Similarity Approach to Chemical Reactivity. A Simple Criterion for Discriminating between One-Step and Stepwise Reaction Mechanisms in Pericyclic Reactivity

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Received April 15, 1993[®]

The similarity index recently proposed as a quantitative measure of the extent of electron reorganization in chemical reactions was generalized to be applicable not only for the discrimination of allowed and forbidden reaction mechanisms of concerted processes but also for a simple evaluation of the relative ease of concerted one-step and nonconcerted stepwise reaction paths. The applicability of the approach is demonstrated by several examples of selected pericyclic reactions, both forbidden and allowed. The resulting theoretical predictions are in remarkable agreement with available experimental and theoretical results.

INTRODUCTION

The crucial question which has to be answered in studying the mechanisms of pericyclic reactions is, whether the reaction proceeds in one elementary step, or whether some, more or less stable intermediates intervene. Especially important is the question of the eventual participation of intermediates in thermally forbidden reactions where the stepwise mechanism via biradical or zwitterionic intermediate was frequently assumed as an alternative to symmetry forbidden concerted processes.[1] The parallel between the forbiddeness and the stepwise nature of the process is not, however, entirely straightforward, since forbidden processes were recently described which are apparently concerted.[2,3] At the same time, the frequently presumed preference of concerted reaction paths for allowed reactions is not apparently guaranteed either, for the so-called multibond processes at least.[4,5] The question of the detailed reaction mechanisms of pericyclic reactions is therefore still the subject of continuing studies, both experimental and theoretical.[6-26] The theoretical studies are, in a majority of cases, based on direct quantum chemical analyses of potential energy hypersurfaces.[14-26] Such calculations, however, critically depend on the quality of the methods used, and their results are frequently contradictory. In discussions concerning the mechanism, the so-called Diels–Alder reaction,[12-22] the Cope and Claisen rearrangement[24-26] may serve as an example. Irrespective of high requirements on the accuracy, such calculations are, moreover, also very time consuming, and their use as a routine means for the rapid qualitative orientation is therefore practically impossible. This of course stimulates the attempts at the creation of new, simpler models, allowing both the rationalization and understanding of the observed trends as well as simple qualitative predictions.[27] Such a philosophy lies also in the basis of the proposed criterion for a simple and rapid discrimination between whether the reaction proceeds as a one-step or stepwise process. Such a criterion is based on the recently proposed topological approach in terms of the so-called similarity indices.[28]

THEORETICAL SECTION

The basic idea of this approach arises from the so-called least motion principle,[29] which is one of the first attempts at the formulation of what is now known as selection rules in chemical reactivity. According to this principle, the condition

for the reaction to proceed easily is the minimal change in both nuclear and electron configurations of reacting molecules. The quantity in terms of which the abstract change in electron configurations can be conveniently measured is the so-called topological similarity index.[28] This index, originally introduced into the chemical theory by Polansky and Carbo,[30,31] has found in recent years numerous interesting applications, especially in the field of pericyclic reactivity.[32] Although examples of extensive use can be found in the original literature,[28,33-36] we consider it convenient to recapitulate briefly the basic ideas of similarity approach to the extent necessary for the purpose of this study.

The basis of this approach is the straightforward incorporation of the similarity index by Carbo[30] into the framework of the so-called overlap determinant method,[37] which is a simple topological procedure invented some time ago for the alternative reproduction of Woodward–Hoffmann rules. Within the framework of this combined approach, the Carbo's original definition of the similarity index (1) can be rewritten in the form of (2), where P_R and P_P are the usual charge density

$$r_{AB} = \frac{\int \rho_A(1)\, \rho_B(1)\, d\tau_1}{\left(\int \rho_A{}^2(1)\, d\tau_1\right)^{1/2}\left(\int \rho_B{}^2(1)\, d\tau_1\right)^{1/2}} \quad (1)$$

$$r_{RP} = \frac{Tr\, P_R \bar{P}_P}{[Tr\, P_R{}^2]^{1/2}[Tr\, \bar{P}_P{}^2]^{1/2}} \quad (2)$$

bond order matrices of molecules R (reactant) and P (product) and where the bar over the matrix $\bar{P}_P$ denotes the similarity transformation (3) with the matrix T. This transformation

$$\bar{P}_P = T^{-1}P_P T \quad (3)$$

enters into the formalism from the overlap determinant method,[37] and its aim is to provide the mutual transformation of AO basis sets on molecules R and P (eq 4), necessary for

