BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN VOL. 42 3399—3409 (1969)

An MO-theoretical Interpretation of the Nature of Chemical Reactions. II. The Governing Principles

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(Received May 19, 1969)

The importance of the overlapping between the highest occupied (HO) molecular orbital (MO) of an electron donor and the lowest unoccupied (LU) MO of an electron acceptor in determining the favorable position and spatial direction of a chemical reaction is emphasized by setting up the following auxiliary principles: the principle of a positional parallelism between the charge-transfer and the bond-interchange, the principle of a narrowing of the inter-frontier energy-level separation, and the principle of a growing frontier density along the reaction path. These sub-principles work in a cooperative manner to enable us to arrive at this general governing principle: most of the chemical interactions are liable to occur at the position and in the direction where the overlapping of the HO and the LU of the respective reactants is at its maximum; in an electron-donating reactant, HO predominates in the overlapping interaction with the MO's of the other reactant, whereas LU does so in an electron-accepting reactant; in the reactants which possess singly-occupied (SO) MO's, these play the part of HO or of LU, or of both. These particular MO's, HO, LU, and SO are "generalized frontier orbitals" in chemical reactions. This principle is applied to uni-centric reactions to give the orientation rule; if it is applied to multi-centric reactions, the stereoselection rule is obtained.

Our previous paper[1] has treated, on the assumption of no nuclear configuration change, the interaction energy between two reactant systems; this energy is partitioned into the Coulomb interaction, exchange interaction, delocalization, and polarization terms. It has been shown that the Coulomb interaction and the delocalization terms are important. The former comes from the net atomic charges and dominates the long-range interaction, while the delocalization term is ascribed to the charge-transfer interaction and is dominant in the usual donor-acceptor interaction energy. The quantity D, which represents the delocalization term, plays a dominant role in determining the energy of charge-transfer interaction, serving as a measure of the reactivity.

The expression of D is analogous to the chemical reactivity indices, superdelocalizability[2] and delocalizability,[3] which were originally defined by the Hückel MO formulation. These indices were derived as being closely related to the frontier electron density. The interrelation of theseq uantities is worth discussing.

In the present paper, we will attempt to investigate the essential features of the charge-transfer interaction in connection with the change in nuclear configuration along the reaction path. It may be permitted to discuss such a problem in the framework of the Born-Oppenheimer approximation. The auxiliary principles which characterize the mode of change will be sought in order to derive the fundamental orientation rule and, at the same time, to disclose the relation between the orientation rule and the reactivity indices.

The Delocalization Term in Degenerate Cases

The delocalization term comes from the mixing of the charge-transfer states into the initial state in an adiabatic interaction of two ground-state reactant molecules. The delocalization term, D, is expressed[1] as:

$$D=\sum_{i}^{\text{occ}}\sum_{l}^{\text{uno}}\frac{|H_{0,i\to l}-S_{0,i\to l}H_{0,0}|^2}{H_{i\to l,i\to l}-H_{0,0}}+\sum_{k}^{\text{occ}}\sum_{j}^{\text{uno}}\frac{|H_{0,k\to j}-S_{0,k\to j}H_{0,0}|^2}{H_{k\to j,k\to j}-H_{0,0}} \tag{1}$$

in which the suffix 0 implies the initial configuration and in which $i\to l$ signifies the monotransferred configuration in which an electron in the ith occupied MO of the reactant A is transferred to the lth unoccupied MO of the reactant B. Similarly, k and j represent an occupied MO of B and an unoccupied MO of A respectively. The corresponding wave-functions are designated as Ψ_0, $\Psi_{i\to l}$ and $\Psi_{k\to j}$ and:

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[1] K. Fukui and H. Fujimoto, This Bulletin, **41**, 1989 (1968).

[2] K. Fukui, T. Yonezawa and C. Nagata, *ibid.*, **27**, 423 (1954).

[3] K. Fukui, H. Kato and T. Yonezawa, *ibid.*, **34**, 1111 (1961).

$$H_{p,q} = \int \Psi_p{}^* H \Psi_q \mathrm{d}\tau \qquad (2)$$

$$S_{p,q} = \int \Psi_p{}^* \Psi_q \mathrm{d}\tau \qquad (3)$$

It is assumed, as has been done in our previous paper,[1] that the wave-function for a certain electron configuration, Ψ_p, of the total system composed of interacting reactants, A and B, is represented by an antisymmetrized product of the MO's of the two reactants, constructed so as to correspond to the electron configuration, in which each MO is made SCF (self-consistent-field) of the Roothaan type with respect to each *isolated* ground-state reactant molecule, taken as constructing an orthonormal set. The symbols $\sum^{\mathrm{occ}}$ and $\sum^{\mathrm{uno}}$ imply the summation over occupied and unoccupied MO's. The Hamiltonian operator, H is that of the combined system consisting of mutually-interacting A and B. For a more detailed explanation, see Ref. 1.

Equation (1) is obtained by the usual configuration interaction procedure as a second-order perturbation term, on the assumption that the interaction is still not very strong.[1] If one of the monotransferred configurations happens to have the same energy as the initial configuration, first-order perturbation term will appear. Such a case can arise in reference to the configuration in which one electron is shifted from the highest occupied (HO) molecular orbital (MO) of the donor molecule to the lowest unoccupied (LU) MO of the acceptor molecule in the case of donor-acceptor interaction. In that case the quantity D will be dominated by the first-order term:

$$D \sim |H_{0,\mathrm{HO}\to\mathrm{LU}} - S_{0,\mathrm{HO}\to\mathrm{LU}} H_{0,0}| \qquad (4)$$

This equation is obtained from Eq. (7′) of Ref. 1.

