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A Novel Approach to the Theory of Catalytic Activity in Terms of Molecular Orbital Mixing

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Abstract: A novel approach is proposed for the estimation of catalytic activity from the change of a frontier orbital, given in terms of general rules which predict the change of a frontier orbital by perturbation of a point charge ("static orbital mixing"), or by overlapping of orbitals ("dynamic orbital mixing") through orbital mixing. These general rules can predict, without calculation, the change of frontier orbitals of a perturbed system from the nonperturbed molecular orbitals. The general rules derived for "static orbital mixing" and for "dynamic orbital mixing" are applied to the Lewis acid-catalyzed Diels-Alder reaction and the Meerwein-Ponndorf reaction, respectively. In both cases, the changes in frontier orbitals and in chemical reactivities under the influence of catalysts could be correctly predicted from the general rules, indicating that this approach should be very useful for the prediction of catalytic reactions. Finally, the meaning of multicenter interactions in catalytic reactions is discussed in connection with enzymatic reactions.

The theory of chemical reactivity has recently been developed so remarkably that organic chemists are able to use it with ease and considerable confidence. This is so mainly because of the simple concepts of the theory, such as HOMO-LUMO interaction in the frontier electron theory developed by Fukui et al.,²⁻⁵ and conservation of orbital symmetry in the Woodward-Hoffmann rule.⁶⁻⁸

In this present article, along with the above-mentioned theories, we wish to present a novel approach for the prediction of catalytic activity in terms of molecular orbitals through orbital mixing.

The usefulness of the idea of orbital mixing has been demonstrated. For example, Zimmerman proposed the concept of MO following to draw correlation diagrams and to follow reactions.⁹ Recently, Fujimoto and Hoffmann calculated the coefficients of orbital mixings of ethylene oxide and acrolein by perturbation of the electric field in connection with catalytic reaction.¹⁰ Moreover, Libit and Hoffmann¹¹ showed that orbital mixing due to overlap integrals plays an important role in the charge distribution of a π electron system with methyl substituent by using the perturbation method¹² developed by Imamura, one of the present authors. A trial¹³ to illustrate catalytic activity by orbital mixing between orbitals with the same symmetry was also made in a manner similar to the Woodward-Hoffmann method.⁶⁻⁸

Our fundamental idea in the present article is as follows. The change in a chemical reactivity by a catalyst is brought about by the change in a frontier orbital concerned, and the change in the frontier orbital should be the result of orbital mixings between the frontier orbital and the other orbitals of the substrate by perturbation due to a catalyst. This perturbation can be classified into two parts, one an electrostatic interaction and the other an overlap of orbitals be-

tween the substrate and the catalyst. The former may be called "static orbital mixing" and the latter "dynamic orbital mixing" (see Figure 1). We derive here general rules to predict the static and dynamic orbital mixings. For examples of application, we have chosen the Lewis acid-catalyzed Diels-Alder reaction and the Meerwein-Ponndorf reaction.

Nowadays, molecular orbital concepts have become working tools for most organic chemists. Our qualitative approach may be of practical value not only for the understanding of the essential feature of a catalysis but also for the prediction or design of a catalytic organic reaction.

Formulas for Static Orbital Mixing

Consider a point charge (Ze) interacting with the molecular orbitals of a substrate. The electric field by the point charge can be regarded as a perturbation to the substrate. That is, the perturbed Hamiltonian H' is represented by eq 1

$$H' = -Ze^2/r_{tk} \quad (1)$$

where r_{tk} is the distance between a point charge at t and an electron k . The usual perturbation theory^{12,14-17} gives the following equation for the coefficient of orbital mixing d_{ij}

$$\begin{aligned} \varphi_i(k) &= \varphi_i^0(k) + \sum_{j(\neq i)} d_{ij} \varphi_j^0(k) + \dots \quad (2) \\ d_{ij} &= \int \varphi_i^0(k) H' \varphi_j^0(k) d\tau_k / (\epsilon_i^0 - \epsilon_j^0) = \\ &= \int \varphi_i^0(k) (-Ze^2/r_{tk}) \varphi_j^0(k) d\tau_k / (\epsilon_i^0 - \epsilon_j^0) \quad (3) \end{aligned}$$

where ϵ_i^0 and ϵ_j^0 are the orbital energies of the i th and j th levels, respectively. The molecular orbital, $\varphi_i^0(k)$, may generally be represented by the linear combination of atomic

orbitals; that is

$$\varphi_i^0(k) = \sum_r C_{ir}^0 \chi_r(k) \quad (4)$$

Substitution of eq 4 into eq 3, followed by CNDO (complete neglect of differential overlap) approximation,¹⁸⁻²⁰ leads to

$$d_{ij} = \sum_r \sum_s C_{ir}^0 C_{js}^0 \int \chi_r(k) (-Ze^2/r_{tk}) \chi_s(k) d\tau_k / (\epsilon_i^0 - \epsilon_j^0) = -Z \sum_r C_{ir}^0 C_{jr}^0 (rr|t) / (\epsilon_i^0 - \epsilon_j^0) \quad (5)$$

where $(rr|t)$ represents the electrostatic interaction energy between the atomic orbital r and a unit point charge at position t .