$$\{\chi_P\} = T\{\chi_R\} \quad (4)$$

the conversion of density matrices into one common basis. The most important feature of matrix T is that its form depends on the detailed reaction mechanism of the transformation R → P, i.e., on whether the transformation proceeds by conrotation or disrotation for electrocyclizations or supra–supra or supra–antara for cycloadditions, etc. Thus, via this
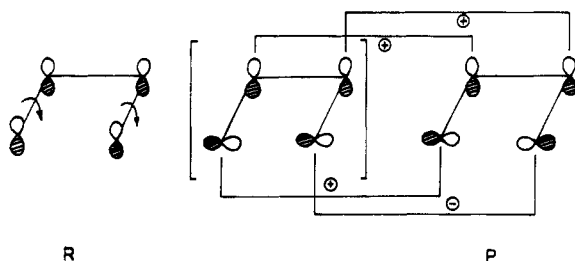

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Chart I

Scheme I

a

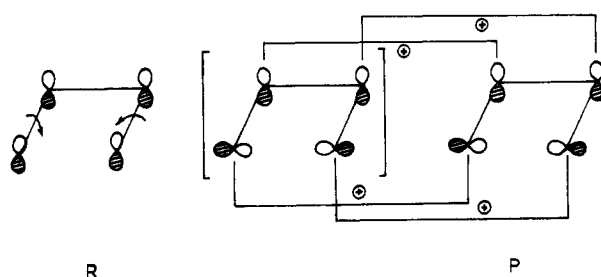R   P

b

R   P

matrix, the possibility to discriminate between the allowed and forbidden reactions enters into the formalism.

Because of the importance of this matrix for the whole formalism, it is perhaps convenient to mention briefly the detailed method of its construction. This can be best demonstrated by a concrete example. We take as an example the electrocyclic transformation of butadiene (R) into the cyclobutene (P).

The structure of both molecules can be described by the approximate wave functions Φ_R and Φ'_P constructed in the form of single Slater determinants (5) from HMO molecular

$$\Phi_R = |\varphi_1\bar{\varphi}_1\varphi_2\bar{\varphi}_2| \tag{5a}$$

$$\Phi'_P = |\psi_1\bar{\psi}_1\psi_2\bar{\psi}_2| \tag{5b}$$

orbitals actively participating in the process. These orbitals are two Π molecular orbitals of butadiene (φ_1, φ_2) corresponding to two dissappearing butadiene double bonds and one Π (Π_{23}) and one σ localized orbital of newly created bonds in cyclobutene (σ_{14}). The individual molecular orbitals can be described as linear combinations of corresponding AO basis set orbitals $\{\chi\}$ and $\{\chi'\}$, where the prime is used to denote the fact that basis sets for molecules R and P are generally different (eq 6) (Chart I).

$$\varphi_i = \sum_\mu c_{\mu i}\chi_\mu \tag{6a}$$

$$\psi_j = \sum_\nu c_{\nu j}\chi'_\nu \tag{6b}$$

In order to determine the mutual relation of both basis sets, which is the necessary prerequisite for both the overlap determinant method and topological similarity index, a procedure was proposed whose principles are based on simple geometric considerations.[37] We analyze first the conrotatory cyclization. This mechanism is characterized by the clockwise

rotation at terminal centers (C_1 and C_4 in our case). During this rotation the original basis orbitals χ_1 and χ_4 change their orientation in space. The construction of the transformation matrix **T** is now based on the comparison of mutual phase relations of rotated atomic orbitals with the orbitals χ'_1 and χ'_4 in the product. As can be seen from Scheme Ia, this relation is given by the simple assignment $\chi'_1 \rightarrow \chi_1$, $\chi'_2 \rightarrow \chi_2$, $\chi'_3 \rightarrow \chi_3$, $\rightarrow \chi'_4 \rightarrow -\chi_4$. This assignment can be alternatively rewritten in the form of (7), which is just the desired matrix **T**. If now the same procedure is applied to the disrotatory

$$\mathbf{T}_{con} = \begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & -1 \end{pmatrix} = \text{diag}\,(1, 1, 1, -1) \tag{7}$$

reaction, it is possible to see (Scheme Ib) that the transformation matrix **T** has the form of the trivial identity matrix (8). These matrices applied according to eq 3 to the density

