(5) R. Bonaccorsi, E. Scrocco, and J. Tomasi, *Theor. Chim. Acta*, **21**, 17 (1971).

(6) B. Levy, P. Millie, J. M. Lehn, and B. Munsch, *Theor. Chim. Acta*, **18**, 143 (1971).

(7) W. England and M. S. Gordon, *J. Am. Chem. Soc.*, **93**, 4649 (1971).

(8) E. Clementi, J. M. André, M. C. André, D. Klint, and D. Hahn, *Acta Phys. Acad. Sci. Hung.*, **27**, 493 (1969).

(9) Such a shape of the pair electrostatic potential, which was obtained without any particular stipulation on the form of the bond orbital, is in accordance with the intuitive description of a σ bond. If such a bond is thought to be described by two atomic hybrids pointing each one toward the other, there will be a larger electron density in the region between the two atoms for two reasons: (a) each atomic hybrid is projected into the internuclear region and consequently the unit positive charge placed on the nucleus becomes relatively more deshielded on the outer region around the bond axis; (b) the formation of the bond produces a further piling up of electrons in the overlap region and consequently the outer regions of the bond become even more depleted of electrons with respect to the simple summation of the two atomic hybrid distributions.

(10) For the definition of the atomic hybrid moments and for the corresponding decomposition of the molecular dipole moment into partial contributions, see, for example, C. A. Coulson "Valence", Oxford University Press, London, 1961.

(11) R. Bonaccorsi, A. Pullman, E. Scrocco, and J. Tomasi, *Chem. Phys. Lett.*, **12**, 622 (1972).

(12) R. Bonaccorsi, A. Pullman, E. Scrocco, and J. Tomasi, *Theor. Chim. Acta*, **24**, 51 (1972).

(13) G. Berthier, R. Bonaccorsi, E. Scrocco, and J. Tomasi, *Theor. Chim. Acta*, **26**, 101 (1972).

(14) The values above reported refer obviously to the summation of model pair potentials. Actual SCF calculations give the following set of minima: CH_3NH_2, −75.9; $C_2H_5NH_2$, −79.7; $(CH_3)_2NH$, −70.0; $(CH_3)_3N$, −64.3. A comparison with the experimental[15] gas phase proton affinities of these amines (in the same order), 218.4, 221.1, 224.9, 229.1 kcal/mol, shows the limits of the electrostatic approximation. Such differences between the trend of experimental PA's and V values can be explained by means of a finer description of the protonation process, including the increasing polarization energies along the set of molecules, the effects due to changes in geometry and the charge transfer contributions.

(15) D. H. Aue, H. M. Webb, and M. T. Bowers, *J. Am. Chem. Soc.*, **94**, 4726 (1972).

(16) Such an effect is also evident in "exact" SCF potential maps: the minimum results of −14.6 kcal/mol in formamide,[10] of −14.6 kcal/mol in adenine,[17] and of +2 kcal/mol in guanine.[17]

(17) R. Bonaccorsi, A. Pullman, E. Scrocco, and J. Tomasi, *Theor. Chim. Acta*, **36**, 339 (1975).

(18) P. Politzer and K. C. Daiker, *Chem. Phys. Lett.*, **34**, 294 (1975).

(19) Cancellation or conservation of such regions can depend in actual cases from the basis set. For instance, recent calculations on ethylene performed with different basis sets[20] show that a small negative in-plane region along the bisecting axis of CH_2 is present only with a minimal basis set wave function. With wave functions of higher quality a notch on the positive isopotential curves in correspondence of the axis is however still evident.

(20) J. Almlöf and A. Stogard, to be published.

(21) I. G. Csizmadia, C. Ghio, and J. Tomasi, unpublished results.

(22) B. H. Solka, A. Y. K. Lau, and A. G. Harrison, *Can. J. Chem.*, **52**, 1798 (1974).

(23) One could object that such comparison is not valid because V_{min} does not have the same coordinates in the two isomers. Actually the effect due to such small difference in position is completely negligible for the present discussion: in fact at the P point, V is equal to 9.7 kcal/mol.

(24) For instance a rationalization of the mutual polarization effects could be obtained by means of a geminal description of the interacting groups.

(25) Differential electrostatic polarization can be usefully introduced, for example, in the interpretation of NMR spectra. Hydrogen exchange is too fast in formamide to permit direct application to this molecule, but in *N*-dimethylformamide there is good evidence that polarization effects due to the CHO group give a noticeable contribution to the difference of chemical shifts and of ^{13}C–H coupling constants between *cis*- and *trans*-methyl hydrogens.[26]

(26) W. T. Raines and T. A. Sutherley, *Mol. Phys.*, **18**, 129 (1970).

(27) G. Alagona, A. Pullman, E. Scrocco, and J. Tomasi, *Int. J. Pept. Protein Res.*, **5**, 201 (1973).

(28) G. Alagona, E. Scrocco, and J. Tomasi, *J. Am. Chem. Soc.*, **97**, 6976 (1975).

Orbital Mixing Rule[1]

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Abstract: The interaction among more than two molecular orbitals is considered. An orbital (ψ_{Ai}) of a system, say A, mixes into itself the other orbital (ψ_{Aj}) of A, which is originally orthogonal to ψ_{Ai}, through the interaction with ψ_{Bk} of the other system, B. The sign relation of ψ_{Ai}, ψ_{Aj}, and ψ_{Bk} in the perturbed orbital ψ_{Ai}' is definitely given by molecular orbital perturbation theory (orbital mixing rule). The rule gives rise to an important view, origin, and direction of nonequivalent orbital extension. The importance of the nonequivalency in frontier orbital extension is exemplified by electrophilic exo additions to norbornenes and related compounds, and by the syn–anti stereoselectivity in Diels–Alder reactions of 5-monosubstituted cyclopentadienes. It is also suggested that a vacant d orbital of sulfur plays a significant role in determining the stereochemical courses of the reactions where thiocarbonyl compounds and thioalkoxy derivatives of ethylene and acetylene accept nucleophilic reagents. A transannular cross σ-bond formation between proximal double bonds caused by electrophiles was explained by the rule. Furthermore, the strength and the direction of π-orbital polarization were predicted and used in interpreting the chemical behavior of π bonds.

The concept of orbital interaction has played a predominant role in the theoretical investigation of the mechanisms of chemical reactions and the electronic structures of molecules. Attention has been paid almost exclusively to interaction between a pair of orbitals. The interaction of an orbital with a second orbital necessarily involves others (orbital mixing), appreciably in some cases. The orbital mixing analyses have been employed by Libit and Hoffmann,[2a] Inagaki and Fukui,[1b] Fujimoto and Hoffmann,[2b] and Imamura and Hirano[2c] to elucidate different chemical phenomena. The purpose of this paper is to clarify, in our own way, the orbital mixing rule on the basis of perturbation theory, and to shed light on the chemical phenomena of which the reasoning remains uncertain or unchallenged.

