

## Orientation in Electrophilic Substitution and Aromaticity

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### Abstract

Orientation in electrophilic aromatic substitution was analyzed in terms of localization energies in a molecule and the graph-theoretically defined polyene reference. For polycyclic benzenoid hydrocarbons, the orientation in substitution scarcely depends on the aromaticity of the molecule; positions of electrophilic attack are determined primarily by the connectivity of carbon atoms in the molecule. In contrast, reactive positions in nonbenzenoid hydrocarbons are determined not only by the connectivity of carbon atoms but also by the aromaticity of the molecule. Some nonbenzenoid aromatic hydrocarbons are predicted to be more reactive toward electrophiles than their respective polyene references.

### Introduction

One of the characteristic properties of aromatic molecules is the ability to undergo substitution reactions with certain electrophiles.<sup>1,2</sup> This property has been used to decide whether a given molecule is aromatic or

not. Electrophilic substitution is a manifestation of the tendency of an aromatic molecule to retain its cyclic conjugated system. When an electrophile attacks an aromatic molecule, it may enter into some specific positions in the molecule. In most polycyclic molecules all peripheral positions are not equivalent and there is usually a preferred orientation (i.e., positional selectivity).<sup>1,2</sup> However, it has not at all been clear whether or not an orientation in electrophilic substitution reflects aromaticity or extra stabilization due to cyclic conjugation.

In the majority of electrophilic substitution reactions, an electrophile attacks in the first step, giving rise to a positively charge intermediate called an arenium ion, and the leaving group departs in the second step.<sup>1-3</sup> The preferred positions for reaction with an electrophile can usually be predicted from relative magnitudes of the localization energies in the substrate.<sup>1,3</sup> In this letter we compare localization energies in a variety of cyclic conjugated molecules with those in their respective polyene references (i.e., olefinic reference structures), and explore theoretical relationships between aromaticity and orientation in electrophilic substitution. All considerations are made within the framework of a simple Hückel model.

### Theory

A hypothetical polyene reference adopted for every cyclic conjugated molecule is that utilized to define the topological resonance energy (TRE).<sup>4,5</sup> A reference (or matching) polynomial of a molecule represents a characteristic polynomial of the polyene reference.<sup>4,5</sup> The percent resonance energy (%RE) is used as a measure of aromaticity in a molecule.<sup>6,7</sup> It is given as 100 times the TRE, divided by the total  $\pi$ -

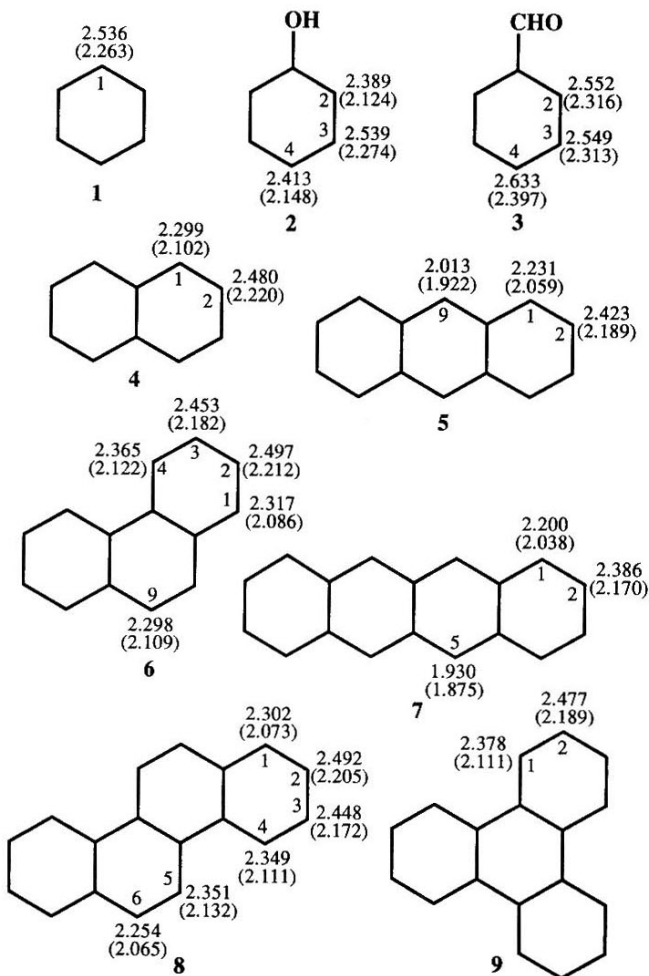
electron energy of the polyene reference. Hückel parameters compiled by Streitwieser<sup>8</sup> were used.