$$\mathbf{T}_{dis} = \begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} = \text{diag}\,(1, 1, 1, 1) \tag{8}$$

matrix of cyclobutene lead to the final values of similarity indices given in eq 9. A greater value of r_{RP} for conrotatory

$$r_{RP}^{con} = 0.724$$

$$r_{RP}^{dis} = 0.500 \tag{9}$$

cyclization was interpreted[28] in the sense of the least-motion principle as indicating a lower extent of electron reorganization in allowed reactions while a lower value for disrotation analogously indicates deeper electron reorganization in forbidden ones. The same general picture was then found to hold for other pericyclic reactions as well.[28,33] The similarity indices thus provide an alternative way to reproduce Woodward–Hoffmann rules.

The formalism proposed in the original study[28] was, however, designed only for processes where the transformation R $\rightarrow$ P proceeds concertedly without the eventual participation of intermediates. Our aim in this study is to generalize the original approach so as to be applicable, besides the discrimination between the allowed and forbidden concerted processes, also for the evaluation of the relative ease of concerted one-step and stepwise reaction paths. For this purpose a simple model is proposed characterizing these stepwise paths in terms of similarity indices for individual elementary steps. In the case of pericyclic reactions the stepwise reaction mechanism is very simple and consists of only two reaction steps involving a common biradical or zwitterionic intermediate.
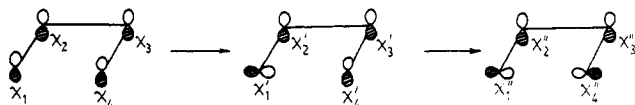
$$R \rightarrow I \rightarrow P \tag{10}$$

The required indices are therefore only r_{RI} and r_{PI}. In terms of these indices, the extent of electron reorganization in each elementary step is given by $1 - r_{RI}$ and $1 - r_{IP}$.[38] If now the individual reaction steps were completely independent, the extent of the reorganization in the whole process (10) would be naturally characterized by the simple sum of these individual terms. Such is not, however, the case. The above idealized expression for the total extent of electron reorganization

SIMILARITY APPROACH TO CHEMICAL REACTIVITY

J. Chem. Inf. Comput. Sci., Vol. 33, No. 6, 1993 **807**
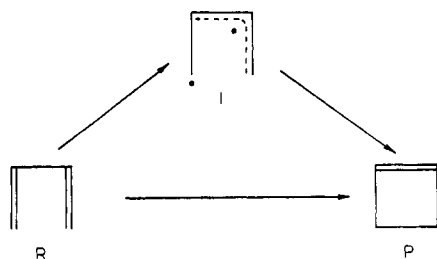
Scheme II

Scheme III

therefore has to be properly modified. Such a modification is given by eq 11, in which the multiplicative correction factor

$$L_{stepwise} = (1 - r_{RI}) + r_{RI}(1 - r_{IP}) = (1 - r_{RI}r_{IP}) \quad (11)$$

r_{RI} was introduced to account for the mutual coupling of the individual steps arising from the fact that the intermediate, before entering as a reactant into the second step, had to be created as a product of the first step.

The relative ease of one step and stepwise reaction paths can be then evaluated by comparing the product $r_{RI}r_{IP}$ with r_{RP}. The reactions for which $r_{RP} > r_{RI}r_{IP}$ are expected to prefer the one-step mechanism, while the criterion for the preference of the stepwise mechanism is $r_{RI}r_{IP} > r_{RP}$. We are of course aware of the fact that the above classification based on the comparison of strictly synchronous one-step and strictly asynchronous stepwise reaction paths represents only an idealized model, but for the purpose of the first qualitative orientation such an idealization seems satisfactory. The practical use of the above criterion will be demonstrated by several examples of selected pericyclic processes.

RESULTS AND DISCUSSION

As the simplest case demonstrating the practical use of the proposed approach, we consider again the electrocyclic transformation of butadiene to cyclobutene, for which the alternative reaction mechanisms are given in the Scheme II. In harmony with the general philosophy of overlap determinant method, on which the whole similarity approach is based, the first step of the analysis requires that the structure of participating molecular species be described by approximate wave functions (12). In these functions the molecular orbitals

$$\Phi_R = |\phi_1\bar{\phi}_1\phi_2\bar{\phi}_2|$$

$$\Phi'_I = \frac{1}{2^{1/2}}(|\psi_1\bar{\psi}_1\psi_2\bar{\chi}'_1| + |\psi_1\bar{\psi}_1\chi'_1\bar{\psi}_2|)$$

$$\Phi''_P = |\pi''_{23}\bar{\pi}''_{23}\sigma''_{14}\bar{\sigma}''_{14}| \quad (12)$$

ϕ_1, ϕ_2, ψ_1, and ψ_2 correspond to occupied HMO orbitals of butadiene and the allyl fragment, respectively, the χ'_1 describes the localized atomic orbital carrying the unpaired electron in the biradical I and the dashes denote again the fact that the AO bases serving to described the molecular orbitals of individual components can be generally different (Scheme III).