Theoretical Background

Let us concern ourselves with two orthonormal sets of orbitals between which interaction is allowed. Orbitals of one set are represented by ψ_{Ai} and ψ_{Aj}, those of the other set being represented by ψ_{Bk}. The orbital energy is denoted by ϵ, with the subscript standing for the orbital. One obtains a theoretical formulation for mixing among nondegenerate orbitals in the second-order perturbed orbital as follows (see Appendix):

$$\psi_{Ai}' = \psi_{Ai} + \frac{h_{ik}h_{jk}}{(\epsilon_{Ai} - \epsilon_{Aj})(\epsilon_{Ai} - \epsilon_{Bk})}\psi_{Aj} + \frac{h_{ik}}{\epsilon_{Ai} - \epsilon_{Bk}}\psi_{Bk} \tag{1}$$

in which the prime stands for the perturbed orbital.

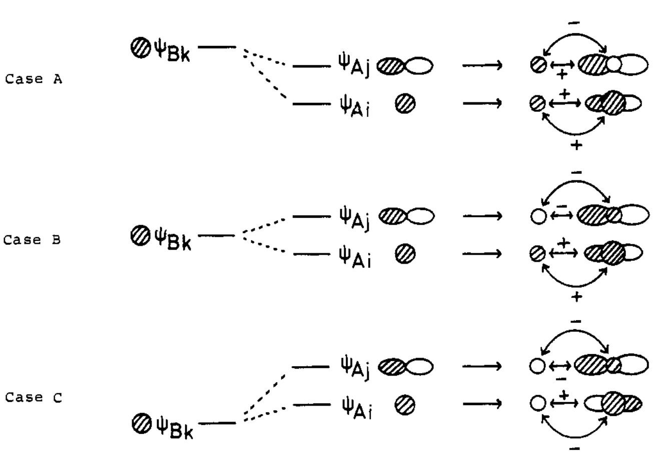


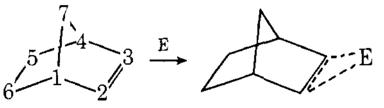
Figure 1. The sign relations upon mixing of three nondegenerate orbitals.

The sign relation among the coefficients of ψ_{Ai}, ψ_{Aj}, and ψ_{Bk} is found in eq 1 to be uniquely determined for a given system. The signs of the resonance integrals (h_{ab}'s) and the relationship of the orbital energies are important factors. One can assume without loss of generality that the signs of all basis orbitals involved, which are arbitrary in principle, are defined so that a positive overlap integral will show bonding character. This assumption is intended to avoid the confusion that negative overlap integrals imply bonding character. Then the resonance integrals (h_{ab}'s) are usually negative. Accordingly, the numerators in eq 1 have the minus sign in the first-order coefficient of ψ_{Bk} and the plus sign in the second-order coefficient of ψ_{Aj}. The signs of the denominators, $(\epsilon_{Ai} - \epsilon_{Bk})$ and $(\epsilon_{Ai} - \epsilon_{Aj})(\epsilon_{Ai} - \epsilon_{Bk})$, are readily derived from the relative energies of the orbitals. For instance, consider the modifications of the lowest lying orbital, say ψ_{Ai}, by mixing in ψ_{Aj} through the interactions of both with ψ_{Bk} ($\epsilon_{Ai} < \epsilon_{Aj}$ and ϵ_{Bk}). The coefficient of the zero-order orbital, ψ_{Ai}, is assumed to be +1. The sign of ψ_{Bk} is plus, since $h_{ik} < 0$ and $\epsilon_{Ai} - \epsilon_{Bk} < 0$. The coefficient of ψ_{Aj}, $h_{ik}h_{jk}/(\epsilon_{Ai} - \epsilon_{Aj})(\epsilon_{Ai} - \epsilon_{Bk})$, has the plus sign, since $h_{ik}h_{jk} > 0$ and the denominator is plus. In other words, ψ_{Aj} and ψ_{Bk} have the same signs. In a similar way, the sign relations in the cases of the other orbital energy relations are drawn from eq 1 and are visualized in Figure 1. Atomic orbitals are used to represent the sign relations. The arrows from the left to the right in Figure 1 connect the unperturbed orbitals, ψ_{Ai} and ψ_{Aj} (left), to the perturbed orbitals (right). The signs, + and −, denote in-phase and out-of-phase combinations, respectively. As a result, one can derive the orbital mixing rule: (1) the lowest orbital, ψ_{Ai} in case A or case B of Figure 1, is modified so that both combinations between ψ_{Ai} and ψ_{Bk} and ψ_{Bk} and ψ_{Aj} are in phase; (2) the highest orbital, ψ_{Aj} in case B or case C, mixes the others into itself so that both combinations between ψ_{Aj} and ψ_{Bk} and ψ_{Bk} and ψ_{Ai} are out of phase; (3) the orbital, ψ_{Aj} in case A or ψ_{Ai} in case C, mixes the others into itself in the opposite phase relations between ψ_{Ai} and ψ_{Bk} and ψ_{Bk} and ψ_{Aj}. The corresponding conclusions can be analogously drawn for the mixing-in of more than three-orbital systems and degenerate orbital systems.

Application and Discussion

The simple formula for orbital mixing can be used to elucidate the mechanisms of a variety of interesting chemical reactions. Most of the applications given here are concerned with intramolecular orbital mixing in the construction of the molecular orbitals of the whole molecules from the orbitals of the composite subsystems. One of the applications is to clarify the origin of the nonequivalent extension of orbitals under the influence of the conjugative entity breaking down the equivalent environments, and in turn to predict the direction. The electronic structures of plane-asymmetrically substituted olefins, predicted from the orbital mixing theory, are found to be consistent with the stereochemical behaviors within the framework of the frontier electron theory or the concept of orbital interaction.[3] Secondly, a rationale is provided for the difference in the regioselectivity of the reactions between oxygen and sulfur analogues. The discussions on the regioselectivity gave an interesting result, that is, theoretical support for the d-orbital participation of the sulfur atom. Thirdly, the direction of polarization of typical olefins by the substituents is discussed. Finally, a rationale for a transannular cross σ-bond formation between proximal double bonds caused by electrophiles is also discussed.

Origin and Direction of Nonequivalent Orbital Extension.[1,4] Exo stereoselection has been observed in the reactions of norbornene with a variety of electrophiles (eq. 2).[5-12] The rationales of the selectivity have been made, to which the solvolysis of 2-norbornyl derivatives has often contributed. Winstein et al.[6] stressed the electronic cause, characteristic of the bicyclo[2.2.1]hydrocarbon skeleton, or the C(1)-C(6) σ-bond participation stabilizing the transition state of the solvolytic reaction of the exo isomers (**1**). Brown[7] and Schleyer[8] attributed this selectivity to stereochemical features of norbornene, i.e., the steric interference by the endo hydrogens at C(5) and C(6) (**2**), and a torsional effect exerted between the bridgehead hydrogens and the neighboring olefinic hydrogens (**3**), respectively. Brown's explanation is questionable. The steric crowding in the exo region, that is, the introduction of methyl groups at the 7 position, did not change the selectivity from exo to endo in the oxymercuration[9,10] or the hydrochlorination[11] of norbornenes. The following experimental results also throw some doubt on the predominant role of Schleyer's torsional effect: (1) the reactions of 1-methylnorbornene with unsymmetrical electrophiles such as mercuric salts[9] and formic acid[12] yielded the possible isomeric exo products in about equal amounts (the torsional effect should have favored the initial attack of the electrophiles on C(2) rather than on C(3)); (2) the hydrochlorinations of 1-methylnorbornene gave the exo products in the inverted ratios of one to the other under slightly different conditions.[12] In this section, we will propose another reason for these matters on the basis of the electronic structure of norbornene predicted by the orbital mixing rule.