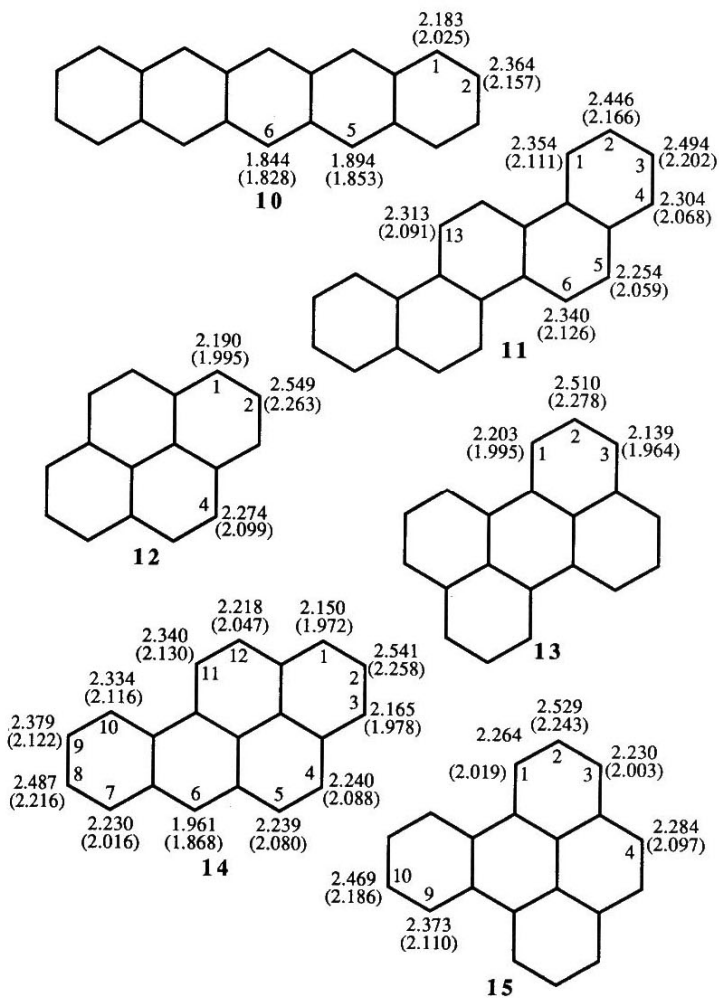
Localization energy (LE) is defined as the  $\pi$ -bonding energy required to attach a proton or an electrophile to a given position in a conjugated molecule.<sup>1,3</sup> In general, a position of small LE is easily attacked by an electrophile whether or not it triggers substitution reaction. Note that the conjugated system of a protonated complex is identical with that of the arenium ion derived from the same molecule. An excellent correlation is observed between calculated LEs and electrophilic reactivities.<sup>1-3</sup> LE can likewise be defined for all positions in the polyene reference of any conjugated molecule.<sup>4,5</sup> It is given as the difference in  $\pi$ -electron energy between the polyene reference of a conjugated molecule and that of the protonated complex. All LEs are given in units of  $|\beta|$ .