$$(rr|t) = \int \chi_r(k) (e^2/r_{tk}) \chi_r(k) d\tau_k \quad (6)$$

The summation in eq 5 can be rewritten as follows

$$\sum_r (C_{ir}^0 C_{jr}^0) (rr|t) = \sum_r (C_{ir}^0 C_{jr}^0) \{ (rr|t) - (r_m r_m | t) \} + (r_m r_m | t) \sum_r (C_{ir}^0 C_{jr}^0) \quad (7)$$

where $(r_m r_m | t)$ is an appropriate integral to cancel all except the few leading terms in eq 7. Therefore, $(r_m r_m | t)$ may tentatively be taken as the average of various $(rr|t)$ terms except the few leading terms which usually include the atomic orbitals on the nearest-neighbor atom to a point charge. From the orthogonality of the molecular orbitals φ_i^0 and φ_j^0 , the second term of eq 7 vanishes, and eq 7 can be rewritten as

$$\sum_r (C_{ir}^0 C_{jr}^0) (rr|t) = \sum_r^{\text{near}} (C_{ir}^0 C_{jr}^0) \{ (rr|t) - (r_m r_m | t) \} + \sum_r^{\text{nonnear}} (C_{ir}^0 C_{jr}^0) \{ (rr|t) - (r_m r_m | t) \} \quad (8)$$

where \sum_r^{near} indicates the summation of atomic orbitals on the nearest-neighbor atom to a point charge and \sum_r^{nonnear} the summation of other atomic orbitals. Considering that $(r_m r_m | t)$ is the average value of the nonnearest neighbor terms and that the integral $(rr|t)$, except for the nearest-neighbor terms, changes its value gradually with the change of the distance between r and t as is shown schematically in Figure 2, we can reasonably neglect the second term of eq 8. Therefore, the mixing coefficient given by eq 5 can be rewritten as follows

$$d_{ij} = -Z \sum_r^{\text{near}} C_{ir}^0 C_{jr}^0 \{ (rr|t) - (r_m r_m | t) \} / (\epsilon_i^0 - \epsilon_j^0) \quad (9)$$

When the substrate is a π electron system, \sum_r^{near} in eq 9 is the summation of the single π atomic orbital on the nearest-neighbor atom to a point charge, leaving only one term

$$d_{ij} = -Z C_{ir}^0 C_{jr}^0 \{ (rr|t) - (r_m r_m | t) \} / (\epsilon_i^0 - \epsilon_j^0) \quad (10)$$

From eq 10 can be derived the following general rule of static orbital mixing.²¹

Case 1: (a) When perturbation is due to a positive charge, the sign of the orbital mixing can be determined by the energy-level difference between the two molecular orbitals concerned and by the sign of the product of two coefficients of the leading term ($C_{ir}^0 C_{jr}^0$), where the atomic orbital r is the nearest neighbor of the point charge concerned. That is, when the sign of the product is positive, a positive contribution is expected from the higher energy level ($\epsilon_j^0 > \epsilon_i^0$) and a negative contribution from the lower energy level ($\epsilon_j^0 < \epsilon_i^0$). When the sign of the product is negative, a positive contribution is expected from the lower energy level ($\epsilon_j^0 < \epsilon_i^0$) and a negative contribution from

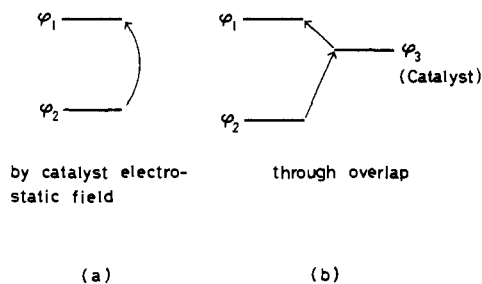


Figure 1. Schematic representations of (a) static and (b) dynamic orbital mixings of substrate molecular orbitals φ_2 into φ_1 .

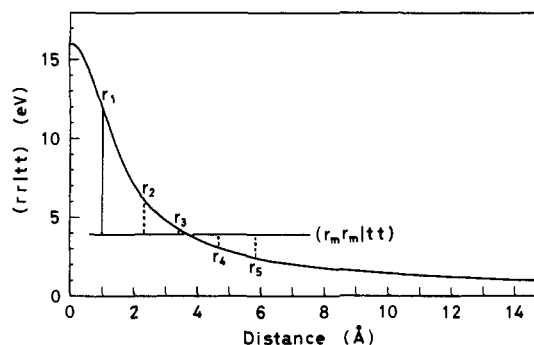


Figure 2. Dependence of $(rr|t)$ on the distance between a point charge at t and the atomic orbital r . The $(rr|t)$ in this figure is for carbon $2s$ -carbon $2s$. The magnitudes of $\{ (rr|t) - (r_m r_m | t) \}$ for an arbitrary set of atomic orbitals r_i ($i = 1-5$) are also given for illustration. In this figure, $(rr|t)$, etc., are replaced by $(rr|tt)$, etc., two-center Coulomb repulsion integral, according to the approximation used in the CNDO/2 method.

the higher energy level ($\epsilon_j^0 > \epsilon_i^0$). (b) The magnitude of the orbital mixing should be approximately proportional to the absolute value of the product of the two coefficients, $C_{ir}^0 C_{jr}^0$, and inversely proportional to the absolute value of the difference of the two energy levels, $|\epsilon_j^0 - \epsilon_i^0|$.