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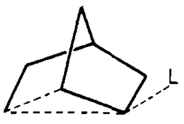

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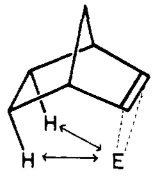

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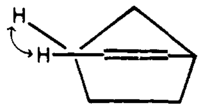


3

According to the concept of orbital interaction,[3] the charge transfer interaction involving the highest occupied molecular orbital (HOMO) is the most important in characterizing the behavior toward electrophile. A detailed description of the HOMO is indispensable in scrutinizing electrophilic reaction mechanisms. Briefly, for the present purpose, an electrophile attacks norbornene in the direction of higher HOMO electron density.

The HOMO of norbornene extends to a nonequivalent degree in the exo and endo directions. This rehybridization originates from mixing of σ orbital(s) in the ethylenic π orbital under the influence of an conjugative entity. The unperturbed π orbital is the predominant component of the norbornene

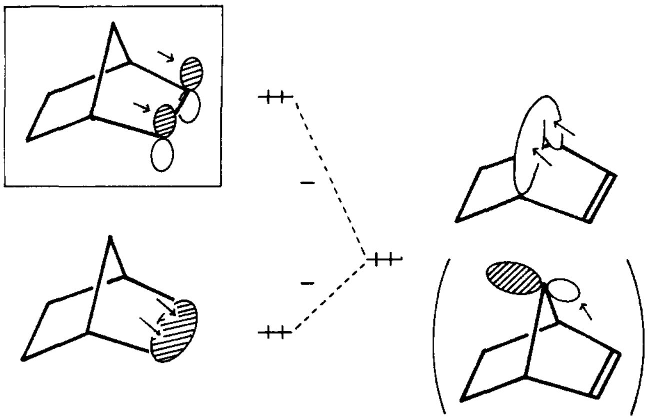


Figure 2. Origin and direction of nonequivalent HOMO extension of norbornene.

HOMO. The σ orbital mixed in order to cause the rehybridization is on the C(2)-C(3) bond. The question is whether the interaction of the π orbital occurs preferentially in the exo direction or in the endo direction. The extended Hückel[13] and CNDO/2[14] MO calculations on the assumed structure constructed by hybridizing norbornane[15] for the saturated part and norbornadiene[16] for the unsaturated part suggest two modes of significant interactions of the π orbital. One is a stronger hyperconjugation with the methano bridge than with the ethano bridge. The methano-bridge orbital is shown in Figure 2. The other important interaction is a back-side interaction with the anti C-H bond at the 7-carbon.[17] Both interactions occur at the exo side of the π orbital. We can now predict that the HOMO extends in the exo direction (see Figure 2). (In this and the following figures the rectangular frame surrounds the perturbed orbital of interest and the arrows attached to the orbital lobes show the interaction points.) The high-lying π orbital is mixed out of phase with the perturbing σ orbital(s) in the exo region and with the σ orbital on the unsaturated carbons in an out-of-phase relation to the exo σ orbital(s) (ψ_{Aj} in case B or case C of Figure 1). The prediction was confirmed by the calculated sign relation between the mixing π and σ orbitals: the s AO's of C(2) and C(3) and the pσ component of the C(2)-C(3) bond have the same signs as that of the exo lobes of the π orbital in the HOMO of norbornene. The mixing-in of the s and pσ orbitals gives rise to greater orbital overlapping or to more electron crowding in the exo region. These can be responsible for the exo electrophilic attack. In order to visualize the spatial extension of the HOMO, a contour map of the plane perpendicular to the C(1)C(2)-C(3)C(4) coplane was examined. A nonequivalent extension along the exo-endo direction is obviously discernible in Figure 3.

This explanation is similarly applicable to the exo stereoselectivity in free-radical reactions of 2-norbornyl[18,19] and 7-oxa-2-norbornyl,[19] and to the relative rate of base-catalyzed deuterium exchange of 2-norbornanones.[20]

Additional support for the direction of nonequivalent orbital extension and its relation to exo-endo stereoselectivity is available, although steric factors are possible and contribute to some degree. The π-HOMO of bicyclo[2.1.0]pentene is predicted to extend in the exo direction. The role of the methano bridge (and the anti C(7)-H bond) in norbornene is considered in this case to be replaced by that of the bridging σ bond of the bicyclopentene bent in the exo direction. The prediction is also confirmed by the contour map depicted in the plane perpendicular to the C(1)C(2)C(3)C(4) coplane (Figure 3). The electron density is calculated by the extended Hückel method.[13] The calculation was carried out on the molecular structure determined by microwave spectra.[21] The electronic

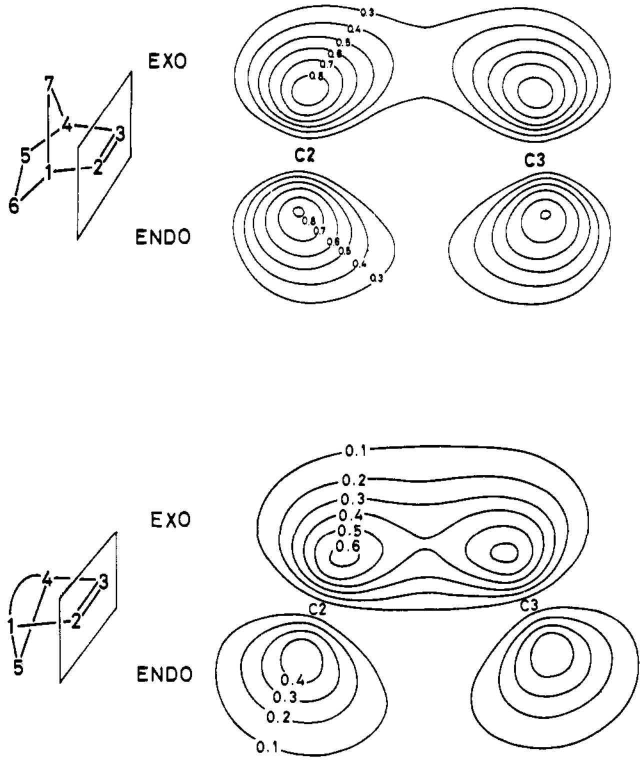
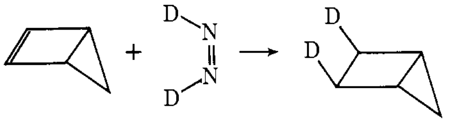


Figure 3. The HOMO electron density distributions of norbornene and bicyclo[2.1.0]pentene.

