrons (sometimes preceded by an arbitrary factor of $1/2$, which we have dropped in our treatment) which can be estimated by the difference of the vertical ionization energy and electron affinity of the system:¹⁵

$$\eta = \left(\frac{\partial^2 E}{\partial N^2} \right)_v \approx I - A \quad (1)$$

Recently, Tozer and De Proft have introduced an approximate method to compute this quantity, requiring only the calculation of the neutral and cationic systems¹⁹

$$\eta \approx (\epsilon_{\text{LUMO}} - \epsilon_{\text{HOMO}}) + 2(\epsilon_{\text{HOMO}} + I) \quad (2)$$

where ϵ_{HOMO} and ϵ_{LUMO} are the Kohn–Sham orbital energies of the highest occupied (HOMO) and lowest unoccupied

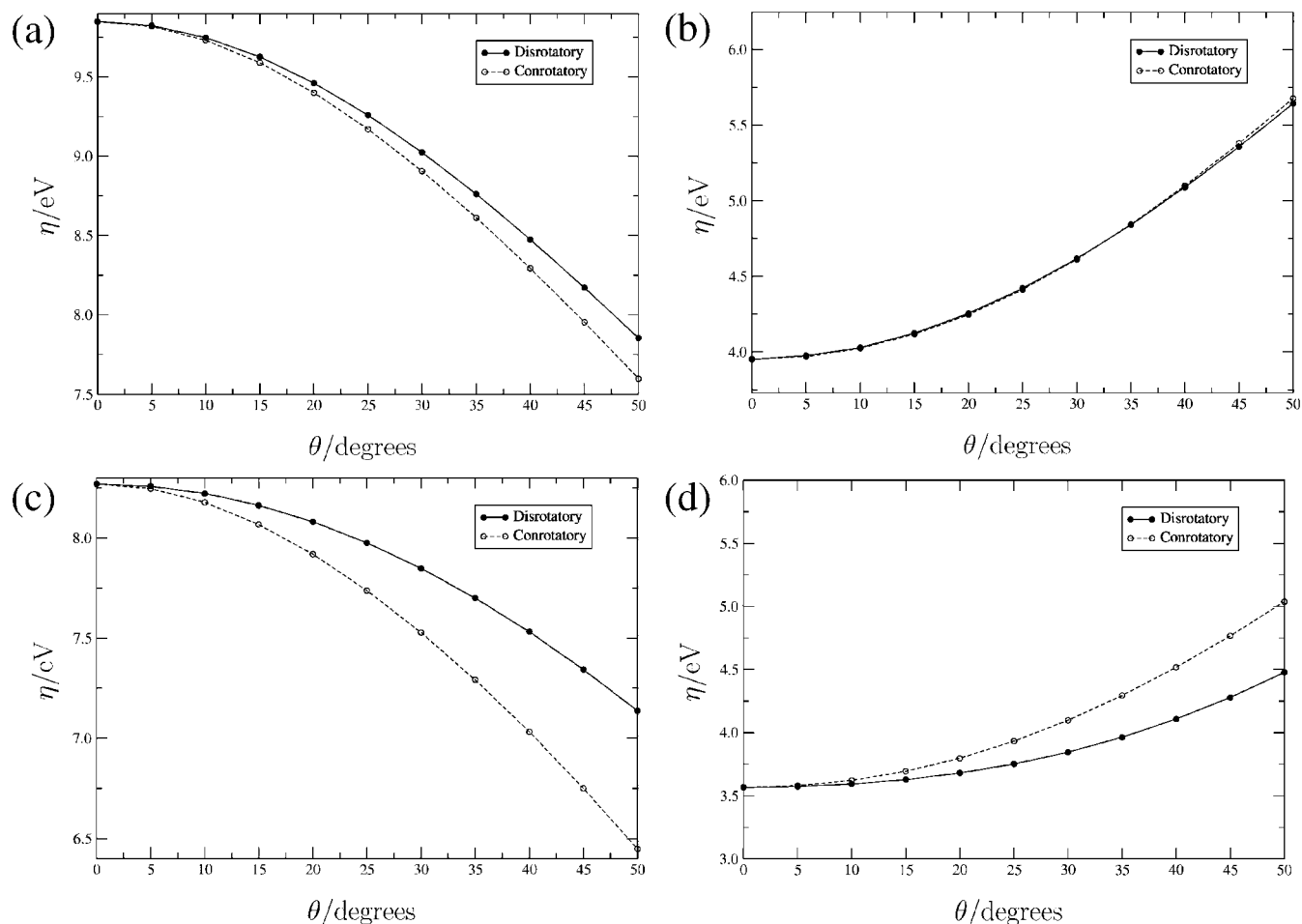


Figure 2. Evolution of the chemical hardness η along a model reaction coordinate, quantified by the dihedral angle θ , for electrocyclization of singlet and triplet 1,3-butadiene (parts a and b, respectively) and 1,3,5-hexatriene (parts c and d, respectively).

(LUMO) molecular orbitals, respectively, obtained using a pure density functional. It was shown that this equation corresponds to eq 1 but using the following approximation for the computation of the electron affinity:^{19,20}

$$A \approx -(\epsilon_{\text{LUMO}} + \epsilon_{\text{HOMO}}) - I \quad (3)$$

This approximate method was shown to give reasonable estimates for the electron affinities of systems possessing metastable anions.^{19,20} In this work, we will need to compute the hardness not only of molecules in their (singlet) ground state but also in the lowest triplet excited state. For the triplet excited state, we need to modify eqs 2 and 3. The vertical electron affinity for a system in the first excited triplet state $A(T)$, using eq 3 for the estimation of the electron affinity of its singlet ground state $A(S)$, can be expressed as