Case 2: When perturbation is due to a negative charge, the reverse of (a) in Case 1 is true for the sign of the orbital mixing, and the same conclusion as (b) in Case 1 is valid for the magnitude of the orbital mixing.

This general rule can be easily extended to a σ electron system. That is, as is apparent from eq 9, $C_{ir}^0 C_{jr}^0$ in the rule may be substituted by $\sum_r C_{ir}^0 C_{jr}^0$ for extension to a σ electron system, since several atomic orbitals on the atom nearest to the point charge have nonzero coefficients. Moreover, when there are many point charges around the substrate, the coefficient of the orbital mixing, d_{ij} , can be given by the summation on point charges, t , in question, giving

$$d_{ij} = -\sum_t Z_t \sum_r^{\text{near}} C_{ir}^0 C_{jr}^0 \{ (rr|t) - (r_m r_m | t) \} / (\epsilon_i^0 - \epsilon_j^0) \quad (11)$$

From eq 11 can be derived a general rule similar to that derived from eq 10.

Application of the General Rule of "Static Orbital Mixing" to Lewis Acid Catalysis in Diels-Alder Reaction

To illustrate the usefulness of the general rule of static orbital mixing of a catalyst given in the preceding section, we studied the catalytic action of Lewis acid in the Diels-Alder reaction. The molecular orbital approach to this problem has already been made by Houk and Strozier, illustrating the change in regioselectivity by Lewis acid,²² comparing the frontier orbitals of acrolein with those of protonated acrolein, considered to be a simple model for a Lewis acid coordinated dienophile, they found that the change in frontier orbitals by protonation indicates an in-

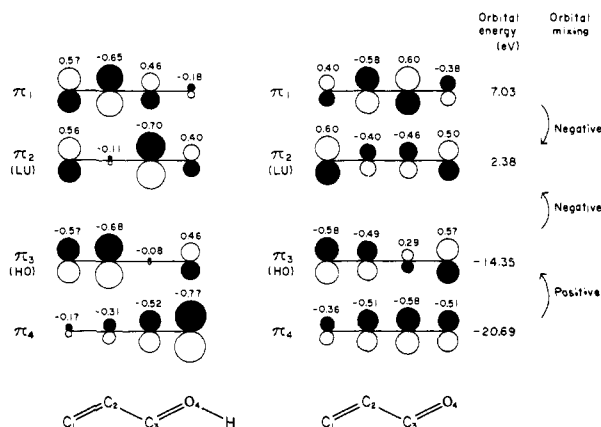


Figure 3. Orbital energies and coefficients of four π orbitals for protonated acrolein (left) and acrolein (right), obtained by CNDO/2 calculation.

crease in regioselectivity, which is in agreement with experimental results. Although their treatment is attractive, they did not give any explanation for the change in the frontier orbitals. Moreover, Fujimoto and Hoffmann also calculated the same system and decomposed the molecular orbitals of protonated acrolein into those of isolated acrolein in order to see the orbital mixing.¹⁰ We have attempted to find the theoretical basis for the change in frontier orbitals through our theory of orbital mixing. The Diels-Alder reaction is most suitable for application of our general rule of static orbital mixing since dynamic orbital mixing vanishes completely, because of the zero overlap between the proton 1s orbital and acrolein π orbitals, and since regioselectivity is related only to the change in the frontier orbital and not to the change in the energy levels concerned.

Figure 3 shows the four π orbitals of protonated acrolein in comparison with those of acrolein calculated by the CNDO/2 method.¹⁸⁻²⁰ From these figures, it is clear that the magnitudes of the coefficients in HOMO and LUMO orbitals change remarkably upon protonation, especially the relative magnitudes of C_{21} and C_{22} in LUMO, which is intimately related to the change of regioselectivity by Lewis acid catalysis as shown by Houk and Strozier.²²

According to our general rule of static orbital mixing, the change in the coefficient of a molecular orbital upon protonation should be represented by the mixing of the molecular orbital with the other molecular orbitals of the substrate itself. The signs of the mixing and the relative magnitudes, determined from this general rule, are summarized in Table I. The table is easily arranged from the molecular orbital of acrolein. For instance, the contribution of the fourth orbital to the third orbital is positive since the product of the coefficients of the third and fourth orbitals on the oxygen atom is negative and since the fourth level is lower than third level, and the magnitude of this contribution is very large since the product of the two coefficients is large and the energy level difference between the third and fourth levels is very small. Table I can be filled out by the same logic.