On the basis of these wave functions the density matrices P_R, P'_I, and P''_P can be straightforwardly determined.

Scheme IV
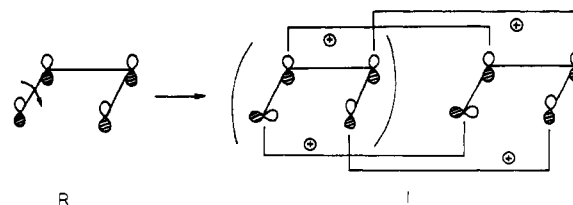
These matrices are then, in the next step, used for the calculation of the similarity indices r_{RI}, r_{IP}, and r_{RP} (eq 13),

$$r_{RI} = \frac{\text{Tr } P_R\bar{P}_I}{(\text{Tr } P_R{}^2)^{1/2}(\text{Tr } \bar{P}_I{}^2)^{1/2}} \quad (13a)$$

$$r_{IP} = \frac{\text{Tr } \bar{P}_I\bar{\bar{P}}_P}{(\text{Tr } \bar{P}_I{}^2)^{1/2}(\text{Tr } \bar{\bar{P}}_P{}^2)^{1/2}} \quad (13b)$$

$$r_{RP} = \frac{\text{Tr } P_R\tilde{P}_P}{(\text{Tr } P_R{}^2)^{1/2}(\text{Tr } \tilde{P}_P{}^2)^{1/2}} \quad (13c)$$

where the density matrices $\bar{P}_I$, $\bar{\bar{P}}_P$, and $\tilde{P}_P$ are given by eq 14.

$$\bar{P}_I = T_{RI}{}^{-1}P'_I T_{RI} \quad (14a)$$

$$\bar{\bar{P}}_P = T_{IR}{}^{-1}\bar{P}_I T_{IP} \quad (14b)$$

$$\tilde{P}_P = T_{RP}{}^{-1}P''_P T_{RP} \quad (14c)$$

As can be seen from these equations, the calculation of similarity indices requires the knowledge of the transformation matrices T_{RI}, T_{IP}, and T_{RP} which thus have to be determined for each elementary step.

$$R \xrightarrow{T_{RI}} I \xrightarrow{T_{IP}} P; \quad R \xrightarrow{T_{RP}} P \quad (15)$$
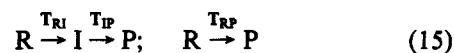
The case of direct one-step reaction $R \rightarrow P$ was analyzed above, and the whole procedure together with the final results can be taken therefrom. It holds that

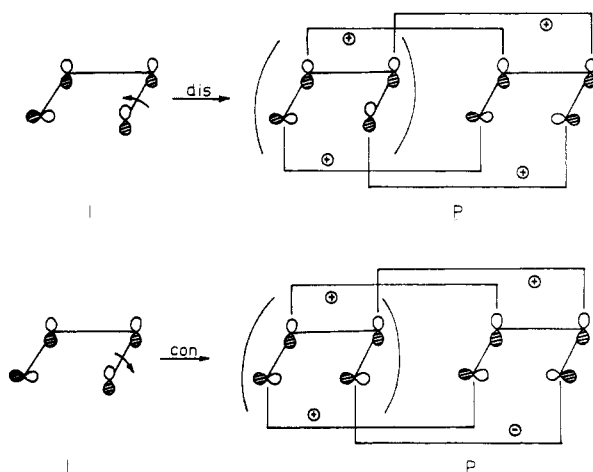$$T_{RP}^{dis} = \text{diag } (1, 1, 1, 1)$$

$$T_{RP}^{con} = \text{diag } (1, 1, 1, -1) \quad (16)$$

If we calculate, using these matrices and definition 14c, the corresponding indices, the values given in eq 9 result. They confirm that the concerted conrotation should be preferred in this case over the concerted disrotation which is really the case.