Even in a not exactly degenerate case, the monotransferred term corresponding to the one-electron transfer from the HO of the donor to the LU of the acceptor can make an overwhelming contribution to the delocalization term when the denominator of this term in Eq. (2) is sufficiently small in comparison with the other monotransferred terms.

$$D \sim \frac{|H_{0,\mathrm{HO}\to\mathrm{LU}} - S_{0,\mathrm{HO}\to\mathrm{LU}} H_{0,0}|^2}{H_{\mathrm{HO}\to\mathrm{LU},\mathrm{HO}\to\mathrm{LU}} - H_{0,0}} \qquad (5)$$

As Mulliken has already pointed out, $H_{0,\mathrm{HO}\to\mathrm{LU}}$ is approximately proportional to $S_{0,\mathrm{HO}\to\mathrm{LU}}$, so that the magnitude of D and, accordingly, the interaction (stabilization) energy can be measured in terms of the extent of orbital overlapping between HO and LU, since:

$$S_{0,\mathrm{HO}\to\mathrm{LU}} \cong \sqrt{2}\, s_{\mathrm{HO,LU}} \qquad (6)$$

where:

$$s_{\mathrm{HO,LU}} = \int a_{\mathrm{HO}}(1) b_{\mathrm{LU}}(1) \mathrm{d}v(1) \qquad (7)$$

and where a_{HO} and b_{LU} are the HO MO of A and the LU MO of B respectively, both being taken as having a real spatial part.

In this way, Eq. (5) leads to the "overlap and orientation" principle of Mulliken.[4] Equation (4) will lead to the same conclusion with regard to the orientation principle. The favorable orientation in such cases can be determined by the rule of the maximum overlapping of HO and LU. Namely, the interaction takes place at the position and in the direction in which the largest overlapping of these particular MO's is attained.

In addition, there are special circumstances which make these particular orbitals, HO and LU, discriminatively important. The importance of the interaction term between HO and LU prevails over a wider range of combination of two reactants; furthermore, it is enhanced in actually-occurring reactions if the nuclear-configuration change along the reaction path is taken into consideration. This point will be discussed on the basis of auxiliary principles later. In any event, the usefulness of the equations of the type of Eq. (4) or (5) is in fact, far more than could be expected simply from the conditions for the fitness of these equations.

The Principle of a Positional Parallelism between the Charge-transfer and the Bond-interchange

It has already been shown[5–7] that the nodal property of HO and LU MO's plays an essential role in determining the steric course of electrocyclic reactions. The same property is important in promoting the alteration of the molecular shape in the case of orbital interaction.

Usually, an atom is, as a whole, bonding with neighboring atoms in occupied MO's and antibonding in unoccupied MO's. This circumstance can be understood by a very simple example which employs the linear-combination-of-atomic-orbitals (LCAO) MO scheme. If we use the Hückel MO theory (overlap neglected) in the frame of π-electron approximation for a planar conjugated molecule, the following relation holds with respect to the rth π AO:

$$(\alpha_r - \varepsilon_i)(C_r{}^{(i)})^2 + \sum_s^{\mathrm{nei}} C_r{}^{(i)} C_s{}^{(i)} \beta_{rs} = 0 \qquad (8)$$

where α_r is the Coulomb integral of the rth AO; β_{rs}, the resonance integral between the rth and the sth AO's; ε_i, the energy of the ith MO, and $C_r{}^{(i)}$, the coefficient of the rth AO in the ith MO. The notation $\sum^{\mathrm{nei}}$ implies summation over all the neighboring AO's of the rth AO. In the case of con-

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[4] R. S. Mulliken, *Rec. Trav. Chim.*, **75**, 845 (1956).

[5] K. Fukui, "Molecular Orbitals in Chemistry, Physics, and Biology," ed. by P.-O. Löwdin and B. Pullman, Academic Press, New York (1964), p. 513.

[6] K. Fukui, This Bulletin, **39**, 498 (1966).

[7] K. Fukui and H. Fujimoto, *ibid.*, **39**, 2116 (1966).

jugated hydrocarbons, all the α_r's and all the β_{rs}'s can be put equal to constant values, α and β respectively. Then, it follows from Eq. (8) that:

$$\sum_{s}^{\mathrm{nei}} C_r^{(i)} C_s^{(i)} = \frac{\alpha-\varepsilon_i}{(-\beta)} (C_r^{(i)})^2 \qquad (9)$$

As usual, the energies of the occupied orbitals are lower than α, while those of the unoccupied orbitals are higher than α. Therefore, the following relations hold for any r: $\sum_{s}^{\mathrm{nei}} C_s^{(i)} C_t^{(i)}$ is positive and proportional to $(C_r^{(i)})^2$ for occupied MO's and is negative and proportional to $(C_r^{(i)})^2$ for unoccupied MO's.

In this way, it is established that the position of the largest HO or LU density is, at the same time, that position which is most liable to weaken the bonds with neighboring atoms in case of electron-releasing or accepting interaction respectively.[8] Namely, the charge-transfer weakens the bonds most greatly at the position of the largest frontier electron density.[5,9]

Some examples of the nodal property of the π HO's and LU's of several conjugated hydrocarbons are shown in Fig. 1, in which the shaded and unshaded areas correspond to the positive and negative regions of the MO coefficients. It can be qualitatively understood from the figure that there is a parallelism between the partial population and the partial sum of the bond-order with neighbors. Even in heteroaromatic systems similar relationships hold. We can see the circumstances in Fig. 2.

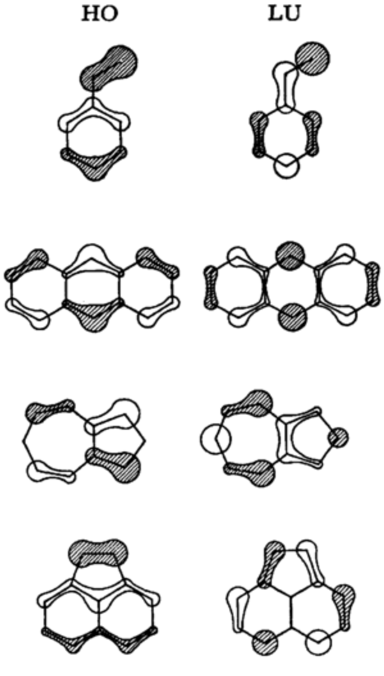

Fig. 1. The nodal property of π HO and LU of some conjugated hydrocarbons.