To investigate the validity of the predictions given in Table I, we decomposed the molecular orbitals of protonated acrolein into the contributions of those of acrolein in the same manner as that employed in our analysis of the rotational strength.²³⁻²⁵ In other words, the molecular orbitals of protonated acrolein were represented as the linear combinations of the molecular orbitals of acrolein. The coefficients of the molecular orbitals of acrolein thus obtained are listed in Table II. The signs of the coefficients in Tables I and II were in complete agreement, without exception. Moreover, the relative magnitude of Table I correctly

Table I. Prediction of the Signs and Magnitudes of Orbital Mixings from the General Rule

Orbital concerned (protonated acrolein)	Contributions of other orbitals (acrolein) ^{a, b}			
	1	2	3	4
1		+L	+S	-S
2	-L		-I	+S
3	-S	+I		+VL
4	+S	-S	-VL	

^a +, - indicate the signs of orbital mixing. ^b VL, L, I, and S indicate the very large, large, intermediate, and small magnitudes of orbital mixing.

Table II. Coefficients of Molecular Orbitals of Acrolein in the Expansion of Molecular Orbitals of Protonated Acrolein

Orbital of protonated acrolein	Contributions of orbitals of acrolein			
	1	2	3	4
1	0.951	0.305	0.020	-0.048
2	-0.287	0.922	-0.253	0.054
3	-0.067	0.206	0.906	0.363
4	0.092	-0.118	-0.339	0.929

predicts the values in Table II. Therefore, it should be concluded that the change in the molecular orbitals by the catalyst attack can be correctly predicted, without calculation, from the molecular orbitals of the isolated substrate through application of our general rule of static orbital mixing. For example, the great decrease in the absolute value of the C_2 coefficient upon protonation in LUMO can be reasonably explained by the large negative contributions of the first and third orbitals to LUMO, as is shown in Table I, since the C_2 coefficients of these orbitals also have large negative values. Other changes in the molecular orbitals upon protonation can also be explained from Table I without any calculation.

Formulas for Dynamic Orbital Mixing

When the molecular orbitals of a substrate overlap with those of a catalyst, the otherwise orthogonal molecular orbitals of the substrate can intermingle with each other through overlap with the molecular orbital of the catalyst. The coefficients of the orbital mixing of the substrate concerned can be derived as the second-order term of the wave function by using the usual perturbation theory. This term has already been derived by many researchers through neglect of the overlap integrals,¹⁷ but recently, Libit and Hoffmann¹¹ derived this term through inclusion of the overlap integral by using the perturbation procedure developed by Imamura.¹² Therefore, only the obtained results will be given in the following discussion.

Consider three molecular orbitals, φ_1 and φ_2 for the substrate and φ_3 for the catalyst; φ_1 and φ_2 are assumed to be orthogonal to each other, while φ_3 has a nonzero overlap integral with φ_1 and φ_2 . φ_1 and φ_2 can intermingle with each other through the overlap integrals between φ_1 and φ_3 as well as those between φ_2 and φ_3 , resulting in an alteration in the shape of the molecular orbitals.

The alteration can be described by the usual perturbation method. Consequently, the perturbed molecular orbital can be expanded as

$$\varphi_1' = d_{11}\varphi_1^0 + d_{12}\varphi_2^0 + d_{13}\varphi_3^0 \quad (12)$$

where φ_1^0 , φ_2^0 , and φ_3^0 are the molecular orbitals of the zeroth order, and their coefficients, d_{11} , d_{12} , and d_{13} , are given by

$$d_{11} = 1 - \beta_{13}^2 / 2(\epsilon_3^0 - \epsilon_1^0)^2 + \dots \quad (13)$$

$$d_{12} = \beta_{13}\beta_{23}/(\epsilon_2^0 - \epsilon_1^0)(\epsilon_3^0 - \epsilon_1^0) + \dots \quad (14)$$

$$d_{13} = -\beta_{13}/(\epsilon_3^0 - \epsilon_1^0) + \dots \quad (15)$$

where ϵ_i^0 is the orbital energy of the i th molecular orbital of the zeroth order, φ_i^0 , and β_{ij} is the core resonance integral between molecular orbitals φ_i^0 and φ_j^0 . Of these equations, eq 15 represents the mixing of φ_3 into φ_1 by direct interaction through β_{13} , while the mixing of φ_2 into φ_1 is represented by eq 14, indicating that the mixing of the molecular orbitals is brought about indirectly through β_{13} and β_{23} . It is the value of d_{12} given by eq 14 that is responsible for the change in the shape of the molecular orbital by the catalyst through dynamic orbital mixing.

Thus, the following general rule of dynamic orbital mixing can be derived from eq 14 according to the relative heights of energy levels of interacting molecular orbitals.

Case 1: (a) When the energy level of a molecular orbital, φ_1 , of a substrate is located between those of two molecular orbitals, φ_2 and φ_3 , of the substrate and the catalyst, and when the sign of the overlap integral between φ_1 and φ_3 is the same as that of φ_2 and φ_3 , a negative contribution of φ_2 to φ_1 is expected. Likewise, a positive contribution is expected when the signs of the overlap integrals differ.

(b) The magnitude of the mixing of the molecular orbital φ_2 should be proportional to the absolute value of the product of the two overlap integrals and inversely proportional to the absolute value of the product of the two energy differences between ϵ_2^0 and ϵ_1^0 and between ϵ_3^0 and ϵ_1^0 .