$$A(T) = A(S) + \Delta E_{\text{ST}} \approx -(\epsilon_{\text{LUMO}}(S) + \epsilon_{\text{HOMO}}(S)) - I(S) + \Delta E_{\text{ST}} \quad (4)$$

where $I(S)$ is the vertical ionization energy of the singlet ground state and ΔE_{ST} is the vertical singlet–triplet gap. The hardness of the first excited triplet state can thus be estimated as

$$\eta(T) = I(T) - A(T) \approx I(T) + I(S) + (\epsilon_{\text{LUMO}}(S) + \epsilon_{\text{HOMO}}(S)) - \Delta E_{\text{ST}} \quad (5)$$

Note that this equation depends not only on the ionization energies and orbital energies but also on the singlet–triplet gap. The singlet–triplet gap can, in this case, be estimated reliably using DFT methods. (For a recent example, see ref 21.)

Gaussian 03 program²² geometries, transition states, and intrinsic reaction coordinates were obtained at the B3LYP²³/6-311+G**²⁴ level; single point hardness calculations using eqs 2 and 5 were performed using the Perdew, Burke, and Ernzerhof (PBE) functional²⁵ with the same basis set.

3. Results and Discussion

In the first part of this contribution, we have computed the hardness response along an initial reaction coordinate of the conrotatory and disrotatory modes of the cyclization of 1,3-butadiene and 1,3,5 hexatriene, both in the singlet and the triplet states. This model reaction coordinate involves a conrotatory or a disrotatory movement of the terminal CH_2 groups of these molecules, as quantified by the angle θ , which is the dihedral angle between the terminal hydrogens and the completely fixed, planar carbon skeleton. It is to be mentioned that the planar C_{2v} conformation of both of these compounds is not a minimum on the potential energy surfaces of these molecules, but this conformation has been used to keep the analysis as simple as possible and in