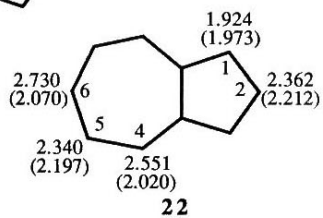
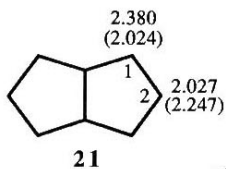
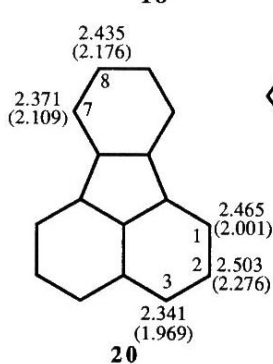
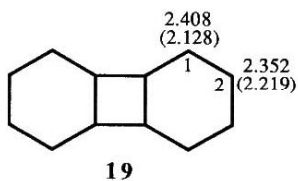
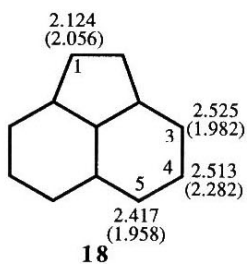
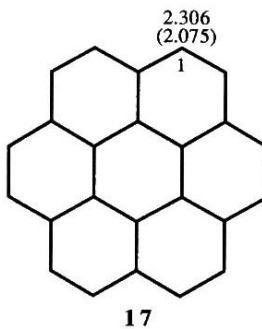
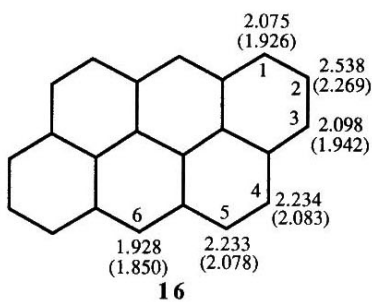
## Results and Discussion

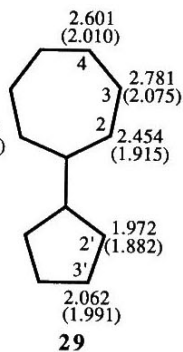
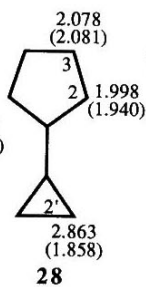
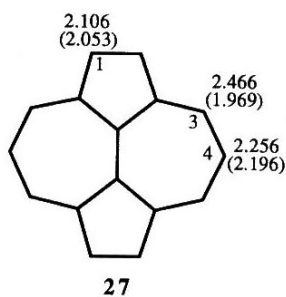
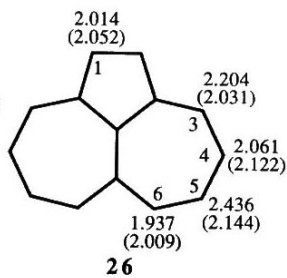
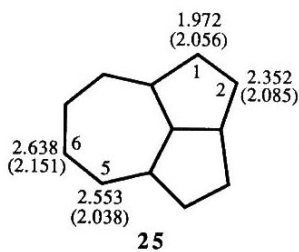
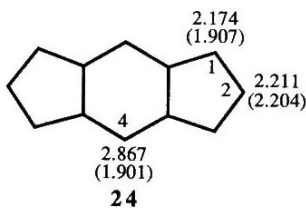
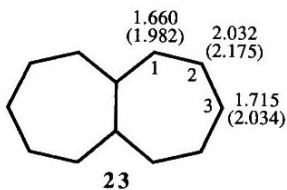
The LEs calculated for all positions in a total of thirty molecules and their polyene references are summarized in Fig. 1. Small LEs point to carbon atoms that should be basic and reactive toward electrophiles. LEs in all molecules investigated range between 1.66  $|\beta|$  and 2.87  $|\beta|$ . Very large or very small LE values are found in nonbenzenoid hydrocarbons. LEs in polyene references lie in the relatively narrow range 1.77-2.40  $|\beta|$ . Relative magnitudes of LEs in every molecule and its polyene reference are listed in Table 1. All LEs in benzene (**1**) and coronene (**17**) are the same because of their highly symmetric structures.