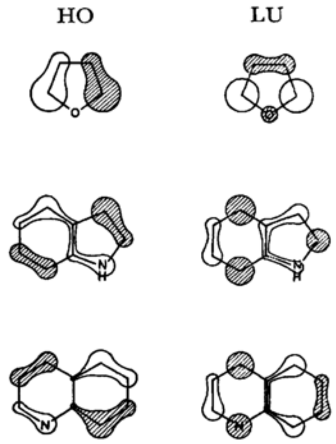

Fig. 2. The nodal property of π HO and LU of some heteroconjugated systems.

Such a character of MO's is to a certain extent perceived in more elaborate calculations, independent of the order of approximation adopted. An example is given in Table 1 using the Pariser-Parr-Pople approximation.[10] The suffix f signifies HO or LU. A distinct parallelism is recognized among the partial population and the partial sum of the bond-order with the neighbors.

Similar circumstances also exist in the extended Hückel treatment[11] of three-dimensional molecules. The orientation in the E2 reaction of halogenated hydrocarbons has previously been discussed.[12,13] If we concentrate our attention on one of the hydrogen 1s AO's, say r, the following equation is

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[8] When the HO energy happens to be higher than α, the electron-releasing will cause bond-strengthening. The result is the same with the electron-accepting in the LU MO when its energy is lower than α.

[9] The extent of this bond-loosening will, therefore, be a measure of the ease of intramolecular electron localization at the reaction center in the case of interaction with another molecule. This may be one of the reasons why the localization energy gives a parallel prediction with the frontier electron density for the chemical reactivity of a majority of conjugated molecules (*cf.* A. Streitwieser, Jr., "Molecular Orbital Theory for Organic Chemists," John Wiley & Sons, New York (1961), p. 305).

[10] See, for instance, R. Pariser and R. G. Parr, *J. Chem. Phys.*, **21**, 466, 767 (1953).

[11] R. Hoffmann, *ibid.*, **39**, 1397 (1963), and subsequent papers.

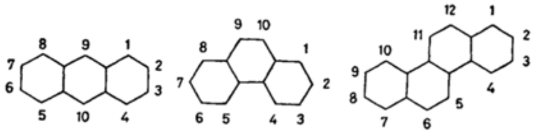
[12] K. Fukui and H. Fujimoto, *Tetrahedron Letters*, **1965**, 4303.

[13] K. Fukui, H. Hao and H. Fujimoto, This Bulletin, **42**, 348 (1969).

TABLE 1. THE POSITIONAL PARALLELISM BETWEEN $(C_r^{(f)})^2$ AND $\sum_s^{\mathrm{nei}} C_r^{(f)}C_s^{(f)}$ IN PARISER-PARR-POPLE CALCULATION

Compound	r	$(C_r^{(f)})^2$	$\sum_s^{\mathrm{nei}} C_r^{(\mathrm{HO})}C_s^{(\mathrm{HO})}$	$\sum_s^{\mathrm{nei}} C_r^{(\mathrm{LU})}C_s^{(\mathrm{LU})}$
Anthracene	1	0.09512	0.03680	−0.03680
	2	0.04770	0.01966	−0.01966
	9	0.19472	0.08745	−0.08745
Phenanthrene	1	0.10550	0.07154	−0.07154
	2	0.00100	0.00034	−0.00034
	3	0.09868	0.06598	−0.06598
	4	0.05843	0.03197	−0.03197
	9	0.16775	0.09051	−0.09051
Chrysene	1	0.07978	0.04403	−0.04403
	2	0.01427	0.00738	−0.00738
	3	0.04871	0.02809	−0.02809
	4	0.06089	0.02985	−0.02985
	5	0.05696	0.02168	−0.02168
	6	0.14446	0.07687	−0.07687

Numberings are as follows:



Anthracene Phenanthrene Chrysene

All C-C distances and all C-C-C angles were assumed to be 1.4Å and 120°, respectively, for the sake of simplicity of computations.

obtained in place of Eq. (8):

$$(h_{rr}-\varepsilon_i)(C_r^{(i)})^2+\sum_{s(\neq r)}(h_{rs}-\varepsilon_i s_{rs})C_r^{(i)}C_s^{(i)}=0 \quad (10)$$

where:

$$h_{rs}=\frac{K}{2}(h_{rr}+h_{ss})s_{rs} \quad (11)$$

where h_{rr}, h_{rs} and s_{rs} are the Coulomb, resonance, and overlap integrals respectively, and where K is the Wolfsberg-Helmholtz constant.[11] The other symbols have the same meaning as in the Hückel scheme. Although the value of the Coulomb integral varies, of course, from one AO to another, it may be possible to employ tentatively, in place of the individual h_{ss}, a sort of mean value, h, which makes the second term of the right side of Eq. (10) equal to:

$$\sum_{s(\neq r)}\left\{\frac{K}{2}(h_{rr}+h)-\varepsilon_i\right\}C_r^{(i)}C_s^{(i)}s_{rs} \quad (12)$$

Hence, it follows that:

$$\sum_{s(\neq r)}C_r^{(i)}C_s^{(i)}s_{rs}=-\frac{h_{rr}-\varepsilon_i}{\frac{K}{2}(h_{rr}+h)-\varepsilon_i}(C_r^{(i)})^2 \quad (13)$$

Then, with respect to LU, the relations $h_{rr}-\varepsilon_{\mathrm{LU}}<0$ and $(K/2)(h_{rr}+h)-\varepsilon_{\mathrm{LU}}<0$ usually hold. The left side of Eq. (13) is equal to $(1/2)v_r^{(i)}$, which is the valence-active part[14] of the partial AO population of the rth AO in the ith MO defined by:

$$v_r^{(i)}=2\sum_{(s\neq r)}C_r^{(i)}C_s^{(i)}s_{rs} \quad (14)$$

Therefore, $v_r^{(\mathrm{LU})}$ must be negative and proportional to $(C_r^{(\mathrm{LU})})^2$, indicating that the hydrogen atom having the largest frontier electron density is most liable to a loosening of the bond with the remaining part of the molecule.