Case 2: (a) When the energy level of φ_1 is higher or lower than both energy levels of φ_2 and φ_3 , the reverse of (a) in Case 1 is true. That is, a positive contribution of φ_2 to φ_1 is expected when the sign of the overlap integrals between φ_1 and φ_3 is the same as that of φ_2 and φ_3 , while a negative contribution is expected when the signs differ.

(b) The magnitude of the orbital mixing is the same as (b) in Case 1.

Thus, according to the general rule derived above, the sign and the magnitude of orbital mixing can easily be estimated from the shapes of the molecular orbitals and relative energy levels in question. It should be noted that these energy levels concerned are not those of the isolated molecules, but those of the electrostatically interacting molecules with no overlap integrals, as will be shown in the following section. Extension of the formulas with more than three energy levels for dynamic orbital mixing is straightforward and the same as that given by Libit and Hoffmann.¹¹ Therefore, the extended formulas will not be given here, but we should add the notation of the summation in eq 13–15.

Application of the General Rule of "Dynamic Orbital Mixing" to the Meerwein-Ponndorf Reaction

In order to ascertain the usefulness of the general rule of dynamic orbital mixing, we applied our formulas to the Meerwein-Ponndorf reaction. As is well known, in this reaction aldehydes and ketones are reduced to alcohols by the catalysis of aluminum isopropoxide. The transition state of this reaction is usually considered to form a cyclic complex by the coordination of the carbonyl oxygen with aluminum, followed by the transfer of the hydride ion, as is shown in Figure 4.^{26,27} Therefore, we calculated by CNDO method^{18–20} the molecular orbitals of isolated formaldehyde as well as those of formaldehyde coordinated to aluminum alkoxide in order to investigate the change in the frontier orbital of formaldehyde upon coordination to the catalyst. Because of the limited memory size of our computer, dimethoxyisopropoxyaluminum was used as the model compound for the catalyst in our Meerwein-Ponndorf reaction; the geometry is given in Table III.

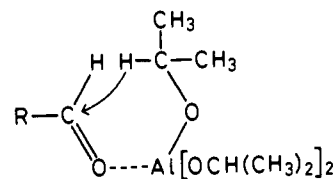


Figure 4. Transition state of the Meerwein-Ponndorf reaction.²⁶

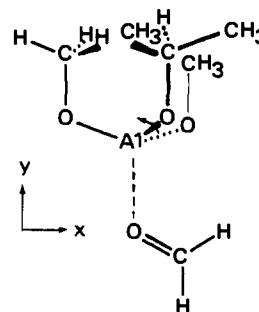


Figure 5. Relative conformation of formaldehyde-aluminum alkoxide complex, used as a model for the analysis of the catalytic effect of Al-alkoxide coordination. Each of the three alkoxy carbons is assumed to be trans with the carbonyl oxygen. The oxygen, carbon, and one methyl hydrogen of one of the methoxy groups are coplanar with the Al atom and the formaldehyde molecular plane. In addition, the Al atom is coplanar with the oxygen, methine carbon, and methine hydrogen of the isopropoxy group.

Table III. The Geometry of Formaldehyde-Aluminum Alkoxide Complex Used in the Calculation^a

Aluminum Alkoxide ^b			
Bond length, (Å)			
Al-O	O-C	C-C	C-H
1.6176	1.45	1.54	1.09
Formaldehyde			
Bond length, Å		Bond angle, deg	
C-H	C=O	∠HCH	∠HCO
1.12	1.21	118	121

^aThe distance between the carbonyl oxygen and the aluminum atom was assumed to be 2.0 Å and the bond angle, ∠COAl, 120°.

^bAll the bond angles in the molecules are assumed to be 109°28'.

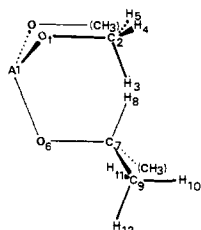
The relative conformation of the substrate and the catalyst is shown in Figure 5, together with the directions of the x , y , and z axes. As shown in Figure 5, the isopropoxy group was tentatively assumed to be located farthest from the carbonyl group, although the true geometry of the transition state for the Meerwein-Ponndorf reaction is not yet disclosed. Because of the large distance between the carbonyl group and the methine hydrogen of the isopropoxy group in this geometry, only the effect of the coordination to the aluminum atom on the frontier orbitals of the carbonyl compound will be included, and the effect of the interaction between the π^* orbital of the carbonyl group and the methine hydrogen, eventually transferred as a hydride ion in the transition state, of the isopropoxy group will be excluded. In other words, in the present model for calculation, we can investigate only the catalytic action of aluminum alkoxide by dropping the interaction between the reagent (the methine hydrogen of the isopropoxy group) and the substrate. In the transition state, however, the isopropoxy group may rotate around the O-Al bond, as shown in Figure 5, so that the methine hydrogen may come close on top of the carbonyl carbon of the substrate. Although the true steric course in the transition state might be different from that assumed in

Table IV. Coefficients of the Atomic Orbitals of Al and Carbonyl π Group in Isolated and Coordinated States