First, we analyze LEs in two substituted benzenes **2**, **3**. All protonated complex derived from monocyclic molecules, such as **2** and **3**, are identical with their respective polyene references since they do not have a cyclic conjugated system. Therefore, the LE for every position in a









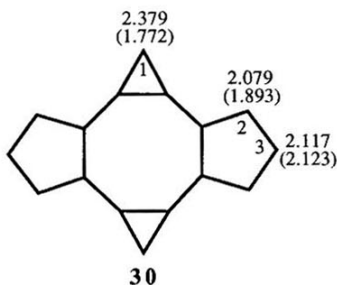


Figure 1. Localization energies (LEs) in typical cyclic conjugated molecules in units of  $|\beta|$ . Values in parentheses are the LEs in the polyene references.

Table 1. Relative magnitudes of localization energies (LEs) in typical cyclic conjugated molecules. Those in the polyene references are given in parentheses.

Species	%RE	Relative magnitudes of the LEs
benzene (1)	3.53	1 (1)
phenol (2)	3.34	1<4<3 (1<4<3)
benzaldehyde (3)	2.49	3<2<4 (3<2<4)
naphthalene (4)	2.92	1<2 (1<2)
anthracene (5)	2.52	9<1<2 (9<1<2)
phenanthrene (6)	2.89	9<1<4<3<2 (1<9<4<3<2)
tetracene (7)	2.27	5<1<2 (5<1<2)
chrysene (8)	2.81	6<1<4<5<3<2 (6<1<4<5<3<2)
triphenylene (9)	3.01	1<2 (1<2)



pentacene (10)	2.11	6<5<1<2 (6<5<1<2)
picene (11)	2.77	5<4<13<6<1<2<3 (5<4<13<1<6<2<4)
pyrene (12)	2.73	1<4<2 (1<4<2)
perylene (13)	2.69	3<1<2 (3<1<2)
benzo[a]pyrene (14)	2.64	6<1<3<12<7<5<4<10<11<9<8<2 (6<1<3<7<12<5<4<10<9<11<8<2)
benzo[e]pyrene (15)	2.87	3<1<4<9<10<2 (3<1<4<9<10<2)
anthanthrene (16)	2.51	6<1<3<5<4<2 (6<1<3<5<4<2)
coronene (17)	2.82	1 (1)
acenaphthylene (18)	2.18	1<5<4<3 (5<3<1<4)
biphenylene (19)	0.75	2<1 (2<1)
fluoranthene (20)	2.64	3<7<8<1<2 (3<1<7<8<2)
pentalene (21)	-2.02	2<1 (2<1)
azulene (22)	1.14	1<5<2<4<6 (1<4<6<5<2)
heptalene (23)	-0.89	1<3<2 (1<3<2)
s-indacene (24)	0.34	1<2<4 (4<1<2)
cyclopent[cd]azulene (25)	0.62	1<2<5<6 (5<1<2<6)
aceheptylene (26)	0.56	6<1<4<3<5 (6<3<1<4<5)
azupyrene (27)	0.99	1<4<3 (3<1<4)
calicene (28)	4.13	2<3<2' (2'<2<3)
sesquifulvalene (29)	1.73	2'<3'<2<4<3 (2'<2<3'<4<3)
cyclic bicalicene (30)	2.96	2<3<1 (1<2<3)

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monocyclic molecule is larger by the TRE of the molecule than that for the same position in the polyene reference. For this reason, any monocyclic

aromatic molecule must be less reactive toward electrophiles than its polyene reference. Relative magnitudes of the LEs in a monocyclic molecule are exactly the same as those in the polyene reference. Thus, the orientation for substitution within a monocyclic molecule is not aromaticity-dependent at all; the most reactive positions remain unchanged on going from a real molecule to the polyene reference. It follows that the ortho/para orientation in phenol (2) and the meta orientation in benzaldehyde (3) are determined solely by the connectivity of conjugated atoms.