feature is consistent with the direction of attack of diimide,[22] which is an electrophilic reagent (eq 3).[23] The similar role of the bent bond was observed in electrophilic additions to bicyclo[3.1.0]hexene (eq 4).[24] The stereochemistry of the methanolysis products from 4-bicyclo[3.1.0]hexenyl trifluoroacetate



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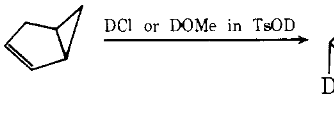

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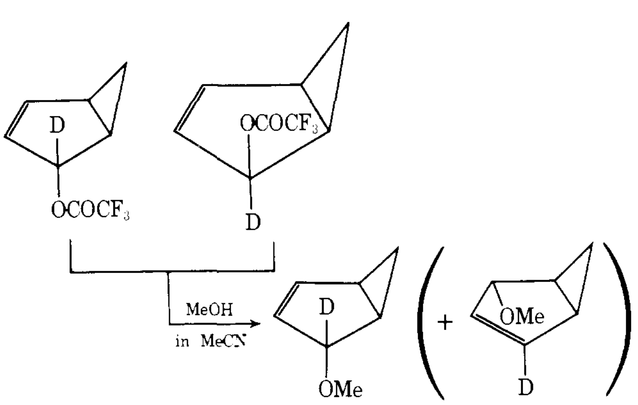


(5)

(eq 5)[25] is also explained by the nonequivalent LUMO extension of the allyl moiety.

Syn-anti isomerism in the Diels-Alder reaction (eq 6) can also be discussed in terms of nonequivalent extension of a frontier orbital. Recently, Williamson and his co-workers systematically investigated an aspect of syn-anti stereoselec-

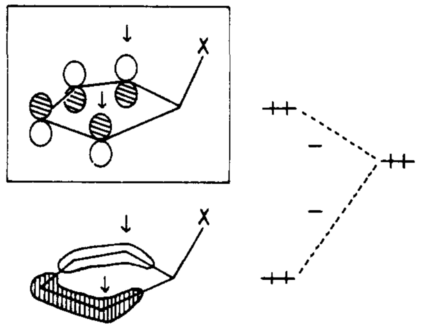
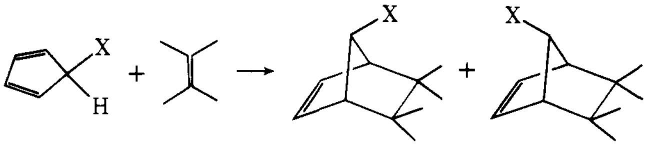


Figure 4. Origin and direction of nonequivalent HOMO extension of 5-substituted cyclopentadienes.

tivity in the cycloadditions of 1,2,3,4,5-pentachlorocyclopentadiene with a variety of dienophiles and demonstrated that the bond formation occurs preferentially at the sterically



(6)

hindered side syn to the 5-chlorine atom.[26] The similar stereoselectivity was also observed in the reaction of ethylene with 5-acetoxycyclopentadiene.[27] On the other hand, the reaction of 5-methylcyclopentadiene with *N*-phenylmaleimide yields both *syn*- and *anti*-methylnorbornenes in about equal amounts.[28]

The dienes favoring the syn orientation bear lone-pair electrons on the 5-substituent. The nonbonding orbital breaks down the symmetry with respect to the molecular plane to a considerable degree. The π-HOMO of the dienes is perturbed only by the nonbonding orbital antisymmetric with respect to reflection in the mirror plane passing through C(5), since the π-HOMO is antisymmetric. The perturbation allows low-lying σ orbitals of the carbon skeleton to mix into the π-HOMO. According to the orbital mixing rule, the π-HOMO combining with the n-orbital out of phase mixes the σ-orbital in such a way that the n-orbital and the σ-orbital are out of phase (Figure 4). It is predicted in Figure 4 that the HOMO of the dienes with an antisymmetrical lone-pair orbital in the 5-substituent extends in the direction of the substituent. In the case of the methyl substituent, the perturbation of the π-HOMO is small, since the energy of the methyl C–H bond orbital lies too low to interact with the π-HOMO as efficiently as the n orbital.

The semiempirical SCF calculations[29] unquestionably show that the HOMO electron cloud of 5-chlorocyclopentadiene is seriously biased in the region syn to Cl, while in the HOMO of 5-methylcyclopentadiene, such deviation of the HOMO electron distribution is small (Figure 5).[30] The HOMO electron density contours were depicted in the plane vertical to the molecular plane. One can say, the syn attack of the electron-accepting dienophile is favored by the nonequivalent extension of the HOMO of dienes. This conclusion is consistent with the reluctance of styrene and propylene to syn attack on 1,2,3,4,5-pentachlorocyclopentadiene[26a] and with the increased probability of syn attack in the presence of aluminum chloride.[26b] These phenomena reflect the poor capacity of styrene and propylene to accept electrons and the enhanced electron affinity of the dienophiles by the complex formation with the Lewis acid, slighting and esteeming the nature of the HOMO of the diene, respectively.[31]

Theoretical Support for d-Orbital Participation of Sulfur. Participation of d orbitals of the second-row elements has been an enduring problem. No unequivocal evidence for d-orbital

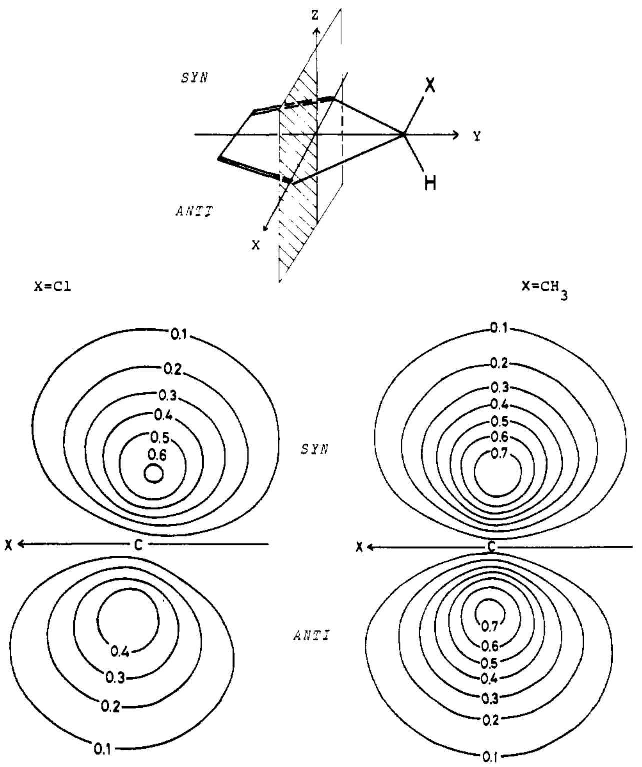
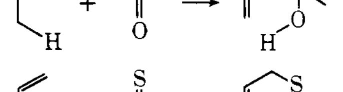
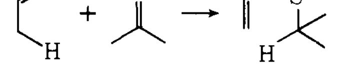