Energy level, eV	Isolated				Coordinated with overlap	Coordinated without overlap ^b			
	Carbonyl	Carbonyl	Al-1 ^a	Al-2 ^a		Carbonyl	Carbonyl	Al-1	Al-2
	-18.57	4.20	3.91	3.95	1.21	-18.95	3.84	4.17	4.22
C 2p _z	0.6447	-0.7644			-0.7977	0.6400	-0.7684	0.0	0.0
O 2p _z	0.7644	0.6447			0.5662	0.7684	0.6400	0.0	0.0
Al 3s			-0.0062	0.0000	0.0002	0.0	0.0	0.0065	-0.0001
Al 3p _x			0.3555	-0.6255	-0.0001	0.0	0.0	-0.3417	0.6332
Al 3p _y			0.0017	0.0000	0.0000	0.0	0.0	-0.0019	0.0008
Al 3p _z			-0.6157	-0.3611	0.1180	0.0	0.0	0.6226	0.3479
Al 3d _z ²			-0.0636	0.1114	0.0003	0.0	0.0	0.0607	-0.1116
Al 3d _{xz}			0.1231	0.0743	-0.0537	0.0	0.0	-0.1223	-0.0702
Al 3d _{yz}			0.4850	0.2791	-0.1413	0.0	0.0	-0.4903	-0.2685
Al 3d _{x-y}			0.0319	-0.0643	0.0003	0.0	0.0	-0.0309	0.0659
Al 3d _{xy}			-0.2800	0.4834	0.0004	0.0	0.0	0.2691	-0.4887

^aTwo molecular orbitals of isolated aluminum alkoxide which have larger aluminum atomic orbital coefficients are conventionally designated as Al-1 and Al-2. ^bCalculated for the electrostatically interacting system without overlap integral between formaldehyde and aluminum alkoxide.

Table V. Charge Distributions of Isolated Aluminum Alkoxide and Formaldehyde



Aluminum Alkoxide						
Al	O ₁	C ₂	H ₃	H ₄	H ₅	O ₆
0.605	-0.324	0.114	-0.002	-0.018	0.016	-0.346
C ₇	H ₈	C ₉	H ₁₀	H ₁₁	H ₁₂	
0.198	-0.022	-0.040	0.017	0.008	0.012	
Formaldehyde						
O	C	H	H			
-0.187	0.222	-0.018	-0.018			

this article, the essential feature of the change in the frontier orbital under the coordination catalyst should properly be revealed by our model described here.

The occupied and unoccupied π molecular orbitals of the carbonyl group in formaldehydes in isolated state and in the state coordinated to aluminum alkoxide are tabulated in Table IV, together with the coefficients of the aluminum 3s, 3p, and 3d atomic orbitals of the isolated and coordinated aluminum alkoxides. It is clear from this table that the coefficient of the carbon π orbital in the unoccupied level of the coordinated formaldehyde is larger than that of isolated formaldehyde. Consequently, this result indicates that aluminum alkoxide increases the reactivity of the carbonyl carbon of formaldehyde toward the hydride ion, which is in agreement with the experimental results.

Why, then, does the interaction between formaldehyde and aluminum alkoxide increase the reactivity of formaldehyde? First, the effect of static orbital mixing, that is, the effect of electrostatic interaction between the catalyst and the substrate, was investigated by dropping all the overlap integrals between the aluminum alkoxide and formaldehyde and by comparing the thus obtained π molecular orbitals of the electrostatically interacting formaldehyde with those of isolated formaldehyde. The calculated π molecular orbitals for the electrostatically interacting formaldehyde are also listed in Table IV. It is obvious that the effect of static orbital mixing is very small, judging from the small difference between molecular orbitals of isolated and electrostatically

interacting formaldehydes. Therefore, dynamic orbital mixing should be responsible for the increase in the frontier electron density on the carbon atom by the interaction between the catalyst and the substrate.

Second, orbital mixing between the two π molecular orbitals of the carbonyl group was analyzed by using the formulas for dynamic orbital mixing. Obviously, the overlap integrals between aluminum atomic orbitals and carbonyl π orbitals should play an important role in orbital mixing. Therefore, among the many molecular orbitals of isolated aluminum alkoxide, two molecular orbitals with relatively large coefficients of aluminum atomic orbitals are picked up and listed in Table IV, together with their orbital energies. The two π molecular orbitals of the carbonyl group of isolated formaldehyde are also tabulated in Table IV. The numerators of eq 14 and 15 can be calculated in a straightforward manner by using the molecular orbitals and the core resonance integrals concerned. As for the denominators of eq 14 and 15, it should be noted that the electrostatic interaction between the catalyst and the substrate may change the relative heights of the orbital energies in question when the molecules are polar, as in this present case. That is, from Table IV, the energy of the unoccupied π orbital of the carbonyl group is 4.20 eV in the isolated state, but 3.84 eV in the electrostatically interacting state without overlap, while that of aluminum alkoxide is 3.91 eV in the isolated state and 4.17 eV in the interacting state due to the positive charge on the aluminum atom and the negative charge on the oxygen atom of the carbonyl group, as is shown in Table V. Therefore, in the isolated state, the energy level of the carbonyl π orbital is higher than that of aluminum alkoxide, while the reverse is true in the interacting state. Obviously, the latter must be used in the denominators of eq 14 and 15. The relative heights of energy levels concerned are shown in Figure 6.