Basically the same procedure can then be used also for the construction of the matrices T_{RI} and T_{IP}, describing the mutual phase relations of AO bases of corresponding components for individual reaction steps. Since, however, the multistep nature of the process introduces into this construction certain specificities, we consider it convenient to demonstrate the whole procedure in more detail. We start by analyzing the first step of the process. This step consists of the rotation of one terminal CH₂ group of butadiene, resulting in the formation of the intermediate biradical. The situation is depicted graphically in Scheme IV, from which it is evident that irrespective of the direction of rotation of CH₂ group, the phase structure of AO bases on both reactant and intermediate is identical. This is due to the fact that the rotation of the first CH₂ group says nothing about what will be the future destiny of the intermediate and both conrotatory and disrotatory reaction

Scheme V

Table I. Calculated Values of Similarity Indices r_{RP}, r_{RI}, and r_{IP} for Several Selected Pericyclic Reactions

reaction	mechanism[a]	r_{RP}	r_{RI}	r_{IP}
butadiene → cyclobutene	conrot	0.724	0.851	0.781
	disrot	0.500	0.851	0.781
hexatriene → cyclohexadiene	disrot	0.759	0.895	0.835
	conrot	0.659	0.859	0.835
ethene dimerization	$s + a$	0.500	0.577	0.866
	$s + s$	0.500	0.577	0.866
Diels–Alder reaction	$s + s$	0.575	0.721	0.859
	$s + a$	0.575	0.721	0.859
butadiene → bicyclobutane	$s + a$	0.500	0.577	0.866
	$s + s$	0.500	0.577	0.866
Cope rearrangement via 1,4-cyclohexadiyl	$s + s$	0.500	0.730	0.730
	$s + a$	0.500	0.730	0.730

[a] Upper value corresponds to the allowed and lower to the forbidden reaction mechanism.

Table II. Calculated Values of Second-Order Similarity Indices g_{RP}, g_{RI}, and g_{IP} for Several Selected Multibond Reactions

reaction	mechanism[a]	g_{RP}	g_{RI}	g_{IP}
ethene dimerization	$s + a$	0.250	0.241	0.724
	$s + s$	0.091	0.241	0.724
Diels–Alder reaction	$s + s$	0.298	0.468	0.711
	$s + a$	0.272	0.468	0.711
Cope rearrangement via 1,4-cyclohexadiyl	$s + s$	0.206	0.481	0.481
	$s + a$	0.206	0.481	0.481

[a] Upper value corresponds to allowed and lower to forbidden reaction mechanism.

paths remain completely opened. As a consequence, the transformation matrix T_{RI} has the form of trivial identity (eq 17). The possibility to discriminate between the alternative

$$T_{RI} = diag\,(1, 1, 1, 1) \qquad (17)$$

conrotatory and disrotatory ring closures thus enters into the formalism only in the second step, where the information allowing one to distinguish between the individual mechanisms comes just from the rotation of the second terminal CH_2 group. The situation is depicted graphically in the Scheme V from which the forms of the corresponding matrices are given in eq 18. Using these relations and the expression for the

$$T_{IP}^{dis} = diag\,(1, 1, 1, 1)$$

$$T_{IP}^{con} = diag\,(1, 1, 1, -1) \qquad (18)$$

calculation of the similarity index, the final values of r_{RI}, r_{IP} can be obtained. Such a calculation demonstrates that in spite of differences in the form of transformation matrices for conrotatory and disrotatory mechanisms, the resulting values of r_{RI} and r_{IP} are in both cases exactly the same. It holds that

$$r_{RI}^{con} = r_{RI}^{dis} = 0.851$$

$$r_{IP}^{con} = r_{IP}^{dis} = 0.781 \qquad (19)$$

In connection with this, at first sight a surprising result, it is, however, necessary to realize that the equivalence of both alternative stepwise reaction paths is completely reasonable and fits well with the well-known lack of stereospecificity of these paths.