This conclusion may be confirmed by actual numerical calculation in which the approximation using the mean h value is, of course, not applied. Examles are shown in Table 2. The table contains the frontier electron density $(C_r^{(\mathrm{LU})})^2$ and the valence-active part of the partial population of the frontier orbital, $v_r^{(\mathrm{LU})}$. Exemplifications by the various calculations mentioned above indicate the existence of a parallelism among actually reactive sites in a molecule; the position of the largest frontier orbital extension is at the same time the position where the bonds with neighboring atoms are, as a whole, most liable to be loosened. Since

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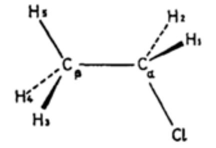
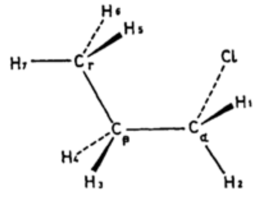
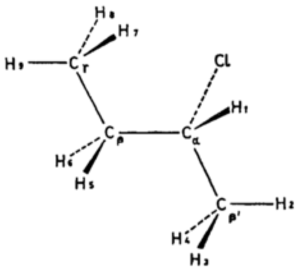
[14] K. Ruedenberg, *Rev. Mod. Phys.*, **34**, 326 (1962).

Table 2. The relation between $v_r^{(LU)}$ and $(C_r^{(LU)})^2$ of hydrogens in several halogenated paraffins

Chlorinated paraffin	r	$(C_r^{(LU)})^2$	$v_r^{(LU)}$
	1	0.01791	−0.01192
	3	0.00124	−0.00062
	5	0.05412	−0.03689
	1	0.01658	−0.01163
	2	0.03135	−0.02134
	3	0.07458	−0.05128
	4	0.00067	−0.00018
	5	0.00096	−0.00071
	6	0.01708	−0.01361
	7	0.00063	−0.00027
	1	0.00978	−0.00661
	2	0.00029	−0.00006
	3	0.06638	−0.04564
	4	0.00044	−0.00011
	5	0.07888	−0.05295
	6	0.00090	−0.00041
	7	0.00158	−0.00131
	8	0.02119	−0.01700
	9	0.00000	−0.00000

the frontier orbital extension is a measure of the ease of charge-transfer interaction, this conclusion represents a parallel relationship between the position of charge-transfer and the position of bond-interchange in a molecule in chemical reactions; it will later be shown to act as one of the two auxiliary principles which lead to the general orientation principle.

The Principle of a Narrowing of the Inter-frontier Level Separation

As has been mentioned above, the charge-transfer interaction takes place at the position of the largest frontier electron density, the position which is simultaneously most susceptible to a weakening of the bonds with the neighboring atoms. This bond-loosening causes the nuclear configuration to change in a definite direction, which should be controlled by the nodal property of the frontier orbitals.

This direction of nuclear-configuration change may be characterized by the mode of change in the energy-level separation between the HO of the donor and the LU of the acceptor. Namely, the HO MO of the donor becomes, in general, higher, while LU of the acceptor becomes lower, in the event of charge-transfer, causing a narrowing of the inter-frontier energy level separation. Sush a conclusion can very easily be understood, since a bonding MO is made unstable by electron-releasing and since an antibonding MO is made unstable by electron-accepting, in both cases through bond-loosening.

Let us consider this problem by quoting several examples. In the first place, let us take the Diels-Alder-type addition of ethylene and butadiene as an instance. The nodal properties of the HO and LU of ethylene and butadiene are shown in Fig. 3, together with the mode of charge-transfer interaction. The HO MO of butadiene is bonding in the region of 1,2- and 3,4-π-bonds and antidonding in the 2,3-region, while the LU of butadiene has the opposite nodal property. The HO of ethylene is bonding, while LU is antibonding. This implies that both

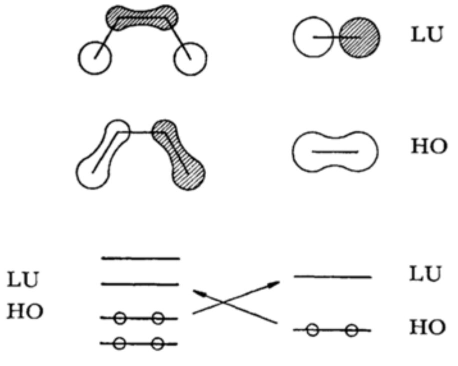
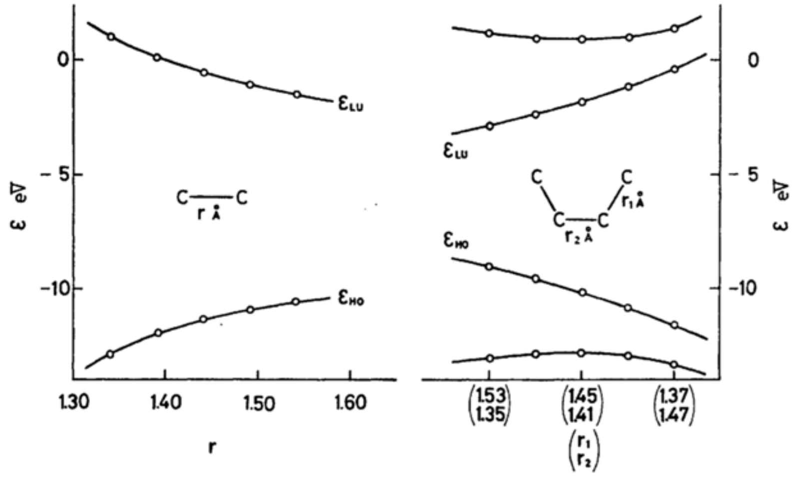


Fig. 3. The nodal property of HO and LU in ethylene and butadiene.



ethylene butadiene

Fig. 4. The change in energy of molecular orbitals in ethylene and butadiene along the reaction path.

the charge-transfer from the HO of ethylene to the LU of butadiene and that from the HO of butadiene to the LU of ethylene will decrease the π bond-order of ethylene and cause a double-bond shift in butadiene.