agreement with the spirit (and the molecular geometry) of the original Woodward–Hoffmann work. Figure 2 depicts the initial hardness changes for these four initial steps. In the case of the ground-state reaction of 1,3-butadiene (Figure 2a), the hardness along the initial reaction path in the forbidden disrotatory mode is higher than along the allowed, conrotatory mode, contrary to our earlier findings for cycloadditions.⁹ In the excited state (Figure 2b), hardness profiles for both the model reactions are almost indistinguishable. Figure 2c depicts the hardness change along the initial model reaction coordinate of the ground-state electrocyclicization of 1,3,5-hexatriene. In this case, one can see that the hardness along the allowed, disrotatory mode is always higher than the hardness along the forbidden mode. In the triplet state, this ordering is reversed, in agreement with the Woodward–Hoffmann rules. Indeed, the results for the electrocyclicization of 1,3,5-hexatriene are in agreement with the fact that the allowed mode of the reaction should have a higher hardness than the forbidden one. In order to gain insight into the apparently contradicting results for 1,3-butadiene, both the conrotatory (allowed) and disrotatory (forbidden) initial reaction coordinate (IRC) paths in the singlet state were computed at the CASSCF(4,4)/6-31G* level of theory. The transition structures for these electrocyclicizations were taken from ref 26. Indeed, in a previous study,⁸ it was found that the transition structure for the allowed process of this electrocyclicization is harder than the one for the forbidden pathway. Along the initial stages of the computed IRC path, the hardness was evaluated at the PBE/6-311+G** level using eq 2. Figure 3 depicts both the energy (Figure 3a) and the hardness profiles of the allowed (Figure 3b) and forbidden (Figure 3c) cyclizations. The reaction path of the cyclization in the allowed mode clearly shows a steeper onset than the forbidden mode; after some point, however, both reaction paths cross, resulting, as could be expected, in an activation barrier for the allowed reaction that is smaller than the forbidden reaction; the difference in activation energy amounts to 13.1 kcal/mol. The hardness profiles are in agreement with the allowed or forbidden character of the reactions. The hardness along the allowed conrotatory mode is always larger than the hardness of the forbidden, disrotatory mode. The hardness shows a very steep decrease in the vicinity of the transition state for the forbidden reaction, with the HOMO–LUMO gap, part of the hardness expression in eq 2, essentially going to zero. This implies that the unexpected result for the initial hardness response for the cyclization of 1,3-butadiene is probably due to the fact that the model reaction coordinate is a rather bad approximation to the IRC for this case. However, the simplified model reaction coordinate performs appreciably better as the size of the molecule increases, because larger molecules have greater conformational flexibility.

The reaction and hardness profiles (Figure 4) for the electrocyclicization of 2,4-hexadiene (reaction c) bear a close resemblance with the ones obtained for 1,3-butadiene, which might be expected since both reactions involve 4 π electrons. Also in this case, a crossing along the IRC occurs, yielding a lower energy transition state for the allowed, conrotatory mode than for the forbidden mode.

