Orbital Phase Explanation of Regioselectivity of Organic Reactions

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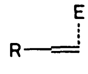
Synopsis. The regioselectivity of such fundamental organic reactions as electrophilic addition to olefins, Diels-Alder cycloaddition, and electrophilic aromatic substitution, can be explained by the phase continuity-discontinuity properties of orbitals involved in cyclic interaction for acyclic delocalization of electrons.

Electron delocalization in acyclic conjugated systems was recently found to involve cyclic interaction of orbitals of subsystems.[1] The acyclic delocalization is under control of the continuity-discontinuity property of orbital phase. The phase continuity requirement is simultaneous satisfaction of the following conditions: (i) the occupied orbitals out of phase; (ii) the vacant orbitals in phase; (iii) the occupied and vacant orbitals in phase. The concept of cyclic orbital interaction in acyclic conjugation has been applied[1–2] to explaining why cross-conjugation is thermodynamically more favorable than linear conjugation in polyanions while the thermodynamic preference is opposite for polyenes. The phase continuity-discontinuity properties of orbitals involved in acyclic delocalization have been employed to design a variety of interesting electron-localizing and delocalizing conjugated systems.[3] We show that acyclic delocalization under control of orbital phase covers the regioselectivity of fundamental organic reactions.

Addition of electrophile (E) to C=C bond (A) with electron-releasing (R) and -withdrawing (W) substituents selectively occurs at the β- and α-carbon, respectively. The transition state is considered as a system where three subsystems, R or W, A, and E interact in an acyclic manner. The electron delocalization from R to E *via* A can be expected to control the regioselectivity of the reactions. The orbitals involved in the delocalization are the occupied orbital (r) of R, the vacant orbital (e*) of E, and the bonding (a) and antibonding (a*) orbital of A. For the β- addition (**1**) the delocalization is favored by the orbital phase continuity (**2**), whereas the phase is discontinuous (**4**) for the α addition (**3**).[4] Similarly, the transition state of the electrophilic addition to W-substituted olefins is considered to be an interacting system composed of W, A, and E. The acyclic delocalization from A to W and E can be expected to



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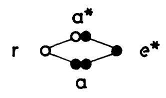

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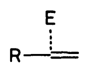

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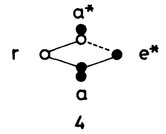

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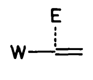

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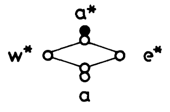

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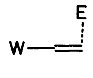

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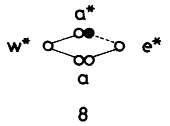

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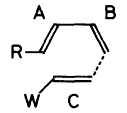

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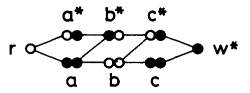

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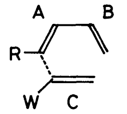

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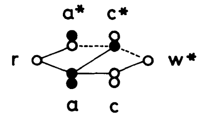

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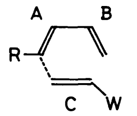

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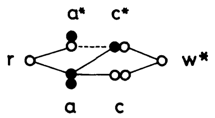

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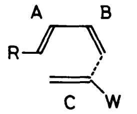

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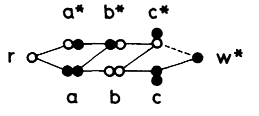

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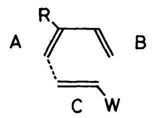

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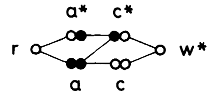

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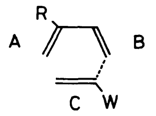

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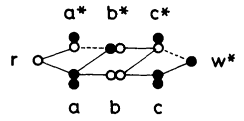

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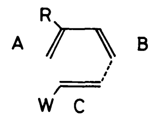

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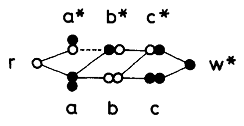

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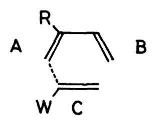

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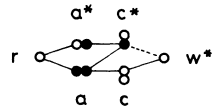

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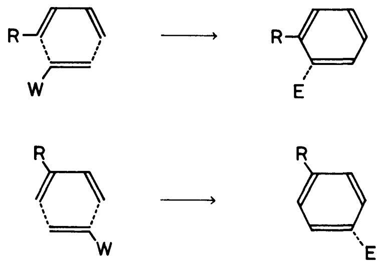
control the regioselectivity. The cyclic orbital interaction involves, a, a*, e*, and w*. The α-addition (**5**) is favored by the orbital phase continuity (**6**), the β-addition (**7**) being disfavored by the phase property (**8**).

A diene with R at a terminal carbon reacts with a W-substituted dienophile to preferentially give an "ortho"-cycloadduct. An R-substituent on an inner carbon leads to a "para"-cycloadduct. There are two pathways for the delocalization from R to W at cyclic transition state. The delocalization occurs through a long path *via* the substituted (A) and unsubstituted (B) double bonds in the diene and that (C) in the dienophile and through a short path *via* A and C. The delocalization along the long R-A-B-C-W path contains cyclic interaction among the occupied orbital (r) of R, the vacant orbital (w*) of W, the bonding (a, b, c) and antibonding (a*, b*, c*) orbitals of A, B, and C. The delocalization along the short R-A-C-W path involves the interaction among r, a, c, w*, c*, and a* orbitals. For the ortho-adduct formation from 1-R-diene the R-A-B-C-W delocalization (**9**) is favored by the orbital phase continuity (**10**), the R-A-C-W delocalization (**11**) being disfavored by the phase property (**12**). Neither is favored by phase property (**14**, **16**) for the meta-adduct formation (**13** and **15**). As a result, the orbital phase favors an acyclic delocalization path (**9**) at the transition state to the ortho-adduct.

A similar argument holds for the Diels-Alder reaction involving 2-R-diene. At the transition state to the para-product the delocalization along the R-A-C-W path (**17**) is favored by the orbital phase continuity (**18**), that along the R-A-B-C-W path (**19**) disfavored (**20**). The acyclic delocalization is disfavored (**22**, **24**) for both paths (**21** and **23**) at the transition state to the meta-cycloadduct.

The transition state model for the aromatic substitution can be formally generated from that for the Diels-Alder reactions as illustrated in Scheme. The incipient σ-bonds between diene and dienophile and π-type interaction between dienophile and W are replaced by π-type interactions in benzene and an incipient σ-bond between benzene and E. The preferential formation of ortho- and para-adducts in Diels-Alder reactions has been shown to be controlled by the acyclic delocalization. At the same qualitative level we can say that the ortho/para-orientation arises from the orbital phase properties for acyclic delocalization.



Scheme

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References

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2) a) S. Inagaki, H. Kawata, and Y. Hirabayashi, *J. Org. Chem.*, **48**, 2928 (1983); b) S. Inagaki, K. Iwase, and N. Goto, *J. Chem. Soc., Perkin Trans. 2*, in press.

3) S. Inagaki, K. Iwase, and H. Kawata, submitted for publication.

4) The neighboring orbitals which meet the phase continuity requirements are linked by solid lines, and otherwise by broken lines.