Figure 5. The HOMO electron density distributions of 5-chloro- and 5-methylcyclopentadiene.

participation has been offered thus far. The authors have met with this problem during the work on thermal 2 + 2 cycloaddition reactions and ene reactions.[32] In a previous paper[32] it was concluded that ene reactions, as well as 2 + 2 cycloadditions of electron-accepting heteronuclear unsaturated bonds with olefins, begin with the three-centered interaction involving two nucleophilic donor atoms and a more electrophilic atom of heteronuclear acceptors. The intermolecular arrangement is most stabilized by the interaction between the HOMO of the olefins and the LUMO of the acceptor. The conclusion is consistent with the observed orientation in ene reactions of carbonyl compounds; the bond formation with olefinic carbon takes place exclusively at the carbonyl carbon with the larger LUMO amplitude (eq 7a).[32] A thiocarbonyl compound, perfluorothioacetone, was surprisingly reported to form a bond with olefins at the sulfur atom (eq 7b).[33] Thiocarbonyl groups have been reported to undergo nucleophilic attacks of organometallic compounds at the sulfur atom (8),[34] in contrast with the oxygen analogues.



(7a)



(7b)

$$\mathrm{Ph_2C{=}S + RMgX \longrightarrow\longrightarrow Ph_2CH_2SR} \qquad (8a)$$

$$\mathrm{R_2C{=}C{=}S + RLi \longrightarrow\longrightarrow R_2C{=}CHSR} \qquad (8b)$$

Orbital energies of the p AO's of our present interest were estimated to decrease in the order of C, S, and O.[35,36] The π MO's of carbonyl and thiocarbonyl, obtained on the basis of the above order, have similar features in the orbital amplitude or larger AO coefficients at the carbon in the π LUMO and the heteroatom in the π HOMO. This suggests that nucleophilic attack occurs preferentially on the carbon of either group. This is inconsistent with the observed orientations. The contradiction between the theoretical prediction and the ex-

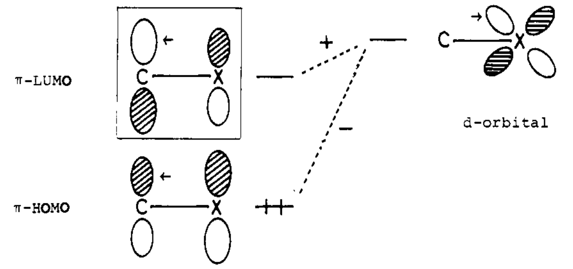
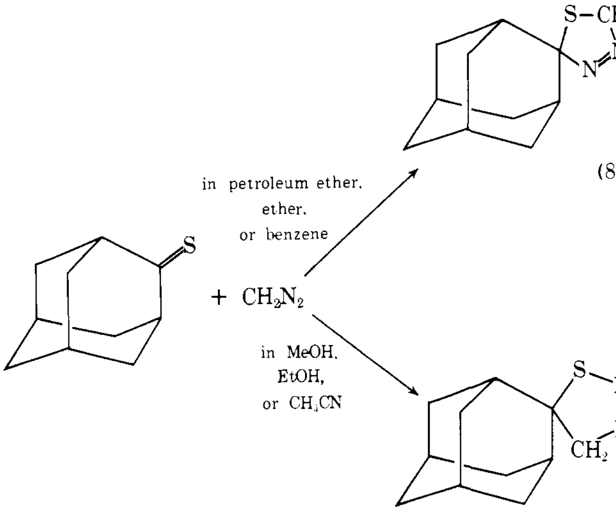


Figure 6. Mixing of a π HOMO into a π LUMO through sulfur d orbitals in thiocarbonyl, giving an AO coefficient ratio reverse to that in the LUMO of the carbonyl group.

perimental results disappears with d-orbital participation of sulfur. If the LUMO of thiocarbonyl is composed mainly of the sulfur d orbital, it is reasonable that nucleophiles should form a bond with the sulfur atom. However, this assumption may not be appropriate. We are interested in the property of the LUMO for the case where the d orbital mixes itself to the LUMO to a lesser, but appreciable degree. This situation is conveniently represented by the case in which the d orbital lies higher than the π LUMO (Figure 6). According to the orbital mixing rule, the π LUMO is combined with the d orbital in phase; the p-orbital component on the carbon and the d orbital may have the same signs at the interacting lobes. In turn, the π HOMO mixes itself into the π LUMO through interaction with the d orbital. The sign of the π HOMO is opposite to that of the d orbital at the interacting carbon p-orbital lobe. The sign relation between the π HOMO and the π LUMO suggests that the π LUMO may be modified by the d-orbital participation in order to have a larger coefficient at the sulfur of thiocarbonyl, since the π HOMO to be mixed into the π LUMO has the same signs at the sulfur atom and the opposite signs at the carbon.

Interestingly, the regioselection in 1,3-dipolar cycloadditions of diazomethane to a thiocarbonyl compound has been reported to change from one to the other under the influence of solvents.[37] In petroleum ether, ether, or benzene as solvents, the orientation is compatible with that of the aforementioned reactions (eq 7b, 8a, and 8b); the nucleophilic carbon of diazomethane is preferentially combined with the thiocarbonyl sulfur atom (eq 8c). In contrast, the reverse orientation is preferred in such solvents as ethanol, methanol, or acrylonitrile (eq 8d). It is believed that the stereochemical difference is due to the occupation of the reactive sulfur atom by active lone-pair electrons of ethanol, methanol, or acrylonitrile prior to the attack of the diazomethane.



(8c)

(8d)

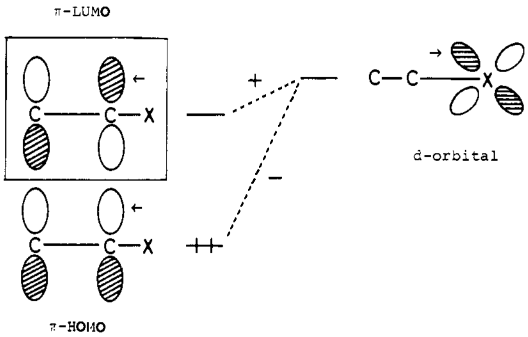
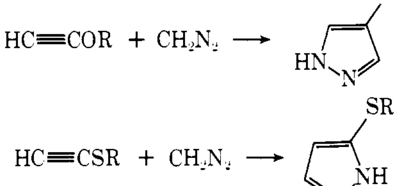


Figure 7. Mixing of a π HOMO into a π LUMO through sulfur d orbitals in thioalkoxy derivatives of ethylene and acetylene, which gives a large AO coefficient at the β carbon in the LUMO.