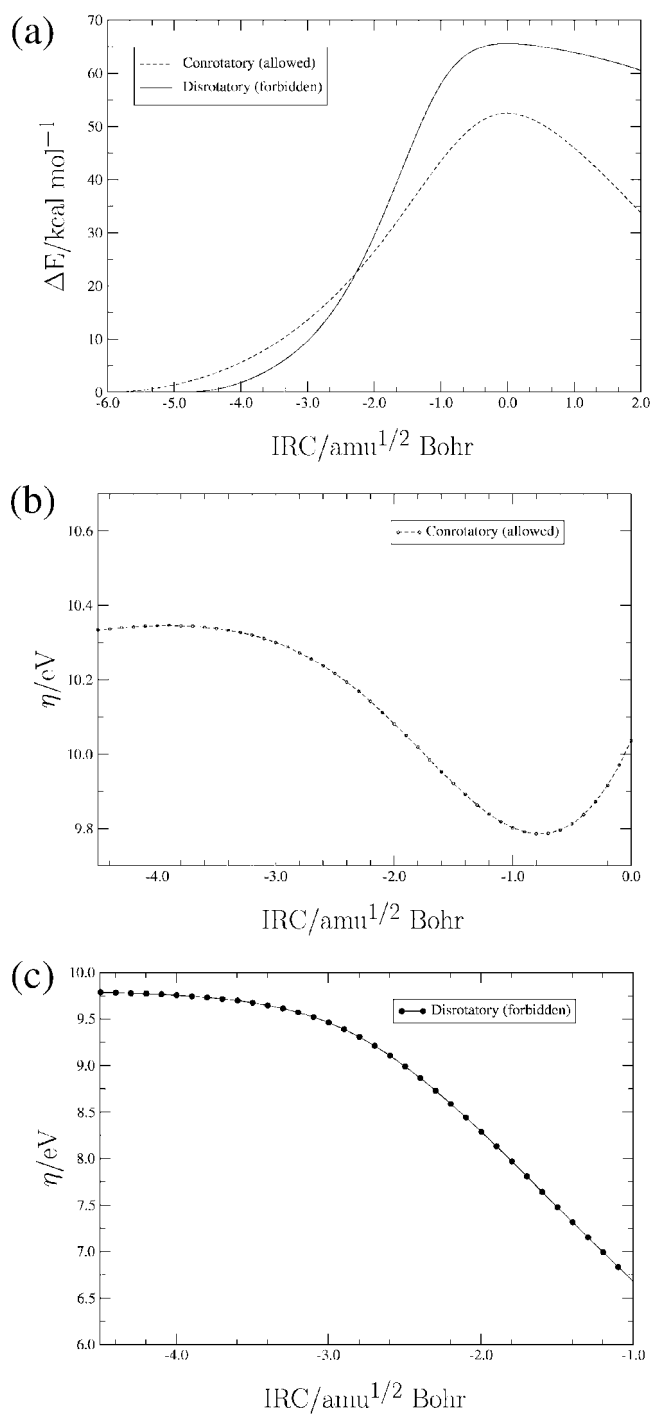


Figure 3. Energetic reaction paths (a) and hardness profiles (b and c) for the conrotatory and disrotatory modes of the electrocyclicization of 1,3-butadiene.

In this case, however, the difference in activation barriers is only 5.2 kcal/mol. On the other hand, this implies that although the calculation of the reaction path was performed using a single reference methodology, the same qualitative results are obtained as in the case of the multi-reference calculations, which is the main aim of our approach. The hardness profile confirms that, for the allowed reaction, the hardness in the neighborhood of the transition state along the IRC path is always larger for the allowed mode. However, initially, the hardness along the forbidden

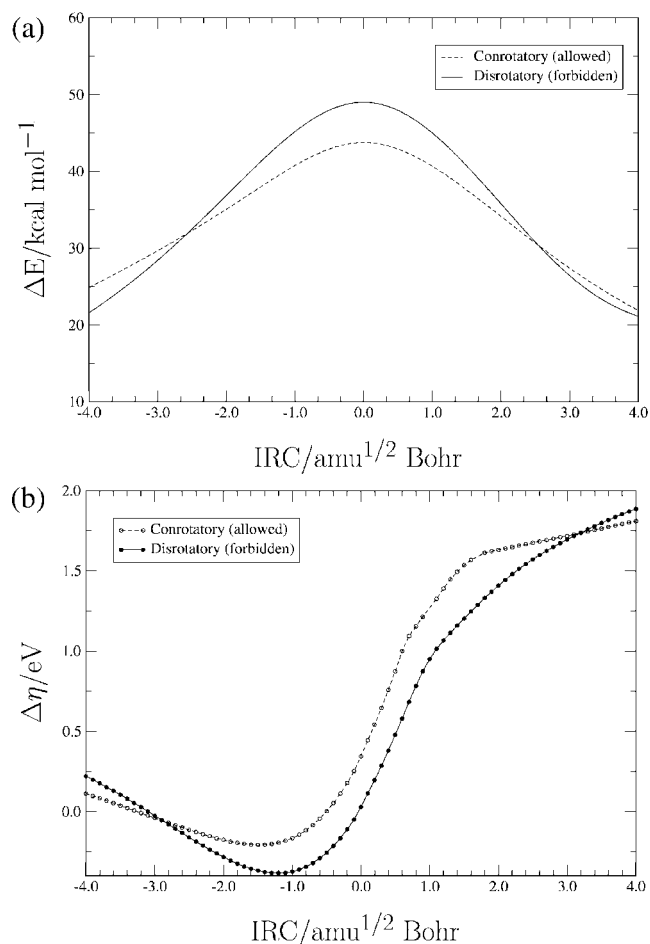


Figure 4. Energetic reaction paths (a) and hardness profiles (b) for the conrotatory and disrotatory modes of the electrocycization of 2,4-hexadiene.

mode pathway is larger, which explains the failure of the initial hardness response observed for the 1,3-butadiene.