The results of calculations by the Pariser-Parr-Pople scheme[10] for several altered nuclear coordinates are shown in Fig. 4. The transient nuclear configurations along the reaction path could reasonably be assumed by considering the direction of charge-transfer and the nodal property of the HO and LU. We can see that the changes in the HO and LU can be clearly distinguished from those of the other orbitals. The separation of these MO levels is considerably contracted as the reaction proceeds. Such a property is common in dienes and dienophiles.

The mode of change in the MO energies of this sort is more conspicuous in the sigma electron systems. As a typical example, let us present the results of an extended Hückel calculation on the SN-2 reaction of methyl chloride by the chloride anion. The reaction coordinates were extracted from the calculation of Kato *et al.*[15] The solid line in Fig. 5 indicates the change in the energy of the LU of methyl chloride, while the broken line shows that of the system composed of methyl chloride and chloride anion. The other unoccupied MO's are located much higher than LU,[16] and the changes in these levels were found to be small in comparison with that in LU.

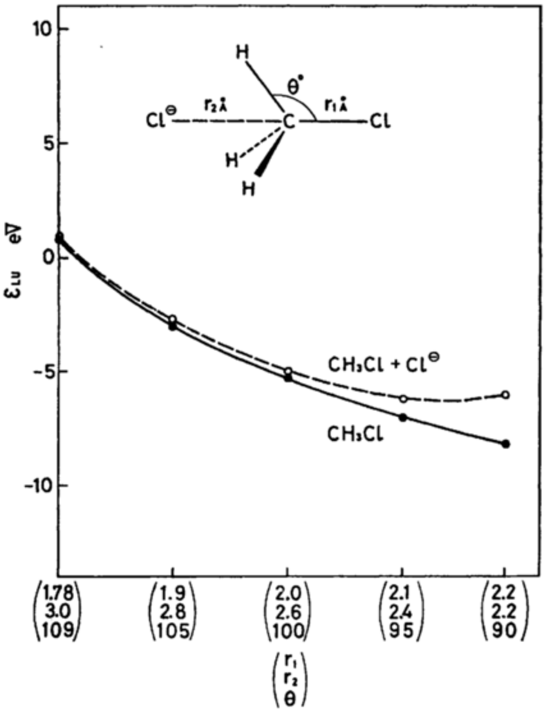


Fig. 5. The change in the energy of LU MO of methyl chloride with and without another approaching chloride anion.

It may be of interest to investigate the content of the activation energy. The stretching of the C–Cl bond in methyl chloride will require enough energy to form an important fraction of the activation energy of the reaction. The LU MO is highly localized at the C–Cl bond and exhibits an antibonding char-

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[15] H. Kato, K. Morokuma, T. Yonezawa and K. Fukui, This Bulletin, **38**, 1749 (1965).

[16] The unoccupied MO's are expressed in terms of a set of limited-basis AO's chosen so as to be suitable in representing the occupied MO's. This is an unsatisfactory point. However, the essential features will never be changed by the employment of any extended-basis set of AO's.

acter. The charge-transfer from the attacking base to LU will, therefore, cause the C–Cl bond stretching. However, this will produce stabilization on account of the lowering of the MO level, as is shown in Fig. 5. In this way, a considerable part of the activation energy is reduced. It can be understood that the charge-transfer and the nuclear configuration change cooperate in driving the chemical reactions.

The circumstances are similar also in nucleophilic elimination reactions. For instance, the LU of ethyl chloride is highly localized at the carbon-chlorine bond, which shows an antibonding nature. Accordingly, the charge-transfer to the LU from the attacking base through *trans*-β-hydrogen may cause a weakening of the C–Cl bond as well as of the β-carbon-hydrogen bond, resulting in a lowering of the LU MO energy. Such a lowering of the MO energy may be of great importance in facilitating the bimolecular elimination of halogenated paraffins by a nucleophile. The results of the numerical calculation have been given in previous papers.[12,13]

Next, let us consider aromatic substitutions. In these reactions the bonds between the reaction center and the neighboring atoms may be lengthened to some extent by the decrease in the π bond-orders of this region. This will cause an elevation of the HO level and a lowering of the LU level. In addition, the leaving hydrogen atom at the reaction center will leave the molecular plane as the reaction proceeds. It may be of interest to examine the energy change in the frontier orbitals in this case. The results of the numerical calculation are shown in Fig. 6.

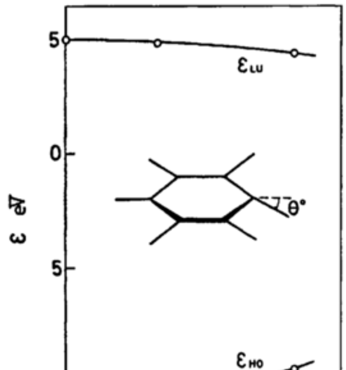

Fig. 6. The change in the energy of HO and LU in benzene due to the C–H bending.

The changes in the energies of HO and LU due to such a change in the bond angle are, in general, small in comparison with those due to the bond-stretching. However, the change is significant in the sense that the effect of valence angles can never be left out of account in discussing the problem.

