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## Sterical index: a novel, simple tool for the interpretation of organic reaction mechanisms

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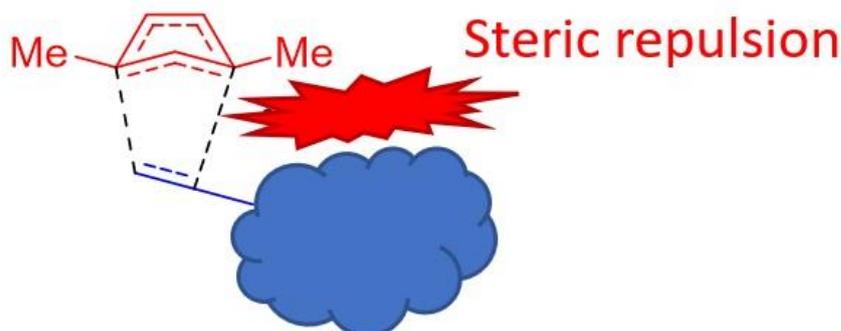
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**Abstract:** A new, simple index for the quantitative description of steric effects was proposed based on the results of DFT calculations. This effect was connected with the disturbance of synchronicity within transition states of the model Diels-Alder reaction. The obtained results offer the possibility of predicting steric effects determined by alkyl groups for a wide range of bimolecular processes.

**Keywords:** Organic reactivity, Steric effect, Cycloaddition

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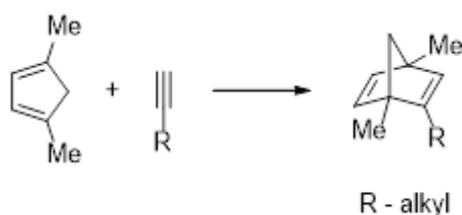
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## Introduction

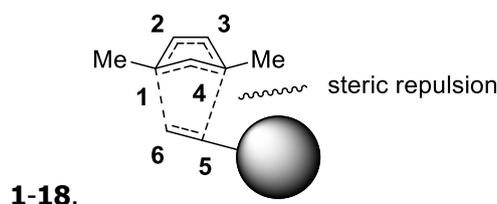
The assessment of the reactivity of chemical compounds is one of the most important problems in modern organic chemistry because it allows estimating a priori the course of a given process without the need to perform long-term and costly experiments. This field is currently developing intensively. Recently, a number of tools for the quantitative description of the electronic properties of molecules and the activity of potential reaction centers have been developed or improved. These include electrophilicity ( $\omega$ ) [1], nucleophilicity (N) [2], chemical softness (S) [3], chemical hardness ( $\eta$ ) [3], chemical electronic potential ( $\mu$ ) [4] and many others. They have a key role in relation to polar reactions. Less attention is paid to the quantitative description of steric effects, which often have a decisive impact on the rate and mechanism of the reaction. This is especially the case in non-polar processes. For the present time, the steric interactions are considered in general, rather in a quality sense ("poor effect", "strong effect"). Within this paper, we proposed a new, very simple descriptor for the quantitative description of steric effects near reaction centers.

## Results and discussion

As the model for our analysis, we applied the simple and good known Diels-Alder reaction [5, 6] with the participation of 1,4-dimethyl-cyclopentadiene and a series of terminal alkynes with different-type alkyl substituents (**1-21**) (Scheme 1).



Scheme 1. Model Diels-Alder reactions between 1,4-dimethyl-cyclopentadiene and alkynes



**1-18.**

$$SI = dC4-C5 - dC1-C6$$

Scheme 2. Steric interactions within Diels-Alder reactions between 1,4-dimethyl-cyclopentadiene and alkynes **1-21**.

Within this model, the degree of polar interactions [7] should be approved as very low and almost identical. On the other hand, the addent's special orientation can be determined by steric repulsion between the methyl group at the diene and the substituent at the alkynyl molecular segment. So, the measure of the steric effect (SI) in this case would be the disturbance of synchronicity, the formation of a new sigma bond (Scheme 2).

The structural base for the estimation of SI indexes was obtained using the DFT B3LYP/6-31G(d) level of theory, which can be conducted on simple stationary computers. On the other hand, this approach was verified in many works as an optimal tool for the quantum chemical study of organic compounds [8-10]. The key geometrical parameters of optimized transition states were collected in Table 1.

Table 1. Steric indexes (SI) and average steric indexes (ASI) for alkyl groups with the same number of carbon atoms calculated for a series of terminal alkynes.