Next, we have analyzed the profiles in the case of two reactions involving 6 π electrons, i.e. the cyclizations of cyclooctatetraene (reaction d) and cycloheptatriene (reaction e). Respective plots are provided in Figures 5 and 6, respectively. As can be seen, in both cases, there is no crossing of the energy profiles and the energy of the disrotatory, allowed mode is always below the energy of the conrotatory, forbidden mode. Also, the hardness along the allowed mode is almost always higher than along the forbidden mode, in agreement with the result presented earlier for the cyclization of the 4 π electron systems. A difference between this case and the former can however be noticed. In the 6 π electron cases, where the allowedness of the reaction can be explained by the Hückel aromaticity of the transition state, the profile for the allowed mode shows an increase in hardness when going from the reactant to the transition state. This sort of “violation” of the maximum hardness principle is not especially uncommon because the requirements for the maximum hardness principle to hold are very stringent.^{18b,c} (refs 27–29 elucidate the reasons for violations of the maximum hardness principle in more detail.)

In the case of the cyclization of the 4 π electron systems, however, involving a Möbius aromatic transition state, the profiles show the inverse trend, i.e. the more “classically”

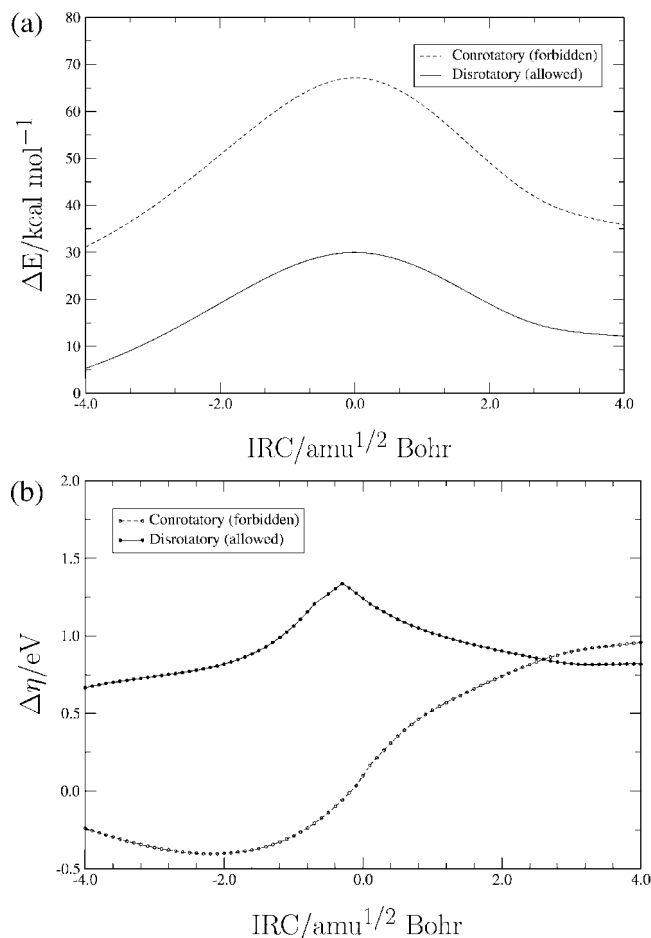


Figure 5. Energetic reaction paths (a) and hardness profiles (b) for the conrotatory and disrotatory modes of the electrocycization of cyclooctatetraene.

observed behavior of decreasing hardness along the reaction path yielding the maximum softness in the vicinity of or at the transition state.

In Table 1, we have listed the activation energies and activation hardnesses³⁰ for reactions c, d, and e. Note that, following ref 30, the activation hardnesses have been computed as the difference of the hardness of the reactants and the transition state. As expected, the allowed reactions always have lower activation barriers and smaller activation hardnesses. The latter finding is consistent with observations in ref 30, where it was stated that the smaller this difference, the faster the reaction.