The ascending HO energy and the descending LU energy of aromatic molecules couple with the descending LU of electrophilic reagents and with the ascending HO of nucleophilic reagents respectively to give rise to a narrowing of the inter-frontier level separation. In the case of liquid-phase ionic reactions, it must frequently be remarked that one should take into account the process of desolvation and solvation in the level change of the reagent orbitals. In homolytic reactions, the ascending HO and descending LU levels both approach the singly-occupied (SO) MO level of reagent radicals, bringing about a simultaneous charge-transfer to and a back-transfer from the SO MO.

In order to confirm these circumstances, the frontier MO's of attacking electrophiles are examined. The hydronium ion is taken as a simple example of solvated electrophiles. The extended Hückel calculation indicates that the LU of hydronium ion lowers as the distance between the proton, which is the bare electrophilic reagent, and the water molecule, that is the solvent, grows with the proceeding of the reaction. The results are shown in Fig. 7.

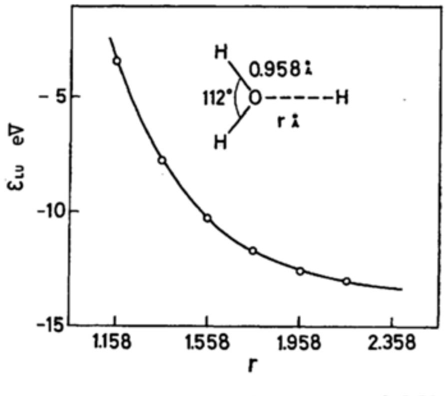

Fig. 7. The change in the energy of LU in hydronium ion due to the O–H stretching.

Lastly, the heterolytic addition to an olefinic double bond will be cited. The reagent is here typified by a chlorine molecule in order to simplify the calculation. The first stage of this reaction is assumed to be the formation of a bridged cation,[17] which may cause the stretching of the carbon-carbon bond.

An extended Hückel calculation is made to obtain a relation between the position of chlorine and the MO energy. The chlorine is shifted in the direction parallel to the carbon-carbon bond. As can be seen in Fig. 8, the total energy, *E*, increases as the chlorine atom separates from the center plane

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[17] An energy minimum arises in the event of approaching the C–C bond on the bisecting line. The stability of triangular interaction is discussed in Ref. 6.

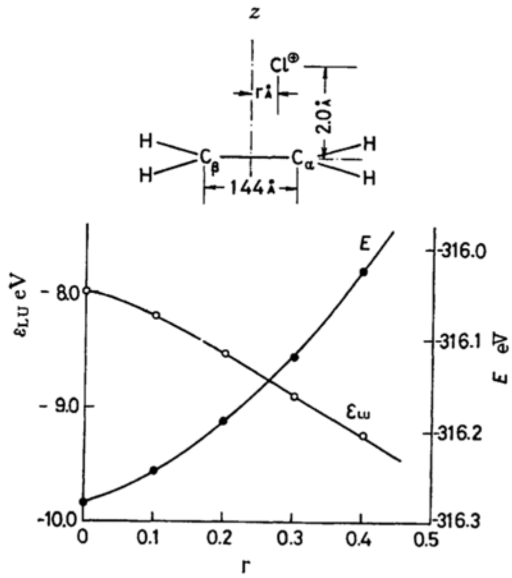


Fig. 8. The change in the energy of LU and in the total energy of ethylene-chorine cation system.

to approach the α-carbon; also, the LU level becomes lower in the event of change in this direction. The progress of the charge-transfer causes the narrowing of the inter-frontier separation, so the contribution of LU of the cation becomes enhanced as the interaction goes on.

The results of numerical calculations with respect to the several examples of chemical reactions cited above suggest the general relationship between the inter-frontier energy level separation and the nuclear configuration change along the reaction path. This implies that the importance of the frontier orbitals is more than would be expected from the case where the separation narrowing is left out of account.

The Principle of a Growing Frontier Electron Density along the Reaction Path

In order to make the third auxiliary principle concrete, it is recommended that we discuss the simplest case first. The well-discussed problem of aromatic substitution fits this purpose. As the reaction proceeds, the sum of the mobile bond-orders of the bonds between the reaction center and the neighboring atoms will decrease according to Eq. (9), causing a loosening of these bonds. The effect of this π-bond weakening may be represented, in the frame of the Hückel MO method, by the decrease in the absolute value of the resonance integrals corresponding to these bonds.

It is important to investigate the change in the frontier electron density at the actual reaction site according to the increase in the resonance integrals (that is, the decrease in the absolute value) with the neighboring atoms. In actual reactions, this change evidently never amounts to as large values as $(-\beta)$, where β is the original value of the resonance integral. However, as an extremely assumptive case, this increment may be taken as $(-\beta)$, so that the general tendency of the effect of such changes might more dinstinctly be realized. In that case the π AO at the reaction center finally becomes isolated (Stage(IV)). Stage (III), immediately before Stage (IV), indicates that a small π conjugation still remains between the reaction center and the neighboring atoms.

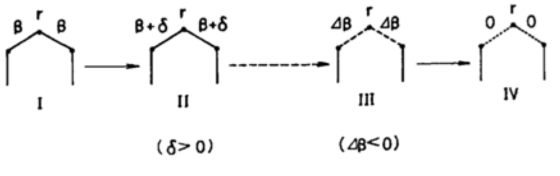
The frontier electron densities, $(C_r^{(\mathrm{HO})})^2$ and $(C_r^{(\mathrm{LU})})^2$, usually increase along the (I)→(II) path. This is valid with respect to the positions in alternant hydrocarbons, and also in a majority of positions of nonalternant hydrocarbons.

