Theory of Substitution in Conjugated Molecules[1]

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(Received May 17, 1954)

I. Introduction

What we call the *frontier electron theory*, which has been put forward to explain the reactivity of conjugated molecules, was first introduced in discussing the orientation in electrophilic substitutions in non-substituted aromatic hydrocarbons.[2] Afterwards, this method has been applied not only to electrophilic, but also to radical and nucleophilic substitutions as well as additions in substituted aromatic, heteroaromatic and other conjugated molecules, showing its utility, through a satis-

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[1] This paper was presented at 7th annual meeting of the Chemical Society of Japan, April 1, 1954.

[2] K. Fukui, T. Yonezawa and H. Shingu, *J. Chem. Phys.*, **20**, 722 (1952); K. Fukui, T. Yonezawa and C. Nagata, ibid., **21**, 174 (1953).

factory agreement of theory with experiment, for predicting the reactivity of the π-electron system.[3]

The frontier electron method is based on the assumption that the reaction should occur at the position of the largest density of the electrons in the frontier orbitals, which are defined according to the type of reaction, namely, the highest occupied orbital in the electrophilic reaction, the lowest vacant orbital in the nucleophilic reaction, and both the above in the radical reaction.

Among the existing theories of the chemical reactivity, the frontier electron method is characterized by the fact that it has not been derived deductively from any physical principle established, but has been found from an intuitive but chemical idea relating to the transition state in the process of substitution. By means of comparing the density distribution of the frontier electrons with the experimental positions of attack in the molecule, it has been recognized, rather as a solid fact than as a theory with a strong physical foundation, that frontier electrons must play some important role in the chemical activation.

In this connection, if a theory of substitution in conjugated molecules could be established in such a form as the frontier electron method which is deduced naturally from the mechanism assumed in the theory, it may be said that this theory would give a physical ground on the frontier electron method, and moreover, the mechanism assumed there would provide us with an important key for obtaining the knowledge of the transition state.

Under these circumstances, the present paper treats a theory of substitution in conjugated molecules, which, therefore, involves not a few assumptions. The validity of them can hardly be demonstrated directly, but can be inferred indirectly on the basis of the availability of the frontier electron method derived from them. This is ture because the agreement of the theory with the experiment proved in the preceding papers[2),3)] is sufficiently satisfactory to convince us that the inference mentioned above is probably reasonable.

II. σ-Part of the Energy of the System

As to the theoretical treatment of a substitution in conjugated molecules, there exists no current theory in which the mechanism of formation and dissociation of σ-bonds is taken into consideration explicitly. Consider a substitution in which the substituent atom X, attached to the rth carbon atom in the substrate π-electron system AX is replaced by a certain atom in a reagent B. The substitution is understood to proceed in such a way that the two σ-electrons shift gradually from AX σ-bond to AB σ-bond. A reaction parameter ρ is introduced, which acts as a measure of proceeding of the reaction and is defined by the following equations:

$$\delta_{AB}=\rho b, \tag{1}$$

$$\delta_{AX}=(1-\rho)a. \tag{2}$$

Here δ_{AB} and δ_{AX} are equal to $\int\chi_A H\chi_B d\tau$ and $\int\chi_A H\chi_X d\tau$, respectively, where χ_A, χ_X are the σ-atomic orbital (real) of the rth atom in A, and of the atom X in AX σ-bond, χ_B is the atomic orbital (real) of B which will form a σ-bond in the reaction, H is the effective Hamiltonian operator for a σ-electron, and a and b are the values of δ_{AX} and δ_{AB} in the isolated molecules AX and AB, respectively. The assumption of (1) and (2) may correspond to the mechanism called "bimolecular" by organic chemists. Then, the initial state is represented by putting ρ equal to zero and the final state by putting ρ equal to unity in the equation.

One electron energy can be obtained by solving the secular equation

$$\Delta\sigma(\varepsilon,\rho)=\begin{vmatrix} \alpha_B-\varepsilon & 0 & \delta_{AB} \\ 0 & \alpha_X-\varepsilon & \delta_{AX} \\ \delta_{AB} & \delta_{AX} & \alpha_A-\varepsilon \end{vmatrix}=0 \tag{3}$$

for any value of ρ, where α_A, α_X and α_B are $\int\chi_A H\chi_A d\tau$, $\int\chi_X H\chi_X d\tau$ and $\int\chi_B H\chi_B d\tau$, respectively.