On the basis of these values and of their comparison with the r_{RP} values for direct reaction the relative ease of the one-step and stepwise reaction paths can be discussed. In our concrete case it can be for example concluded that the direct cyclization should be preferred over the stepwise path for allowed conrotation ($r_{RP} > r_{RI}r_{IP}$), while in the case of forbidden disrotation the preferred reaction path is the stepwise one. This result is very interesting not only for being in complete harmony with what was intuitively expected from Woodward–Hoffmann rules but also for remarkably corresponding with what is predicted for the mechanism of this reaction from available theoretical data.[23,39–42] Especially interesting in this connection is the case of forbidden disrotatory reaction for which both semiempirical and ab initio calculations predict the reaction path to be very asynchronous. The limiting

case of this asynchronous reaction path is then our idealized stepwise mechanism via the biradical intermediate.

Such a qualitative confirmation of previous intuitive ideas is not, however, the only output of the proposed approach. Another interesting possibility of exploitation consists of allowing a simple semiquantitative estimate of which of the corresponding reaction steps will be rate determining. Such an estimate is based on a simple comparison of individual values of r_{RI} and r_{IP}, characterizing the extent of the changes of electron configurations in the individual reaction steps. Thus, e.g., in our case such a comparison suggests that the extent of reorganization is higher in the second step. We can thus expect this step to be rate determining. The reaction profile of such a process thus corresponds to what Dewar calls the two-step process.[4] It would be certainly interesting to confront this theoretical prediction with experiment or independent theoretical calculations, but unfortunately the lack of convenient data makes so far such a comparison unfeasible. As we shall see, however, below, such a comparison is possible in other cases and some of them will be discussed in the subsequent part. The calculated values of similarity indices for the set of selected pericyclic reactions for both parent nonsubstituted and model substituted systems are summarized in Tables I and III and in the Scheme VI.

We discuss now some general features arising from the above results, first for the case of parent nonsubstituted systems where the corresponding intermediates can be expected to correspond to pure biradicals. The simplest situation is in the case of electrocyclic transformation of hexatriene to cyclohexadiene where the calculated values strongly suggest the preferrence of a concerted mechanism for allowed disrotation while for the forbidden conrotation the favorable reaction path should be the stepwise one. All these predictions are again in complete harmony with the intuitive expectation of Woodward–Hoffmann rules.

A little bit more complex situation is in the case of cycloadditions and sigmatropic reactions, the specific position

Table III. Comparison of First-Order Similarity Indices for One-Step and Stepwise Reaction Paths for the Diels–Alder Reaction of Butadiene with Substituted Ethenes

reaction[a]	$\alpha(\beta)$[b]	r_{RP}	r_{RI}	r_{IP}	$r_{RI}r_{IP}$
I	0	0.575	0.721	0.859	0.619
	±1	0.591	0.782	0.809	0.632
	±2	0.616	0.818	0.833	0.681
	±3	0.632	0.835	0.844	0.704
II	0	0.575	0.721	0.859	0.619
	±1	0.591	0.736	0.859	0.632
	±2	0.616	0.767	0.859	0.659
	±3	0.632	0.784	0.859	0.673

[a] For numbering see the Scheme VII. [b] Positive values correspond to donor and negative to acceptor substitution.

Scheme VI
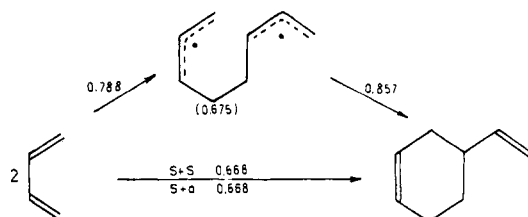
of which was already stressed.[4,43] The most delicate situation is in the case of ethene dimerization, where the equality of r_{RP} for both $s + s$ and $s + a$ mechanisms as well as of the product $r_{RI}r_{IP}$ suggests that any discrimination between alternative reaction paths is impossible in this case. Fortunately there is a possibility of overcoming this drawback. This is due to the fact that the insufficiency of the first-order index r_{RP} to discriminate between allowed and forbidden mechanisms for multibond reactions was found already in a previous study,[43] and in this case the insufficiency was remedied by replacing the similarity index r_{RP} (first-order index) by the so-called second-order similarity index g_{RP}. If now the same remedy is applied to the discrimination between one-step and stepwise mechanisms, the original criterion based on comparison of r_{RP} with the product $r_{RI}r_{IP}$ analogously requires the comparison of g_{RP} with the product $g_{RI}g_{IP}$. Similarly as with first-order indices, the concerted one-step mechanisms can be expected to be preferred for $g_{RP} > g_{RI}g_{IP}$, while when $g_{RP} < g_{RI}g_{IP}$, the stepwise mechanism should be favored. The calculated values of second-order similarity indices for several selected multibond processes are summarized in Table II. As can be seen from this table, the values of g_{RP} do indeed remedy the insufficiency of the first-order index r and correctly predict the reaction preferred for the concerted process by Woodward–Hoffmann rules. Much more interesting than this reproduction of Woodward–Hoffmann rules is, however, the comparison of g_{RP} with the product $g_{RI}g_{IP}$ since just such a comparison is in this case required for the discrimination between the concerted one-step and nonconcerted stepwise mechanisms. Thus, e.g., in the case of 2 + 2 ethene dimerization where the original criterion based on first-order indices failed, the new enhanced criterion based on the index g clearly suggests that the preferred mechanism of forbidden $s + s$ dimerization is the stepwise one. This is in complete agreement with both experimental and theoretical data for this process.[44,45]