In order to understand these circumstances qualitatively, although not in a mathematically strict sense, it is convenient to consider Stage (III). In this stage it is very easy to prove that:

$$\lim_{\Delta\beta\to 0}(C_r^{(\mathrm{HO})})^2 \quad \text{and} \quad (C_r^{(\mathrm{LU})})^2 = \frac{1}{2} \qquad (15)$$

provided that the system obtained by deleting the atom r from the original hydrocarbon has a nonbonding level, $\varepsilon=\alpha$.[18] Since the original values of $(C_r^{(\mathrm{HO})})^2$ and $(C_r^{(\mathrm{LU})})^2$ are usually far less than 0.5, this result suggests that the frontier electron density increases along the path (I)—(III). The relation of Eq. (15) holds in alternant hydrocarbons and also in several, actually reactive positions of some nonalternant hydrocarbons, like the $(C_1^{(\mathrm{HO})})^2$ of fulvene, the $(C_1^{(\mathrm{HO})})^2$ of acenaphthylene, and the $(C_7^{(\mathrm{HO})})^2$ of fluoranthene.[19]

When the remaining system has no nonbonding MO, the following two sub-cases are possible. Let



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[18] If the remaining system possesses n nonbonding MO's, $(C_r^{(\mathrm{HO})})^2$ and $(C_r^{(\mathrm{LU})})^2$ become $1/(n+1)$.

[19] The numbering of these nonalternants conforms to: K. Fukui, T. Yonezawa and C. Nagata, This Bulletin, **34**, 37 (1961).

the number of occupied MO's of the original system be n, and let the number of occupied MO's of the remaining system obtained by deleting the atom r from the original system be m. The first sub-case is the one where $m=n$. In this case it follows that:

$$\lim_{\Delta\beta\to 0}(C_r^{(\mathrm{LU})})^2 = 1 \tag{16}$$

Such a relation holds in the position 6 of fulvene, the position 5 of acenaphthylene, the position 6 of azulene, and the position 3 of fluoranthene. The second sub-case is specified by $m=n-1$, so that:

$$\lim_{\Delta\beta\to 0}(C_r^{(\mathrm{HO})})^2 = 1 \tag{17}$$

which is actually satisfied in the position 1 of azulene. All of these cases indicate that the rule of growing frontier electron density might hold in actually reactive positions.

One of the few exceptions is $(C_3^{(\mathrm{HO})})^2$ of fluoranthene. In this case we have $m=n$, so that $\lim_{\Delta\beta\to 0}(C_3^{(\mathrm{HO})})^2=0$. However, it should be noted that in this case the HO MO energy of the remaining system is very close to the nonbonding orbital energy ($\varepsilon=\alpha+0.1317\beta$) whereas the energy of the isolated AO of the position 3 will easily become lower than $\varepsilon=\alpha$ under the influence of an approaching electrophile, so that the isolated AO energy might not become higher than the HO MO of the remaining system. In this way, it is possible even in this case that:

$$\lim_{\Delta\beta\to 0}(C_3^{(\mathrm{HO})})^2 = 0.5 \text{ or } 1 \tag{18}$$

Such a Coulombic effect of the attacking reagent should be considered in the other cases which have already been mentioned. In all of these cases, however, the circumstances are more favorable, in view of this effect, for the validity of the rule of growing frontier electron density along the reaction path.

The heterolytic addition of chlorine to a C=C bond (discussed in preceding section) is also an example. Figure 9 shows that the partial valence-inactive population of the $2p_z$ AO of β-carbon in the LU increases with the progress of the reaction.

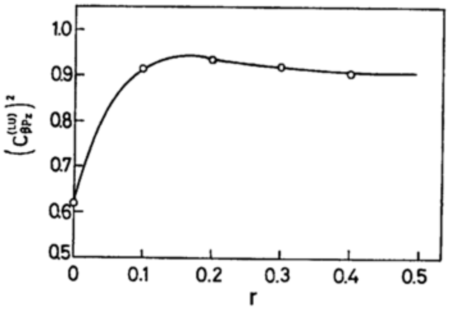

Fig. 9. The change in the partial population of p_z orbital at β-carbon of ethylene-chlorine cation system.

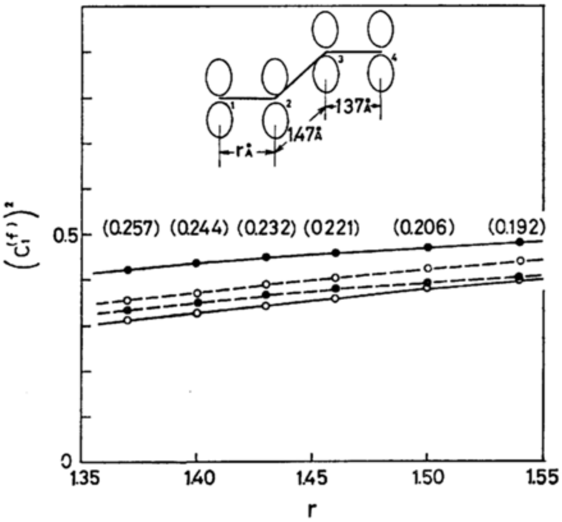

Fig. 10. The change in frontier electron density in the π electronic part of *trans*-butadiene along the departing of the end carbon atom.

—●— LU including overlap
—○— HO including overlap
--●-- LU neglecting overlap
--○-- HO neglecting overlap

(The values in parenthses indicate the overlap integral between two $p\pi$ atomic orbitals at the carbon atoms 1 and 2.)

This rule is not essentially violated by the adoption of more elaborate methods of calculation. With the change in the nuclear configuration, the overlap integrals between the AO's belonging to the departing atom and the AO's belonging to the remainder of the molecule vary. In order to discuss the change in the magnitude of the frontier electron density as a measure of the numerator of Eq. (1), the effect of the change in the overlap integrals upon the frontier electron density through the normalization condition can never be neglected. Figure 10 gives the change in the $(C_r^{(f)})^2$ in the π electronic part of butadiene due to the stretching of the C=C bond. We can see that the essential conclusion mentioned above also holds in the extended Hückel calculation, explicitly including overlap integrals.