For simplicity, the changes of α_A, α_B and α_X due to the change of ρ are ignored, because they are expected to have less serious influence upon the essence of the theory than the changes of δ_{AB} and δ_{AX}.# The following results are obtained by some algebraic manipulations of Equation (3):

(1) Among three roots $\varepsilon_1(\rho)$, $\varepsilon_2(\rho)$ and $\varepsilon_3(\rho)$ of Equation (3) $(\varepsilon_1<\varepsilon_2<\varepsilon_3)$, $\varepsilon_1(\rho)$ has a maximum value when ρ varies from zero to unity if either one of the following two conditions, i and ii, is satisfied.

i $\alpha_B>\alpha_X$ and $(\alpha_B-\alpha_X)(\alpha_A-\alpha_X)<b^2$, (4)

ii $\alpha_B<\alpha_X$ and $(\alpha_X-\alpha_B)(\alpha_A-\alpha_B)<a^2$. (5)

(2) As long as the condition (4) or (5) is satisfied, $\varepsilon_1(0)$ is equal to the lower σ-level of AX σ-bond in the isolated AX molecule and $\varepsilon_1(1)$ is the lower σ-level of AB σ-bond in the isolated AB molecule. In this case two σ-electrons in AX σ-bond enter into AB σ-bond across a point of the maximum energy along a continuous curve $\varepsilon_1(\rho)$. Thus (4) or (5) may be regarded as the condition which must be satisfied when the substitution

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3) K. Fukui, T. Yonezawa, C. Nagata and H. Shingu, *J. Chem. Phys.*, **22**, 1433 (1954); K, Fukui, T. Yonezawa, C. Nagata and H. Shingu, Summary of the Symposium on Atoms and Molecules, *Japan Phys. Soc.*, p. 27 (1953).

But this is a point which may need further investigation. Especially, it should be noted that the assumption of constancy of both α_A etc. and δ_{AB} etc. sometimes leads us to an unreasonable result (compare e.g. the calculation of H_3 molecule by Van Vleck and Sherman (*Rev. Mod. Phys.*, **7**, 167 (1935)), which is, however, not the present case, where the mode of change of δ's is assumed by the equation (1) and (2).

proceeds adiabatically. In the present paper only the case when this condition is satisfied is treated.

(3) The maximum value of $\varepsilon_1(\rho)$, $\varepsilon_1^{\ddagger}$, is given by

$$\varepsilon_1^{\ddagger}=\frac{1}{2}[\alpha_A+\alpha_{BX}-\{(\alpha_A-\alpha_{BX})^2+c^2\}^{1/2}], \tag{6}$$

and $\rho^{\ddagger}$, the value of ρ at the maximum point, is also given by

$$\rho^{\ddagger}=\frac{1}{2(a^2+b^2)}[[2a^2+(\alpha_B-\alpha_X)[\alpha_A-\alpha_{BX} + \{(\alpha_A-\alpha_{BX})^2+c^2\}^{1/2}]]], \tag{7}$$

where $\alpha_{BX}=(a^2\alpha_B+b^2\alpha_X/(\alpha^2+b^2)$, and $c^2=4a^2b^2/(a^2+b^2)$. Conditions (4) and (5) correspond to the condition that $\rho^{\ddagger}$ is in the range from zero to unity.

(4) The higher level $\varepsilon_2(\rho)$, which varies continuously from α_B to α_X when ρ changes from zero to unity, has neither maximum nor minimum at $0<\rho<1$, when the condition (4) or (5) is satisfied.

(5) When the eigenfunctions belonging to the eigenvalues $\varepsilon_i(\rho)$ (i=1, 2, 3) are written as

$$\psi_\sigma{}^{(i)}=c_A{}^{(i)}\chi_A+c_X{}^{(i)}\chi_X+c_B{}^{(i)}\chi_B,$$

the following relations always hold between the coefficients in the wave functions.

$$c_X{}^{(1)}\cdot c_B{}^{(1)}>0$$
$$c_X{}^{(2)}\cdot c_B{}^{(2)}<0$$
$$c_X{}^{(3)}\cdot c_B{}^{(3)}>0$$

All of these characteristics derived mathematically from Equation (3) have an important meaning in constructing the theory of substitution.