Polycyclic benzenoid hydrocarbons 4-17 have been called polycyclic aromatic hydrocarbons (PAHs), all of which are highly aromatic with many  $(4n+2)$ -membered conjugation circuits.<sup>9-11</sup> In general, the LE for each arenium ion derived from a given PAH molecule is smaller than that for the polyene reference of the ion. Therefore, every position in a PAH molecule is less reactive than the corresponding one in the polyene reference. We can say that thermodynamically stable PAH molecules are kinetically stable. In most PAHs the most reactive positions remain unchanged on going from a real molecule to the polyene reference. Highly reactive positions in PAHs are still highly reactive even if they are deprived of aromaticity; aromaticity scarcely disturb the positional selectivity in electrophilic substitution. For example, in naphthalene (4) the 1-position is more susceptible to electrophilic attack than the 2-position. The same is true of its polyene reference, in which the 1-position is predicted to be more reactive than the 2-position. Among the PAHs studied, phenanthrene (6) may be exceptional. In this molecule the 9-position is the most reactive, whereas in the polyene reference the 1-position is the most reactive. This anomaly is associated with the fact that 1- and 9-phenanthrenium ions happen to be similar in energy .

It would seem appropriate to classify molecules **18-20** as semibenzenoid hydrocarbons because they have two or more benzene rings in addition to other rings. The main origin of aromaticity in these molecules is still six-membered conjugation circuits.<sup>10,11</sup> Positions of highest electrophilic reactivity in acenaphthylene (**18**) and biphenylene (**19**) differ from those in their respective polyene references. In **18** the most reactive 1-position is located at the olefinic CC double bond, whereas all other carbon atoms lie along the aromatic delocalization pathway. Accordingly, the LE for the 1-acenaphthylenium ion is smaller than that for any other protonated species. In contrast, the entire polyene reference of **18** is olefinic in nature, so the polyene reference of the 1-acenaphthylenium ion is no longer the lowest in energy. In **19** the four-membered ring is a main destabilization factor, but is not so in the polyene reference. This accounts for the displacement of the most reactive positions on going from **19** to its polyene reference. Fluoranthene (**20**) has marked benzenoid character as it consists of benzene and naphthalene nuclei. It has neither olefinic CC double bonds nor 4n-membered rings. A five-membered ring in **20** is a neutral factor as to aromaticity.<sup>10-12</sup> Streitwieser and coworkers determined a relative reactivity order of 3>8>7>1>2 by the nitration of **20**.<sup>13</sup> Relative magnitudes of the LEs in this molecule are fairly consistent with this experiment. As in the case of PAHs, the most reactive positions in **20** stay there in the polyene reference.

Molecules **21-30** are nonalternant nonbenzenoid hydrocarbons, in which there are no six-membered conjugation circuits. Some nonbenzenoid molecules are aromatic, and others are not.<sup>14</sup> For example, azulene (**22**) is moderately aromatic, whereas pentalene (**21**) and heptalene (**23**) are antiaromatic with negative %REs.<sup>4,5</sup> Electrophilic substitution cannot be expected for anti- or nonaromatic molecules, but these molecules would

still bond to electrophiles. The primary positions in **21-30** for bonding to an electrophile can likewise be predicted from the LEs. The LEs in **22** give the 1-position as the most reactive one. In fact, the azulene 1-position is by far the most reactive.<sup>14</sup> LEs predict that the 1-position in the polyene reference of **22** should again be the most reactive. However, this might be a coincidence. The most reactive positions in many other nonalternant hydrocarbons differ from those in their respective polyene references. For example, azupyrene (**27**) undergoes electrophilic substitution at the 1-position associated with the lowest LE,<sup>15</sup> whereas in the polyene reference the 3-position is predicted to be more reactive. Thus, aromaticity or antiaromaticity plays an important role in determining highly reactive positions in nonbenzenoid hydrocarbons.

It is interesting to see that aromaticity enhances the reactivity or kinetic instability of some nonbenzenoid hydrocarbons. One or more positions in these molecules are predicted to be more reactive toward electrophiles than the corresponding positions in their respective polyene references even if the entire molecule is moderately aromatic. An example is the 1-position in azulene (**22**). The LE for the 1-azulenium ion is slightly smaller than that for its polyene reference. This fact is particularly significant as it does not conform to our traditional view that aromaticity is a stabilizing factor for a cyclic conjugated system. Thermodynamic stability of the 1-azulenium ion arises from the highly aromatic tropylium-like substructure. Fulvalenes **28** and **29** tend to form protonated complexes containing cyclic  $(4n+2)$ - $\pi$ -electron subsystems.