The Co-operation of Sub-principles and the General Orientation and Stereoselection Rule

It is obvious that the three sub-principles work co-operatively in promoting the chemical reaction. The charge-transfer interaction takes place predominantly at the position and in the direction in which the overlapping of the HO and LU of the two reacting species is largest, as is to be expected from Eqs. (5) and (6). This interaction brings about a local bond-weakening, which is mainly controlled by the nodal property of the frontier orbitals. The extent of bond-weakening positionally parallels the frontier-orbital extension according to the first sub-principle. The bond-loosening leads to the nuclear configuration change in a definite direction, which causes the narrowing of the inter-frontier energy level separation according to the second sub-principle and, at the same time, the increase in the frontier electron density at the reaction center according to the third sub-principle. These make the denominator on the right side of Eq. (5) smaller and the numerator larger, so the contribution of the frontier orbital interaction term to the delocalization part (Eq. (1)) of the interaction energy becomes larger. Hence, the charge-transfer interaction increases, resulting again in a bond-interchange near the reaction center, a molecular shape deformation, a narrowing of the inter-frontier separation, and an increase in the frontier electron density, in turn. The importance of the term of Eq. (5) thus becomes greater and greater, the form of the delocalization term approaching that of Eq. (4).

It should be remarked in this connection that the MO's which can participate in such a type of co-operation are obviously restricted to the HO and LU. The energies of the other MO's undergo only the minimum change which is absolutely needed for the occurrence of the reaction and is assumed to be almost constant with respect to every possible position of the reaction. This is because a stable molecule originally takes the nuclear configuration which is energetically most favorable, and, in the event of reaction, any change in the nuclear configuration will be accompanied by an unstabilization which resembles the promotion in atoms in the case of molecule formation. Therefore, the change in the nuclear configuration will take place in such a direction that the unstabilization will be most effectively reduced, while a direction of change in which no energetical advantage can be expected will be avoided. As has already been mentioned, the charge-transfer between the HO and LU causes an alteration in the molecualr shape at the site of the greatest HO or LU MO density. In this way, the change in molecular shape is automatically limited to the proximity of the particular position in the reacting species. This self-controlling action seems to underlie the empirical rule which has been known as "the principle of least motion" or "the principle of least molecular deformation."[20]

It is evident from the above discussion that the most effective means to promote a chemical reaction smoothly by reducing the unstabilization attributable to the nuclear configuration change due to the interaction is to give rise to a change by which the charge-transfer from the HO of one species to the LU of the other is effectuated. This charge-transfe rmay be uni-directional or mutual according to the magnitude of the difference between the electron-donating power of one reactant and the electron-accepting power of the other. Other directions of nuclear configuration change are all rejected as bringing about little gain in stabilization energy.

In this way, the reaction pathway becomes dominantly controlled by the frontier-orbital interaction. The position of the reaction will be determined, through Eq. (6), by the rule of the maximum overlapping of the HO and LU (sometimes the SO in place of the HO or LU) of the two reacting species. The general orientation principle is, therefore, as follows: *"A majority of chemical reactions are liable to take place at the position and in the direction where the overlapping of the HO and LU of the respective reactants is at its maximum; in an electron-donating species, HO predominates in the overlapping interaction, while the LU does so in an electron-accepting reactant; in the reacting species which possess SO MO's, these play the part of the HO or of the LU, or of both."*

In some intramolecular reactions, like the cyclization of a conjugated olefinic chain, the dominantly controlling factor seems to be the first-order inteaction term,[6,21] in which the HO-LU interaction is concealed; however, the same reaction can be discussed by considering the HO-LU interaction between two parts of a molecule.[22] The HO-LU interaction has also been considered between the sigma- and pi-parts of conjugated molecules in order to derive a stereoselection rule.[7]

In this view, the particular MO's which control the reaction pathway in chemical reactions in general, *i.e.*, HO, LU, and SO, are referred to as "generalized frontier orbitals."

It seems in this way that the principle presented above is a general one which will qualitatively govern almost all sorts of chemical interactions, including intermolecular and intramolecular as well as unicentric and multicentric. The principle can be applied to a unicentric reaction to derive an orientation rule; and if it is employed to discuss multicentric reactions, the result is the stereoselection rule, which has already been discussed.[7,21,22]

The reactivity indices, the frontier electron density, the delocalizability, and the superdelocalizability, are those for unicentric reactions and give predictions consistent with the general orientation principle. In this connection, it is worthwhile to mention the relation between these chemical reactivity indices and the general orientation rule. These indices are derived from Eq. (1), in which the nuclear-configration change along

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[20] See, for example, J. Hine, *J. Org. Chem.*, **31**, 1236 (1966), and the references cited therein.

[21] K. Fukui, *Tetrahedron Letters*, **1965**, 2009.

[22] K. Fukui and H. Fujimoto, "Mechanism of Molecular Migrations," Vol. 2, ed. by B. S. Thyagarajan, Wiley-Interscience (1969).

the reaction path is left out. Namely the indices, like most other reactvity indices ever proposed, are calculated with regard to an isolated, undeformed molecule. If the molecular deformation along the reaction path is taken into consideration, the values of these indices will be changed. The change in the value of delocalizability and superdelocalizability will be controlled by the sub-principles discussed above, so the contribution of the terms corresponding to the frontier orbitals will become more dominant than in the original expression.

In the superdelocalizability thus modified, the frontier terms should be weighted more. The index of the type of Eq. (5), the one-term approximation of superdelocalizability,[23] and Brown's Z-value[24] are all this line. We prefer the frontier terms and recommend that the frontier electron density be used as a reactivity index.

The calculations have been carried out partly on the HITAC 5020E computer at the Computer Center of the University of Tokyo and partly on the FACOM 230·60 computer at the Computer Center of Kyoto University.

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[23] K. Fukui, T. Yonezawa and C. Nagata, *J. Chem. Phys.*, **27**, 1247 (1957).

[24] R. D. Brown, *J. Chem. Soc.*, **1959**, 2232.