In addition to this prediction of the preferred reaction mechanism, the individual values of similarity indices g_{RI} and g_{IP} (and also the values of r_{RI} and r_{IP}) which provide a measure of the extent of electron reorganization in individual steps R → I and I → P can be used, similarly as the indices r_{RI} and r_{IP} to estimate which of the two reaction steps can be expected to be rate determining. As can be seen from both Tables I

and II, the rate determining step for the $s + s$ stepwise ethene dimerization should be the formation of the intermediate ($g_{RI} < g_{IP}$ and/or $r_{RI} < r_{IP}$). Although the lack of appropriate experimental data prevents direct verification of this theoretical prediction, it is interesting that our theoretical prediction is in complete agreement with the available theoretical calculations.[44,45] In a completely analogous way it would be possible to analyze any other multibond reaction. Especially interesting in this respect is the Diels–Alder reaction, for which the question of the eventual participation of nonconcerted stepwise mechanism was suggested some time ago by Dewar.[15,16] It is therefore of interest to us to know what will be the prediction of our model. As can be seen from Tables I and II, the comparison of concerted and stepwise mechanisms seems to suggest, irrespective of whether the first-order or second-order indices are used, the preference of the stepwise mechanism ($g_{RP} < g_{RI}g_{IP}$ as well as $r_{RP} < r_{RI}r_{IP}$) with the first step being rate determining ($g_{RI} < g_{IP}$; $r_{RI} < r_{IP}$). This corresponds to the reaction of the two-stage type. In this connection it is interesting that the same type of mechanism, combining the observed kinetic concertedness with the possibility of certain asynchronization in the formation of the bonds was proposed for the Diels–Alder reaction some time ago by Woodward and Katz.[46] The preference for an asynchronous stepwise reaction path is in this case also in harmony with the results of semiempirical calculations by Dewar.[14–16] Since, however, these results were questioned by more sophisticated ab initio techniques[18–22] and since the parent unsubstituted systems behave frequently atypically,[16] we will take our predictions in this case with prudence. Nevertheless it is interesting that similar prediction of a two-stage reaction mechanism in the case of closely related 2 + 4 dimerization of butadiene (Scheme VI) is in complete harmony with experimental results by von Doering.[47]

After this discussion of the simplest cases of parent nonsubstituted systems, we continue with the similar analysis of reactions of substituted systems. Although the analysis of these systems is methodologically entirely analogous to what was described above, the presence of the substituents brings nevertheless some specificities which are worth mentioning.

One of these specificities consists of the existence of a greater number of nonequivalent stepwise reaction paths arising from the substituent induced decrease of symmetry. Another complicating factor which has to be generally taken into account in the case of substituted systems concerns the increased variability in the structure of the corresponding intermediates, since, as a consequence of substituent induced polarity, the corresponding intermediates need not already correspond to pure biradicals, but, in highly polar systems represented, e.g., by the substitution of the push–pull type, the contributions of the zwitterionic states may become important.

In the following part the practical applicability of the proposed analysis will be demonstrated by the concrete example of the Diels–Alder reaction substituted in the dienophilic component. The substitution was modelled by the change of the Coulombic integral α on the corresponding center. In order to model the effect of both the nature and the "strength" of the substitution, the calculations were performed for a series of α systematically varying from $+3\beta$ to -3β. The calculated values of similarity indices for one-step concerted and both alternative stepwise reaction paths (Scheme VII) are given in Tables III and IV.