The energy $\Delta\varepsilon\sigma$, which is twice as much as the difference between $\varepsilon_1^{\ddagger}$ given by Equation (6) and $\varepsilon_1(0)$ and hence may be considered as the σ-part of the activation energy in the substitution, is given by

$$\Delta\varepsilon\sigma=\frac{a^2(\alpha_B--\alpha_X)}{a^2+b^2}+\sqrt{(\alpha_A-\alpha_X(^2+4a^2}$$
$$-\sqrt{\left(\alpha_A-\frac{a^2\alpha_B+b^2\alpha_X}{a^2+b^2}\right)^2+\frac{4a^2b^2}{a^2+b^2}}. \tag{8}$$

The fact that $c_X{}^{(2)}$ and $c_B{}^{(2)}$ have opposite signs is important in connection witn the statement in the next section.

III. Hyper Conjugation in the Transition State

In Section II, it is stated that the coefficients $c_X{}^{(2)}$ and $c_B{}^{(2)}$ in the eigenfunction belonging to $\varepsilon_2(\rho)$ always have opposite signs. Here it is desired to examine generally the quantitative relation between $|c_X{}^{(2)}|^2$ and $|c_B{}^{(2)}|^2$ when ρ is equal to $\rho^{\ddagger}$, but this is too complicated to be carried out analytically. For this reason the case when B is equal to X is at first considered. We could distinguish B from X e.g. by means of labelling them isotopically. In this case eigenfunctions and $\rho^{\ddagger}$ are easily written explicitly as

$$\begin{aligned}\psi_\sigma{}^{(1)\ddagger}&=2^{-1/2}A^{-1/2}\{(A-\alpha_A+\alpha_B)^{1/2}\chi_A\\&\quad+2^{-1/2}(A+\alpha_A-\alpha_B)^{1/2}(\chi_B+\mathrm{c}_X)\}\\ \psi_\sigma{}^{(2)\ddagger}&=2^{-1/2}(\chi_B-\chi_X)\\ \psi_\rho{}^{(3)\ddagger}&=2^{-1/2}A^{-1/2}\{(A+\alpha_A-\alpha_B)^{1/2}\chi_A\\&\quad-2^{-1/2}(A-\alpha_A+\alpha_B)^{1/2}(\chi_B+\chi_X)\}\\ \rho^{\ddagger}&=1/2\end{aligned} \tag{9}$$

where $\psi_\sigma{}^{\ddagger}$ corresponds to ψ_σ when ρ is equal to $\rho^{\ddagger}$, and $A=\{(\alpha_A-\alpha_B)^2+2a^2\}^{1/2}$. The orbital $\psi_\sigma{}^{(2)\ddagger}$ in Equation (9) is antisymmetric with respect to the plane which is perpendicular to the line connecting B to X across its middle point.

As the reagent B is believed to approach to the rth atom in A from the direction perpendicular to the plane in which all the carbon atoms of AX lie, this plane is considered to cross the line BX at its middle point when ρ is equal to $\rho^{\ddagger}$. Thus the orbital $\psi_\sigma{}^{(2)\ddagger}$ is parallel to the π-orbitals in A and is antisymmetric to the above-stated plane. This fact is, therefore, sufficient to make us believe the possibility of a hyperconjugation between the π-orbitals in A and the orbital $\psi_\sigma{}^{(2)\ddagger}$.* It is not so unreasonable to consider that the hyperconjugation may take place more or less even when B is not equal to X. It is our opinion similar to Mulliken et al. that this hyperconjugation, taking part in the electronic interaction of the system near the transition state, causes a delocalization of π-electrons from A to the reaction center or vice versa and plays an important role in decreasing the activation energy.