In a final part, we quantitatively assess the initial hardness responses $(\partial\eta/\partial Q)_N$ for all the reactions considered in this work. In the case of the ground- and excited-state cyclizations of 1,3-butadiene and 1,3,5-hexatriene, Q corresponds to the dihedral angle θ , described above, which was used to construct a simple reaction coordinate for these cases. For the other cases, Q is the mass-weighted internal coordinate corresponding to the reactive mode. Table 2 lists the finite difference approximations to the initial hardness responses. As can be seen, in all but one of the cases, the initial hardness response for the allowed reaction is larger than that of the forbidden one. The only exception, the electrocycization of 1,3-butadiene in the singlet state, is most probably due to the fact that the simplified reaction coordinate used in this

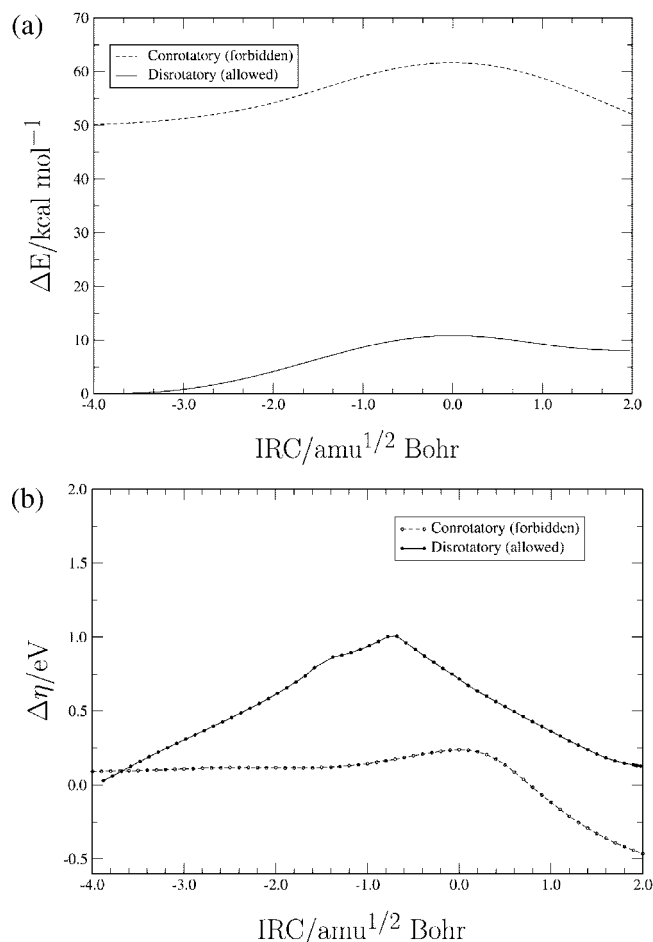


Figure 6. Energetic reaction paths (a) and hardness profiles (b) for the conrotatory and disrotatory modes of the electrocyclization of cycloheptatriene.

Table 1. Activation Energies ΔE^\ddagger and Hardnesses $\Delta\eta^\ddagger$ of the Allowed (A) and Forbidden (F) Modes of the Electrocyclizations of 2,4-Hexadiene, Cyclooctatetraene, and Cycloheptatriene^a

reactant	mode	ΔE^\ddagger	$\Delta\eta^\ddagger$
2,4-hexadiene ^b	conrotatory (A)	43.8	-0.343
	disrotatory (F)	49.0	-0.028
cyclooctatetraene ^c	disrotatory (A)	30.0	-1.212
	conrotatory (F)	67.2	-0.098
cycloheptatriene ^d	disrotatory (A)	10.9	-0.715
	conrotatory (F)	61.7	-0.238