No.	Substituent		Interatomic distances		SI	ASI
	Formula	Structure	d [Å]			
			C <sub>4</sub> -C <sub>5</sub>	C <sub>1</sub> -C <sub>6</sub>		
<b>1</b>	H	H	2.254	2.254	0	0
<b>2</b>	CH <sub>3</sub>	Me	2.418	2.124	0.293	0.293
<b>3</b>	C <sub>2</sub> H <sub>5</sub>		2.422	2.122	0.300	0.300
<b>4</b>	C <sub>3</sub> H <sub>7</sub>		2.425	2.112	0.313	0.339
<b>5</b>			2.450	2.107	0.343	
<b>6</b>	C <sub>3</sub> H <sub>5</sub>		2.455	2.093	0.362	
<b>7</b>	C <sub>4</sub> H <sub>9</sub>		2.466	2.087	0.379	0.400
<b>8</b>			2.430	2.107	0.323	
<b>9</b>			2.625	2.039	0.586	
<b>10</b>	C <sub>4</sub> H <sub>7</sub>		2.431	2.119	0.312	
<b>11</b>	C <sub>5</sub> H <sub>11</sub>		2.420	2.122	0.299	0.401
<b>12</b>			2.451	2.110	0.340	
<b>13</b>			2.637	2.026	0.611	
<b>14</b>	C <sub>5</sub> H <sub>9</sub>		2.456	2.102	0.354	

<b>5</b>			2.421	2.122	0.299	
<b>16</b>	C <sub>6</sub> H <sub>13</sub>		2.451	2.110	0.341	0.415
<b>17</b>			2.669	1.999	0.670	
<b>18</b>	C <sub>6</sub> H <sub>11</sub>		2.454	2.106	0.349	

It was found that the interatomic distance at the screened center C<sub>5</sub> can adopt values in the range of 2.254÷2.669 Å. So, the estimated SI indices for alkyl C<sub>1</sub> – C<sub>6</sub> substituents are equal to 0.293÷0.670. In consequence, the sterical effect of the cyclohexyl group should be considered as more than two times stronger than in the case of the methyl group. Next, the average steric indexes (ASI) indices exist in the range of 0.293÷0.415. It was found that within C<sub>1</sub>-C<sub>3</sub>, the SI value for most branched alkyl groups is lower than the respective indices for the cycloalkyl group.

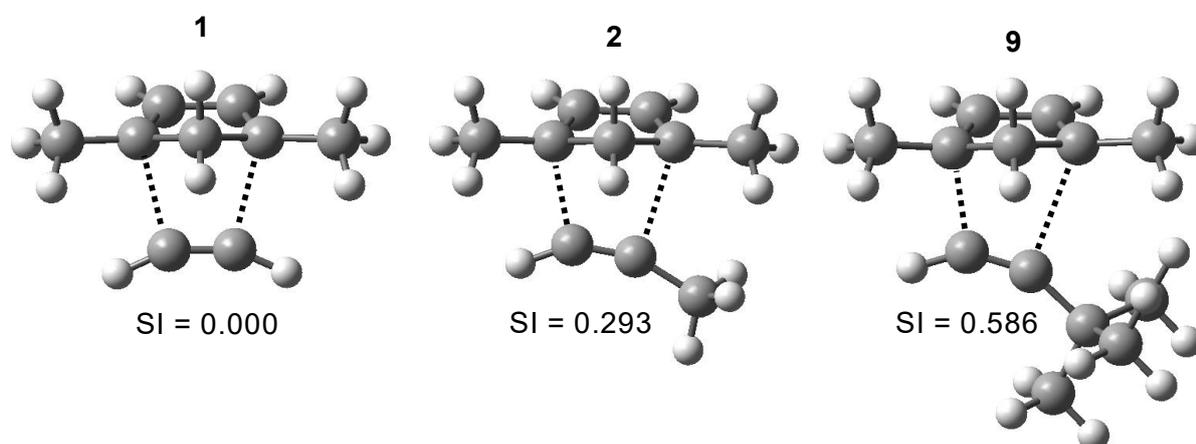


Fig. 1. The 3D presentation and the SI for compounds **1**, **2**, and **9**.

### Computational details

All calculations reported in this paper were performed on "Prometheus" cluster in the "Cyfronet" computational center in Cracow. Hybrid functional B3LYP with the 6-31G(d), basis set included in the GAUSSIAN 09 package [11] was used. Previously we have found that the B3LYP/6-31G(d) calculations illustrate well the structure of transition states in different-type cycloaddition processes [9, 10]. First-order saddle points were localized using QST2 and Berny procedures. The transition states were

verified by diagonalization of the Hessian matrix and by analysis of the internal reaction coordinate (IRC). Calculations of all structures were performed at the temperature  $T=298\text{K}$  and pressure  $p=1\text{atm}$ . The results are collected in Table 1.

## Conclusions

From our considerations, it is evident that based on simple DFT calculations, you can diagnose the strength of predictable steric effects using specific numerical indicators. In our opinion, these indicators can be adapted to the description of any bimolecular reaction.

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