The vacant d-orbital effect of sulfur may be responsible for the opposite regioselections in the 1,3-dipolar cycloaddition reactions of alkoxy and thioalkoxy derivatives of acetylene with diazomethane (eq 9a and 9b).[38] It has theoretically been proposed that the bond formation in 1,3-dipolar cycloadditions take place in such a way that the atom of the larger AO coefficient of the donor HOMO combines with that of the larger AO coefficient of the acceptor LUMO.[39] Diazomethane, the electron-donating partner in 1,3-dipolar cycloaddition reactions,[40] has larger HOMO amplitude at the carbon. The LUMO of alkoxyacetylene has a larger AO coefficient on the α carbon because of the influence of the oxygen lone-pair electrons (this is inferred from the orbital mixing rule). Accordingly, the regioselectivity with alkoxyacetylene is consistent with the present knowledge. The similar property of the LUMO of thioalkoxyacetylene can be concluded as long as only the effect of the sulfur lone-pair electrons on π-orbital polarization is taken into account. The perturbation of the π LUMO by a vacant d orbital, but not by the n orbital, gives rise to the LUMO of thioalkoxyacetylene compatible with the regioselectivity. The LUMO is constructed by first mixing the vacant d orbital in phase with the π LUMO and then by mixing the π HOMO out of phase with the d orbital (Figure 7). It is suggested here that the LUMO of thioalkoxyacetylene has the larger molecular orbital amplitudes at the β carbon. This explains the contrasted regioselectivity of the sulfur analogue.



(9a)

(9b)

Such a d-orbital participation is compatible with the β attack of the anionic hydrocarbon groups of organolithium compounds to vinyl sulfides (eq 10).[41]

$$\mathrm{PhSCH{=}CH_2 + RLi \longrightarrow PhSCHLi{-}CH_2R} \qquad (10a)$$

$$\mathrm{EtSCH{=}CH_2 + RLi \longrightarrow EtSCHLi{-}CH_2R} \qquad (10b)$$

Direction of Polarization and Chemical Properties of Ethylene Derivatives. Recently Libit and Hoffmann[2a] examined the substituent effect on π-electron distribution of olefins and aromatics. The polarization effect can be used to interpret the familiar facts that the addition of hydrogen halide to alkylethylenes and butadiene occurs according to Markownikoff's rule, while that to acrylic acid occurs in the anti-Markownikoff manner.[42] The HOMO electron distribution has a maximum at the β carbon of alkylethylenes, at the terminal carbon of butadiene, and at the α carbon of acrylic acid. The key factor

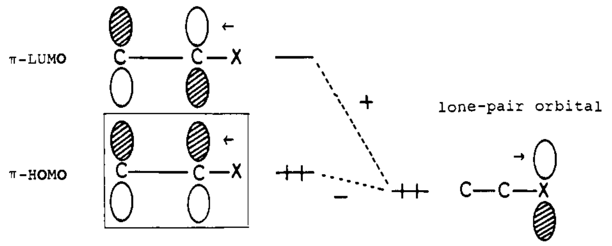
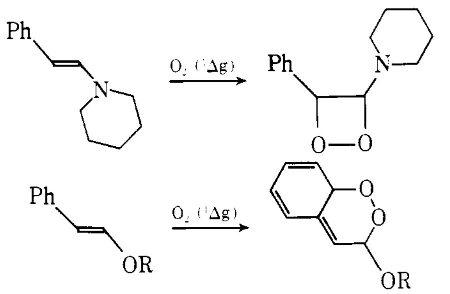


Figure 8. Mixing of a π-LUMO into a π-HOMO through a lone-pair orbital which gives a large AO coefficient at the β carbon in the HOMO

determining the direction of polarization is the relative energy of the perturbing orbital of the substituent group. The HOMO electron density of ethylenic compounds is concentrated on the β carbon when the perturbing orbital lies at equal (the π HOMO of the other ethylenic moiety in butadiene) or lower (C-CH$_3$ σ orbital in alkylethylene) energy levels. The case is reversed with the high-lying orbitals (the π LUMO of the carboxylic group in acrylic acid). The above discussions are based on the orbital mixing rule.

The polarization effect on the ethylenic π orbital is applicable to a recent interesting observation; see the pair of reactions in eq 11.[43] The difference in the course of the reaction is



(11a)

(11b)

attributable to the strength of the polarization by the substituents. The lone-pair orbitals of nitrogen and oxygen presumably lie between the energy levels of the σ CH in propylene and the perturbing ethylenic π orbital in butadiene. Accordingly, the n orbitals are expected to concentrate the HOMO electron density on the β carbon, with respect to its own position, or on the α carbon of the styrene derivative of interest. However, the perturbation by the phenyl π orbitals leads to the opposite trend, concentrating it on the β carbon of styrene. The n orbital of nitrogen, higher in energy than that of oxygen, is likely to polarize the ethylenic π orbital appreciably more, overcoming the effect of the phenyl ring. The mechanism of the polarization by the n orbital is schematically represented in Figure 8. The degree of polarization is seen in the denominator of eq 1 to depend on the energy separation between the π HOMO and the n orbital.

The present authors have pointed out previously that the 2 + 2 cycloaddition reactions and ene reactions between donor and acceptor begin with a three-centered interaction among the nucleophilic atoms of the donors and an electrophilic atom of the acceptors.[32,44] The model holds for a slightly polar π bond of the donors. In the case of the amino substituent, the transient three-membered ring structure may collapse at an earlier stage of the reaction; the oxygen atom attacking the olefinic π bond tends preferentially to come to the α carbon of styrene with the higher HOMO electron density. It follows that the 4 + 2 cycloaddition reaction invoving the β carbon of styrene is disfavored in the enamine.

Transannular Cross-Bond Formation. A transannular σ-bond formation between proximal double bonds (eq 12) has recently been reported[45-48] to take place on attacks by an electrophile, and subsequently by a nucleophile. These reactions proceed by cross bonding.

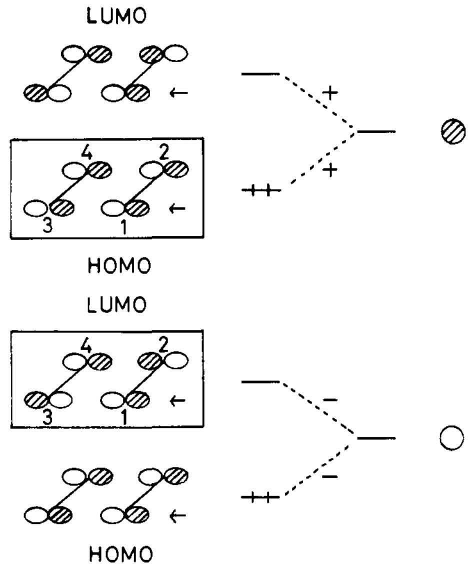
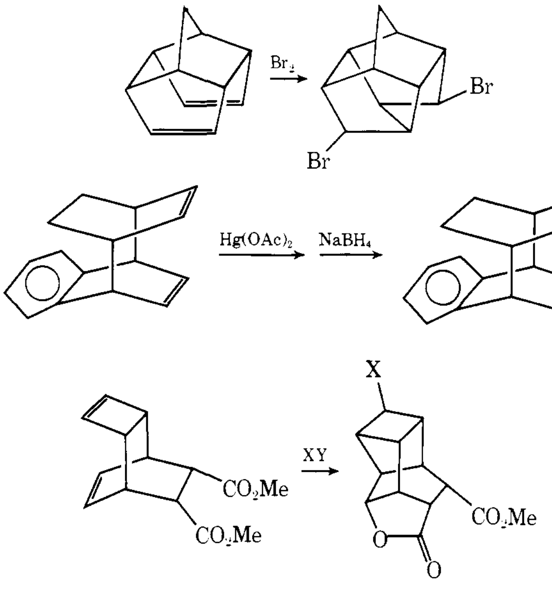


Figure 9. Mixing of a π HOMO and a π LUMO of a double-bond system into each other through the LUMO of an electrophile.