Next, orientation in electrophilic substitution is analyzed in relation to local structures in a conjugated system. CC bonds in PAHs may be classified as NN, NJ, or JJ if, respectively, neither, one or both carbon atoms are at ring junctions.<sup>16</sup> Pairing of these bond types leads to a

classification of carbon atoms, of which three can carry hydrogen atoms. The larger orders for NN and NJ bond leads to an increasing sequence of free valences for nonhindered positions in PAHs as follows:<sup>16</sup> (a) non-peri (flanked by NN and NN); (b) peri (flanked by NN and NJ); and (c) peri-peri (flanked by NJ and NJ). This regularity indicates that a relatively stable arenium is formed by protonating a PAH molecule at a peri-peri or peri position. It is true that in PAH molecules the most reactive carbon atoms are located next to ring junctions.

In this context, it is noteworthy that the polyene references of all polycyclic hydrocarbons, both benzenoid and nonbenzenoid, exhibit the same regularity as to reactive positions. The polyene reference of a complex formed by attaching a proton to a peri-peri or peri carbon atom is relatively low in energy. Peri-peri carbon atoms, if any, would be chosen preferentially. Thus, positions of electrophilic attack in polyene references of polycyclic conjugated hydrocarbons are determined primarily by the connectivity of carbon atoms. On this basis, we can say that relative magnitudes of the LEs in a PAH molecule reflect those in the polyene reference straightforwardly. This is consistent with the fact that the TREs of all arenium ions derived from the same PAH are fairly similar to each other. For example, the TREs of 1-, 2-, and 9-anthracenium ions are 0.303, 0.241, and 0.383  $|\beta|$ , respectively.

The situation is different, however, for many nonbenzenoid molecules; the TREs of protonated complexes vary widely, depending on the position of protonation. For example, the TREs of 1-, 2-, 4-, 5-, and 6-azulenium ions are 0.200, 0.001, -0.380, 0.007, and -0.508  $|\beta|$ , respectively. Note that the 1-azulenium ion is highly aromatic, but that the 4- and 6-azulenium ions are highly antiaromatic. Since the LEs are highly correlative with the negatives of the TREs, such a large variation in the

TREs causes the displacement of highly reactive positions on going from a real molecule to the polyene reference. This also constitutes the reason why some positions in some nonbenzenoid aromatic hydrocarbons are more reactive than the corresponding positions in their respective polyene references. For many benzenoid and nonbenzenoid species, the preferred positions for reaction with electrophiles correspond to the arenium ions of highest aromaticity.

### Concluding Remarks

The lack of consideration of electron-repulsion effects is a major weakness of the present Hückel approach. This may lead to a poor correlation between LE values and electrophilic reactivity. The use of highly sophisticated molecular orbital (MO) methods would predict the much more reasonable orientation for substitution within a molecule. However, these MO methods are not suited for defining appropriate polyene references of aromatic molecules. Gutman proved that the polyene references adopted by us can be regarded as a kind of alternant hydrocarbons, in which  $\pi$ -electrons are uniformly distributed.<sup>17</sup> Therefore, as in the case of real PAH molecules, one does not need to worry about the effect of  $\pi$ -electron densities on the electrophilic reactivity of the polyene references. In this sense our Hückel method presumably yields reasonable LE values for all positions in the polyene references.

We previously pointed out that highly aromatic molecules in general are kinetically very stable, so are poor in chemical reactivity.<sup>6</sup> For example, naphthalene (**4**) is more reactive than benzene (**1**) and substitution is faster. Similarly, anthracene (**5**) and phenanthrene (**6**) are substituted faster than **1**. The ease of electrophilic substitution is never an

indication of higher aromaticity. This is another feature of electrophilic aromatic substitution.

### Acknowledgment

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