The values of orbital mixing derived by using eq 14 and 15 are given in Table VI. From these results, two molecular orbitals of aluminum alkoxide can reasonably be expected to give negative contributions to result in an increase in the frontier electron density on the carbonyl carbon atom and a decrease on the carbonyl oxygen atom, in complete agreement with the numerical results in Table IV.

In order to confirm this conclusion, the molecular orbital of the formaldehyde-aluminum alkoxide complex was decomposed into those of isolated formaldehyde and isolated aluminum alkoxide in a manner similar to that employed for the analysis of static orbital mixing given above. In Table VII is listed the expansion coefficient of molecular

Table VI. The Coefficient of Orbital Mixing

	d_{13} (eq 15)	d_{12} (eq 14)	
Al-1 ^a	-2.22	-0.231	} -0.299
Al-2 ^a	-1.13	-0.068	

^a Al-1 and Al-2 represent the molecular orbitals of aluminum alkoxide listed in Table IV with the orbital energies of 3.91 and 3.95 eV, respectively.

Table VII. Coefficients of Molecular Orbitals of Aluminum Alkoxide and Formaldehyde in the Expansion of Molecular Orbitals of Aluminum Alkoxide-Formaldehyde Complex

	Contributions of isolated molecular orbitals			
	Carbonyl π	Carbonyl π^*	Al-1 ^b	Al-2 ^b
Carbonyl π^* MO	-0.0814	0.9748	-0.1725	-0.0991
Carbonyl π MO ^a	-0.0061	0.99998		

^aThe molecular orbitals of the complex interact only electrostatically. ^bThe same notation used in Table IV.

orbitals of the isolated system for the carbonyl π orbital of the complex, together with those obtained by dropping all the overlap integrals between the catalyst and the substrate. As Table VII shows, static orbital mixing is found to be negligibly small, which is in agreement with the results mentioned above. On the other hand, the mixing coefficients due to dynamic orbital mixing are very large in magnitude for both the Al-1 and Al-2 levels of aluminum alkoxide, the former being about twice as large as the latter, in harmony with the values of d_{13} in Table VI. Furthermore, the orbital mixing of carbonyl π molecular orbital into carbonyl π^* molecular orbital in Table VII has an order of magnitude similar to that of the sum of d_{12} in Table VI, since the orbital mixing of carbonyl π orbital should be the sum of the contributions through the Al-1 and Al-2 levels. It should be pointed out that the signs of the orbital mixing are also in complete agreement with each other. Therefore, the increase in chemical reactivity by the catalyst in the Meerwein-Ponndorf reaction was found to be the result of the dynamic orbital mixing of the occupied carbonyl π molecular orbital with the unoccupied carbonyl π^* molecular orbital by way of the molecular orbitals of the aluminum alkoxide catalyst, as is shown in Figure 6.

Further Development of the Theory of Orbital Mixing

In the preceding sections, we derived the formulas and general rules for static and dynamic orbital mixings and applied them to the Diels-Alder and Meerwein-Ponndorf reactions with remarkable success. The most useful aspect of the general rules is that the change in molecular orbitals by the attack of a catalyst can easily be predicted from the molecular orbitals of the isolated substrate and the position of the attack. Molecular orbital drawings of representative substrates are now readily accessible in a recently published book.²⁸ Combination of an orbital drawing with our general rules for orbital mixing can give the prediction of the change in a frontier orbital concerned without molecular orbital calculations. It is needless to say that these general rules for static and dynamic orbital mixings can be applied not only to catalytic reactions but also to other fields in which orbital mixing plays an important role.

The general rules are to be considered valid only qualitatively and not quantitatively, since the formulas by the perturbation method are obtained by neglecting the changes in the electron-electron repulsion terms in the usual SCF procedure, i.e., by uncoupled approximation. As shown in the application of dynamic orbital mixing to the Meerwein-

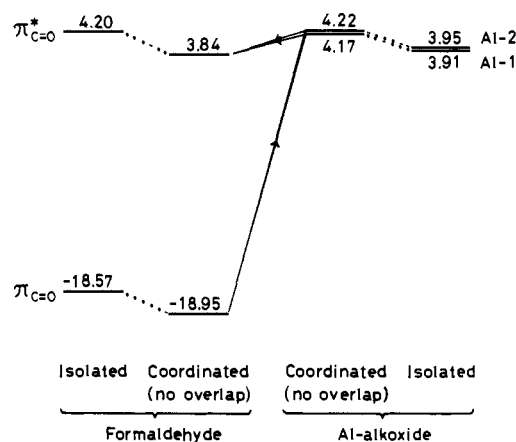


Figure 6. Schematic representation of dynamic orbital mixing (solid lines) in the Meerwein-Ponndorf reaction and of the change of the energy levels on coordination (with no overlap). The numbers are the energy levels of the molecular orbitals in eV.