We discuss now some general conclusions which can be deduced from these tables. The first, most important

Scheme VII
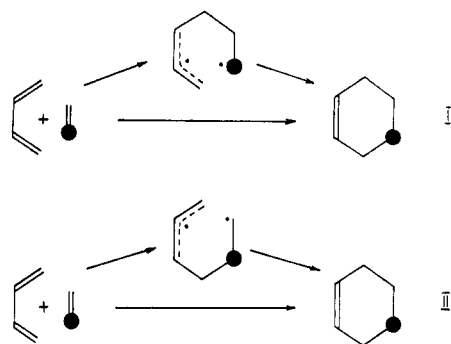
Table IV. Comparison of First-Order Similarity Indices for One-Step and Stepwise Reaction Paths for the Thermally Allowed *s* + *s* Diels–Alder Reaction of Butadiene with Substituted Ethenes

reaction[a]	$\alpha(\beta)$[b]	g_{RP}	g_{RI}	g_{IP}	$g_{RI}g_{IP}$
I	0	0.298	0.468	0.711	0.332
	1	0.316	0.585	0.608	0.356
	−1	0.316	0.583	0.616	0.332
	2	0.342	0.643	0.650	0.417
	−2	0.342	0.639	0.657	0.419
	3	0.360	0.671	0.671	0.450
	−3	0.360	0.667	0.677	0.451
II	0	0.298	0.468	0.711	0.332
	1	0.316	0.498	0.711	0.354
	−1	0.316	0.494	0.711	0.351
	2	0.342	0.542	0.711	0.385
	−2	0.342	0.535	0.711	0.380
	3	0.360	0.571	0.711	0.406
	−3	0.360	0.562	0.711	0.399

[a] For numbering see the Scheme VII. [b] Positive values correspond to donor and negative to acceptor substitution.

conclusion concerns the regular increase of corresponding indices (both *r* and *g*) with increasing |α| for all types of reaction paths. This suggests that irrespective of the reaction mechanism the reaction can be expected to be facilitated by the substitution. Moreover, the symmetry with respect to |α| indicates that both donor and acceptor substituents of the comparable "strength" should behave in influencing the reaction analogously. This result seems to be completely reasonable since for the "normal" Diels–Alder reaction, to which our system belongs, the same activating effect of both donor and acceptor substitution is predicted by the perturbation theory.[48]

More interesting than this simple qualitative estimate of the effect of substitution on the ease of the reaction are, however, mechanistic predictions concerning the relative ease of one-step concerted and stepwise reaction paths. Here it is possible to see again that irrespective of whether first- or second-order indices are used, the two-stage mechanism, becomes favored with increasing substitution more strongly than the concerted one. This seems to suggest that the stepwise mechanism will apparently dominate in this case.

This result is supported not only by the direct quantum chemical calculations[16,49] but also by experiment. As an example may serve, e.g., the analysis of substituent effect on the Diels–Alder addition of maleinanhydride to substituted furanes[12] and a kinetic study[5] confirming the presence of a biradical intermediate in the gas-phase reaction of 1,3-cyclohexadiene with acrylonitrile.

The confirmation of the stepwise nature of the reaction is not, however, the only point in which our calculations agree with experimental data. Interesting is also the close correspondence of experiment and our calculations in the question

of the rate determining step, which was found to correspond to the formation of intermediate.[5]

Another important mechanistic conclusion which can be extracted from the proposed model concerns the prediction of the character of the asymetry of the stepwise reaction path. As can be seen from Tables III and IV, the preferred reaction path corresponds to reaction A, the typical feature of which is that the first of the C···C bonds is created between nonsubstituted carbon centers. It is interesting that even this relatively subtle mechanistic detail is in complete harmony with independent quantum chamical calculations in which either the true intermediate or at least the asynchronous transition state was found,[16,49] the structural features of which closely correspond to what is predicted by our model. If we realize how simple the model is, such a close correspondence is really encouraging.

Even if we are aware of the fact that the presented examples are far from covering all possible types of pericyclic reactions, it is perhaps possible to express our belief that the basic mechanistic features are nevertheless well reproduced by the model. In this connection it is, however, important to emphasize that the aim of the proposed model is not to substitute the sophisticated MO calculations, but rather to allow the synthetic organic chemist to exploit the obtained qualitative picture of the reaction mechanism in the design of optimal strategy for the synthesis of the desired products. In this respect the proposed approach is ideally suited for incorporation into the programs for computer designed synthesis.[50]

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