^a All values are relative to the minimum energy structure along the reaction path of the allowed mode of each reaction. Energy differences were obtained at the B3LYP/6-311+G** level and are given in kilocalories per mole; hardness differences were obtained using eq 2 at the PBE/6-311+G** level and are given in electronvolts. ^b $E(\text{B3LYP}/6-311+\text{G}^{**}) = -234.700014 \text{ au}$, $\eta(\text{PBE}/6-311+\text{G}^{**}) = 9.395 \text{ eV}$. ^c $E(\text{B3LYP}/6-311+\text{G}^{**}) = -309.669028 \text{ au}$, $\eta(\text{PBE}/6-311+\text{G}^{**}) = 8.012 \text{ eV}$. ^d $E(\text{B3LYP}/6-311+\text{G}^{**}) = -271.584515 \text{ au}$, $\eta(\text{PBE}/6-311+\text{G}^{**}) = 8.906 \text{ eV}$.

case is not a good approximation to the IRC. We finally mention that, for this case, we carefully investigated the step-size dependence of the numerical differentiation. Computing the derivative using a very small step size (a 1° change in the dihedral angle, θ), did not change the trends in the magnitudes of the derivatives and the conclusions drawn remain unchanged.

Table 2. Initial Hardness Responses $(\partial\eta/\partial Q)_N$ of the Allowed (A) and Forbidden (F) Modes of the Electrocyclizations of 1,3-Butadiene, 1,3,5-Hexatriene, 2,4-Hexadiene, Cyclooctatetraene, and Cycloheptatriene^a

reactant	multiplicity	mode	$(\partial\eta/\partial Q)_N$
1,3-butadiene	S	conrotatory (A)	-0.00733
	S	disrotatory (F)	-0.00498
	T	disrotatory (A)	0.00496
1,3,5-hexatriene	T	conrotatory (F)	0.00228
	S	disrotatory (A)	-0.00240
	S	conrotatory (F)	-0.00469
	T	conrotatory (A)	0.00273
2,4-hexadiene	T	disrotatory (F)	0.00130
	S	conrotatory (A)	-0.152
	S	disrotatory (F)	-0.210
cyclooctatetraene	S	disrotatory (A)	0.0952
	S	conrotatory (F)	-0.158
cycloheptatriene	S	disrotatory (A)	0.310
	S	conrotatory (F)	0.00816

^a In the first two cases, this derivative is evaluated for the reactant in its C_{2v} symmetry and is expressed in electronvolts per degree. For the three other cyclizations, the derivative has been evaluated at the mass-weighted coordinate of -4.0. All derivatives were obtained numerically at the PBE/6-311+G** level (in the first two cases, with a step size of 5° in Q and 0.1 in the other cases).

4. Conclusions

In our ongoing investigation to cast the Woodward–Hoffmann rules for pericyclic reactions into density functional reactivity theory, we have investigated a number of electrocyclizations involving both 4 and 6 π electrons.

First, we have investigated the hardness response along the initial stages of the conrotatory and disrotatory modes of the electrocyclization of 1,3-butadiene and 1,3,5-hexatriene, both in the singlet and the triplet states; previously, this quantity was found, through its connection with the maximum hardness principle and the aromatic transition state concepts, to predict the allowedness of a cycloaddition reaction. In the 6 π electron case, the allowed mode of the electrocyclization was found to correspond to the highest initial hardness, whereas in the 4 π electron case, this result was not recovered. Upon consideration of the fully relaxed IRC path of this reaction, however, the expected result, i.e. higher hardness for the allowed mode, was recovered.

In the second part, we have studied the full IRC reaction and hardness profiles for the electrocyclization of 2,4-hexadiene, a 4 π electron case, and the cyclizations of cyclooctatetraene and cycloheptatriene, two 6 π electron cases. In all of these cases, the hardness of the allowed mode is higher than the hardness of the forbidden mode; also, the activation hardnesses for the former processes are always smaller than those of the latter ones.

Upon consideration of the magnitudes of the initial hardness response along the IRC, it can be concluded that for the electrocyclizations considered in this work, this quantity can be invoked to recover the Woodward–Hoffmann rules within the framework of the DFT-based perturbative perspective on chemical reactivity. In general, allowed electrocyclization reactions always have a higher initial hardness response than forbidden ones. This result, with the results in our earlier papers, supports the identification of the initial hardness response (or the closely related dual

descriptor) as the right key DFT-based reactivity indicator for describing pericyclic reactions.

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