Ponndorf reaction, the change in the relative heights of energy levels of a substrate and a catalyst may have a serious effect on the results. In order to develop a more quantitative approach, the change in the relative heights of energy levels concerned should be taken into explicit account. However, there is a relatively simple method to see whether or not the relative heights of the energy levels of a substrate and a catalyst do reverse. That is, the energy levels of the molecular orbitals go down when they interact with positive charges but go up with negative charges. On the other hand, the relative heights of energy levels of a substrate and a reagent can reasonably be expected to be not as serious as that of a substrate and a catalyst, since the electrostatic field due to a catalyst influences both the energy levels of a substrate and a reagent. The strength of the electrostatic field on a substrate might be different from that on a reagent due to the difference in the relative distance between the catalyst and the substrate, and between the catalyst and the reagent. However, this difference is probably not very important for the qualitative approach developed here. Moreover, it should be pointed out that we consider only the change in a frontier orbital and neglect the contribution of other orbitals to the change in chemical reactivity. This approximation can be rationalized from the fact that the change in chemical reactivity by a catalyst is brought about predominantly by the change in the frontier orbital, judging from the definition of superdelocalizability by Fukui et al.^{4,5} In order to obtain the quantitative measure for catalytic activity, we need to formulate the interaction energy between a reagent and a substrate under the influence of a catalyst including a change in electron-electron repulsion terms, as we are so doing at this time.

Finally, the meaning of multicenter interactions between a substrate and a catalyst may be derived from these general rules of orbital mixing. In other words, whether multicenter interactions strengthen or weaken orbital mixing, i.e., increase or decrease in chemical reactivity, can be predicted from the sign of molecular orbitals. For example, in static orbital mixing, a simultaneous interaction with two point charges (four-center interaction) gives the following coefficient of orbital mixing from eq 11

$$d_{ij} = -Z_{i1}C_{ir_1}^0C_{jr_1}^0\{(r_1r_1|t_1) - (r_m r_m|t_1)\}/(\epsilon_i^0 - \epsilon_j^0) - Z_{i2}C_{ir_2}^0C_{jr_2}^0\{(r_2r_2|t_2) - (r_m r_m|t_2)\}/(\epsilon_i^0 - \epsilon_j^0) \quad (16)$$

where t_1 and t_2 are designated as two point charges interacting with a substrate, and the neighbor term nearest to t_1 and t_2 is assumed to contain only one term, r_1 and r_2 , re-

spectively, for the sake of simplicity. From eq 16, it can be predicted that when $Z_{i_1}C_{ir_1}^0C_{jr_1}^0$ has the same sign as that of $Z_{i_2}C_{ir_2}^0C_{jr_2}^0$, the absolute value of d_{ij} increases in magnitude by the four-center interaction, in comparison with that by a two-center interaction, to lead to a larger change in chemical reactivity. On the other hand, when two terms have different signs, the reverse is true to lead to a smaller change in chemical reactivity. Similar features are expected for multicenter interactions for dynamic orbital mixing as well as combinations of static and dynamic orbital mixings. Consequently, catalytic activity for multicenter interactions should depend upon the symmetry of molecular orbitals, which is in harmony with the Woodward-Hoffmann rule⁶⁻⁸ of chemical reactivity already proven to be very useful for the prediction of catalytic activities.¹³ However, it should be worthwhile to note that our general rules can also be applied to the system lacking molecular symmetry. This conclusion has led us to the probability that catalytic action of enzymatic reaction can be illustrated by orbital mixings from signs of molecular orbitals concerned, since multicenter interactions are usually found in many enzymatic reactions. Studies on applications of orbital mixing to enzymatic reactions are now in progress and will be reported in the near future.

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Substituent Effects on Subjacent Orbital Control

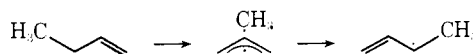
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Abstract: One electron MO theory indicates that subjacent orbital control is important in nonpolar 1,3 sigmatropic shifts but not in highly polar 1,3 shifts. This conclusion is supported by Mulliken-Wolfsberg-Helmholz, SCF-MO-INDO, and ab initio (STO-4G) calculations.

The Woodward-Hoffmann theory^{2a} of sigmatropic reactions has been the first systematic attempt to rationalize and predict the stereochemical outcome of these migrations. Recently, the limitations of one-determinant MO theory were pointed out and new *guidelines* for the prediction of the stereochemistry of pericyclic reactions in which the two interacting molecules or fragments bear substituents of varying electronic nature were proposed on the basis of a qualitative configuration interaction (CI) treatment.^{2b-d} In another recent development, Berson and Salem discussed "subjacent orbital control" as an important electronic factor which determines the stereochemistry of sigmatropic shifts.³ This treatment was carried out within the confines of one-determinant MO theory and the model reaction examined was the 1,3 sigmatropic shift of a methyl group

across an allyl framework, e.g., a nonpolar sigmatropic shift.



In our laboratories we have been interested in the effect of substituents upon the rates, stereoselectivity, and regioselectivity of pericyclic reactions. Thus, it became of interest to study the effect of substituents upon "subjacent orbital control" in 1,3 sigmatropic shifts, the reactions examined by Berson and Salem in their original publication. In this work we provide a general theoretical argument supported by Mulliken-Wolfsberg-Helmholtz (MWH) empirical,⁴ SCF-INDO semiempirical,⁵ and ab initio (STO-4G basis set)⁶ calculations which show that "subjacent orbital con-