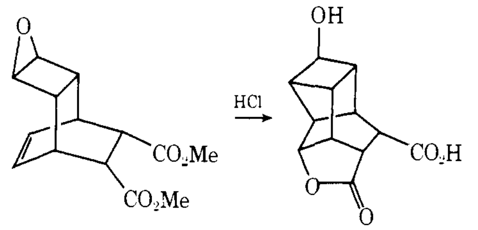


(12a)

(12b)

(12c)

An electronic factor of the cross linkage between the double bonds is given by the orbital mixing rule. The modifications of the HOMO and LUMO of the double-bond system interacting with the LUMO of electrophiles are depicted in Figure 9. The original HOMO of the double-bond system has in-phase relations between the p AO's on the carbons linked by the π bonds and out-of-phase relations between the double bonds. The HOMO electrons contribute to the repulsion between the double bonds. When an electrophile approaches a terminus of a double bond, say C(1), the LUMO of the double-bond system is mixed in the HOMO through the interaction with the LUMO of electrophiles. According to the orbital mixing rule, the signs of the HOMO and the LUMO coefficients at C(1) are the same (Figure 9). The modified HOMO has larger amplitudes at C(1) and C(4) and smaller amplitudes at C(2) and C(3) (Figure 9). As a result, the anti-bonding property in the HOMO decreases between C(2) and C(3) and increases between C(1) and C(4). This is partially the reason that cross linkage occurs. The modified LUMO of the double-bond system is similarly shown by the orbital mixing rule to have larger amplitudes at C(1) and C(4). It follows that the attack of a nucleophilic entity occurs preferentially at C(4) rather than at C(3). The change of the HOMO and the LUMO of the double-bond system by an attacking electrophile is clearly shown to favor the cross bonding. A related reaction accompanied by the ring opening of epoxide under the influence of acids (eq 13)[49] is similarly explained.



(13)

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Appendix

Consider a molecule A subjected to the effect of an outer field due to an approaching molecule B. Let the MO's of A and B be $\psi_{\mathrm{A}i}$ and $\psi_{\mathrm{B}k}$ and their energies $\epsilon_{\mathrm{A}i}$ and $\epsilon_{\mathrm{B}k}$. The one-electron Hamiltonian of the total system is h, and h_{A}' is the change of the one-electron Hamiltonian of molecule A due to the approach of molecule B, h_{B}' being the analogous quantity for molecule B. The following integrals are defined for constructing the perturbed secular determinant.[50]

$$s_{ik} = \int \psi_{\mathrm{A}i}\psi_{\mathrm{B}k}\,\mathrm{d}v$$

$$h_{ik} = \int \psi_{\mathrm{A}i} h \psi_{\mathrm{B}k}\,\mathrm{d}v$$

$$h_{ij}' = \int \psi_{\mathrm{A}i} h_{\mathrm{A}}' \psi_{\mathrm{A}j}\,\mathrm{d}v$$

$$h_{kl}' = \int \psi_{\mathrm{B}k} h_{\mathrm{B}}' \psi_{\mathrm{B}l}\,\mathrm{d}v$$

On solving the perturbed secular equation, the perturbed MO's and their energies of A are obtained as

$$\begin{aligned}\psi_{\mathrm{A}i}' = {} & \left\{1 - \sum_{k}^{\mathrm{B}} \frac{s_{ik}(h_{ik} - s_{ik}\epsilon_{\mathrm{A}i})}{\epsilon_{\mathrm{A}i} - \epsilon_{\mathrm{B}k}} - \frac{1}{2}\sum_{k}^{\mathrm{B}} \frac{(h_{ik} - s_{ik}\epsilon_{\mathrm{A}i})^2}{(\epsilon_{\mathrm{A}i} - \epsilon_{\mathrm{B}k})^2} \right.\\ & \left. - \frac{1}{2}\sum_{j(\neq i)}^{\mathrm{A}} \frac{h_{ij}'^2}{(\epsilon_{\mathrm{A}i} - \epsilon_{\mathrm{A}j})^2}\right\}\psi_{\mathrm{A}i} + \sum_{j(\neq i)}^{\mathrm{A}} \left\{\frac{h_{ij}'}{\epsilon_{\mathrm{A}i} - \epsilon_{\mathrm{A}j}} \right.\\ & \left. + \sum_{k}^{\mathrm{B}} \frac{(h_{ik} - s_{ik}\epsilon_{\mathrm{A}i})(h_{jk} - s_{jk}\epsilon_{\mathrm{A}i})}{(\epsilon_{\mathrm{A}i} - \epsilon_{\mathrm{A}j})(\epsilon_{\mathrm{A}i} - \epsilon_{\mathrm{B}k})} - \frac{h_{ij}'(h_{ii}' - h_{jj}')}{(\epsilon_{\mathrm{A}i} - \epsilon_{\mathrm{A}j})^2}\right\}\psi_{\mathrm{A}j}\\ & + \sum_{k}^{\mathrm{B}} \left\{\frac{h_{ik} - s_{ik}\epsilon_{\mathrm{A}i}}{\epsilon_{\mathrm{A}i} - \epsilon_{\mathrm{B}k}} + \sum_{j(\neq i)}^{\mathrm{A}} \frac{h_{ij}'(h_{jk} - s_{jk}\epsilon_{\mathrm{A}i})}{(\epsilon_{\mathrm{A}i} - \epsilon_{\mathrm{A}j})(\epsilon_{\mathrm{A}i} - \epsilon_{\mathrm{B}k})} \right.\\ & - \frac{s_{ik}h_{ii}'}{\epsilon_{\mathrm{A}i} - \epsilon_{\mathrm{B}k}} + \sum_{l(\neq k)}^{\mathrm{B}} \frac{h_{kl}'(h_{il} - s_{il}\epsilon_{\mathrm{A}i})}{(\epsilon_{\mathrm{A}i} - \epsilon_{\mathrm{B}k})(\epsilon_{\mathrm{A}i} - \epsilon_{\mathrm{B}l})}\\ & \left. - \frac{(h_{ik} - s_{ik}\epsilon_{\mathrm{A}i})(h_{ii}' - h_{kk}')}{(\epsilon_{\mathrm{A}i} - \epsilon_{\mathrm{B}k})^2}\right\}\psi_{\mathrm{B}k} + 0(\Delta^3) \qquad \text{(A-1)}\end{aligned}$$

and

$$\begin{aligned}\epsilon_{\mathrm{A}i}' = {} & \epsilon_{\mathrm{A}i} + h_{ii}' + \sum_{k}^{\mathrm{B}} \frac{(h_{ik} - s_{ik}\epsilon_{\mathrm{A}i})^2}{\epsilon_{\mathrm{A}i} - \epsilon_{\mathrm{B}k}} + \sum_{j(\neq i)}^{\mathrm{A}} \frac{h_{ij}'^2}{\epsilon_{\mathrm{A}i} - \epsilon_{\mathrm{A}j}}\\ & + 2\sum_{\substack{j<m\\(j,m\neq i)}}^{\mathrm{A}} \frac{h_{ij}'h_{im}'h_{jm}'}{(\epsilon_{\mathrm{A}i} - \epsilon_{\mathrm{A}j})(\epsilon_{\mathrm{A}i} - \epsilon_{\mathrm{A}m})}\\ & + 2\sum_{j(\neq i)}^{\mathrm{A}}\sum_{k}^{\mathrm{B}} \frac{h_{ij}'(h_{ik} - s_{ik}\epsilon_{\mathrm{A}i})(h_{jk} - s_{jk}\epsilon_{\mathrm{A}i})}{(\epsilon_{\mathrm{A}i} - \epsilon_{\mathrm{A}j})(\epsilon_{\mathrm{A}i} - \epsilon_{\mathrm{B}k})}\\ & + 2\sum_{k<l}^{\mathrm{B}} \frac{h_{kl}'(h_{ik} - s_{ik}\epsilon_{\mathrm{A}i})(h_{il} - s_{il}\epsilon_{\mathrm{A}i})}{(\epsilon_{\mathrm{A}i} - \epsilon_{\mathrm{B}k})(\epsilon_{\mathrm{A}i} - \epsilon_{\mathrm{B}l})}\\ & - 2\sum_{k}^{\mathrm{B}} \frac{s_{ik}h_{ii}'(h_{ik} - s_{ik}\epsilon_{\mathrm{A}i})}{\epsilon_{\mathrm{A}i} - \epsilon_{\mathrm{B}k}} - \sum_{j(\neq i)}^{\mathrm{A}} \frac{h_{ij}'^2(h_{ii}' - h_{jj}')}{(\epsilon_{\mathrm{A}i} - \epsilon_{\mathrm{A}j})^2}\\ & - \sum_{k}^{\mathrm{B}} \frac{(h_{ii}' - h_{kk}')(h_{ik} - s_{ik}\epsilon_{\mathrm{A}i})^2}{(\epsilon_{\mathrm{A}i} - \epsilon_{\mathrm{B}k})^2} + 0(\Delta^4) \qquad \text{(A-2)}\end{aligned}$$

where Δ signifies the first-order quantities like s_{ik}, h_{ik}, h_{ij}', h_{kl}', and so on, and $0(\Delta^3)$ implies a small quantity of order Δ^3.[50]

An important consequence of these equations may be the rule of intramolecular orbital mixing by the orbitals of a different molecule, which is given by the coefficient of $\psi_{\mathrm{A}j}$ in $\psi_{\mathrm{A}i}'$. This is written as

$$\frac{h_{ij}'}{\epsilon_{\mathrm{A}i} - \epsilon_{\mathrm{A}j}} + \sum_{k}^{\mathrm{B}} \frac{(h_{ik} - s_{ik}\epsilon_{\mathrm{A}i})(h_{jk} - s_{jk}\epsilon_{\mathrm{A}i})}{(\epsilon_{\mathrm{A}i} - \epsilon_{\mathrm{A}j})(\epsilon_{\mathrm{A}i} - \epsilon_{\mathrm{B}k})} \qquad \text{(A-3)}$$

if we neglect the remaining terms as less important than these two. The first term originates from the "static" effect of the field of molecule B upon the Hamiltonian for molecule A, while the second is caused by the "dynamic" effect of the orbitals of the second molecule.[2c] Both constitute the effect of polarization of molecule A.

Next, we take only the direct, "dynamic" orbital effect among three orbitals, $\psi_{\mathrm{A}i}$, $\psi_{\mathrm{A}j}$, and $\psi_{\mathrm{B}k}$, into account, and consider the phase relation in the perturbed orbital $\psi_{\mathrm{A}i}'$ represented by eq 1 in the text, where the overlap integrals are neglected as small.

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charge transfer from the n orbital on the 5-substituent to the LUMO of the dienophile. However, this mode of nonbonded interaction may occur at the cost of more significant interaction between the π HOMO of the diene and the π LUMO of the dienophile indispensable to the cycloaddition. The HOMO of the cyclopentadiene with an n orbital at the 5 position is out-of-phase combination of the π HOMO and the n orbital. Accordingly, if the nonbonded attraction occurs effectively, or if the LUMO of dienophile is in-phase combined with the n-orbital component of the HOMO, the antibonding nature appears between the π HOMO component of diene and the LUMO of dienophile. This suggests that the nonbonded attraction of the n orbital with the reaction center of the dienophile disfavors the leading interaction in the Diels-Alder reactions.

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Molecular Orbital Studies of the Protonation of the Methylanisoles

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Abstract: Application of the STO-3G method to the energetics of protonation of the ambident methylanisoles shows the predominance of ring protonation for all three isomers. The method further indicates that oxygen protonation is only competitive for the para isomer. Comparison of these results with those for the methylphenols allows prediction of differences between the hydroxy and methoxy substituents in a typical system, and the predictions are in close accord with experimentally well known trends.

We report herewith a study of the site of protonation of the methylanisoles using the STO-3G method.[1] The methylanisoles are of special interest as a test of theory because the site of protonation experimentally is not always the same as in the corresponding methylphenols. We have previously performed similar calculations on the methylphenols using both the STO-3G and INDO programs.[2] The ab initio results for the methylphenols correctly predicted the order of stability of the neutral compounds and also the favored protonation sites. The INDO method failed to yield results concordant with experiment for either the neutral methylphenols or the protonated forms of these compounds. In light of these shortcomings of the semiempirical method, we have elected to perform only STO-3G calculations in the present study.

The geometries used for the neutral methylanisoles are shown in Figure 1. The aromatic ring was constructed from standard model geometries.[3] Since results on the methylphenols agree with experiment and those on proton affinity differences of alkylbenzenes are within 600 cal mol^{-1} of observed differences,[4] we assume that the standard model geometry is a reliable guide for the study of these compounds. We selected substituent geometries (the C-O bond lengths and the angle β) on the basis of INDO energy minimization, the agreement between INDO results[5] and STO-3G results[6] for bond lengths in hydrocarbon ions being within 0.01 to 0.02 Å. The same standard substituent bond lengths and angles were used for all three isomers.

Figure 2 represents the geometries used for the ring-protonated methylanisoles. The ring structure is based upon the model for protonated benzene reported by Hehre et al.,[4] with the exception noted in ref 7. The substituent geometries are the same as for the neutrals and are constant for all protonated forms.

The geometries for the oxygen-protonated forms are illustrated in Figure 3. The aromatic ring is assumed to have the same model geometry as the neutral compounds. The substituent geometries were again chosen on the basis of INDO energy minimization. Unlike the methylphenols,[2] there was