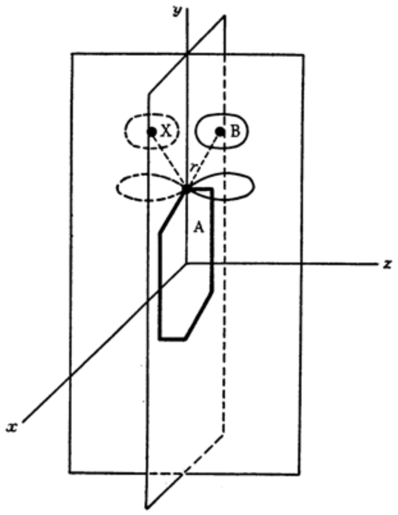

Fig. 1. Schematic diagram of hyperconjugation in the transition state.

IV. π-Part of the Energy of the System

As can be seen in Equation (9) the orbitals $\psi_\sigma{}^{(1)\ddagger}$ and $\psi_\sigma{}^{(3)}$ in which coefficient of χ_B is equal to that of χ_X, are free from conjugation with A. In calculating the π-part of the energy, therefore, these orbitals are left out of consideration, even when B is not equal to X, according to the relation mentioned in (5).

The state, in which the total energy of the whole system is maximum, is not always equal to the state $\rho=\rho^{\ddagger}$, except when B is equal to X. Thus, in a strict sence, it is not correct to regard the state $\rho=\rho^{\ddagger}$ as the transition state. But, in order to avoid complicating the problem and missing more

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* This consideration was first introduced by Mulliken et al. (L. W. Pickett, N. Muller, and R. S. Mulliken, *J. Chem. Phys.*, **21**, 1400 (1953).) to explain the stabilization of $C_6H_7^+$ ion. Their work modifies the excessively large value of localization energy reported by Wheland (*J. Am. Chem. Soc.* **64**, 900 (1940)).

important conclusions, it might be allowable here to proceed with the discussion taking the state $\rho=\rho^{\ddagger}$ as the transition state. The eigenvalue ε_2 belonging to $\psi_\sigma{}^{(2)\ddagger}\equiv\psi_h$ is denoted by α_h, and the orbital ψ_h is referred to as a *pseudo-π-orbital.*

The empirical classification of substitution reached by organic chemists, i.e. electrophilic, radical and nucleoppilic is naturally introduced into the theory in the following manner. Namely, acoording as the the reagent B is electrophilic, radical or nucleophilic, the orbital ψ_h is considered to be occupied by 0, 1 or 2 electrons, respectively.

Now the π-energy in the transition state can be calculated by means of ordinary LCAO method. The secular equation for the transition state is written as

$$\Delta_\pi=\begin{vmatrix} \alpha_h-\varepsilon & \gamma & 0 & \\ \gamma & \alpha_r-\varepsilon & \beta_{r,r+1} & \\ 0 & \beta_{r,r+1} & \alpha_{r+1}-\varepsilon & \\ \vdots & & \begin{pmatrix}\text{Secular equation}\\ \text{for AX}\end{pmatrix} & \end{vmatrix}=0, \qquad (10)$$

where each α_s and β_{st} is the Coulomb integral of the sth atom and the resonance integral between the sth and the tth atomic orbitals in the isolated AX molecule, and γ is the resonance integral of the quasi-bond between the pseudo-π-orbital and the rth atom in A. The values of these integrals in Equation (10), which concerns the transition state, differ from those in the isolated molecule, but these differences, which are believed to have no any serious influence on the present theory, are here ignored.

In fact, the change in the Coulomb integral α_r caused electrostatically by the approaching reagent in a heterolytic substitution has no longer any essential significance,* so long as a considerable amount of delocalization of electrons, which will be stated below, takes place.

It is rather easy to extend the present theory to the case when a conjugation occurs between AX and B which possesses π-electrons, but this extension is not included in the present paper[4]

Making use of the perturbation theory by regarding γ as small, the π-activation energy for a non-degenerate system** is obtained as

$$\Delta E_\pi=\sum_{j=1}^{N}\frac{(\nu_j-\nu)C_r{}^{(j)2}}{\varepsilon_j-\alpha_h}\gamma^2+\nu(\alpha_h-\alpha_B), \qquad (11)$$

where N is the total number of π-orbitals in the isolated AX molecule, ν_j and $C_r{}^{(j)}$ are the number of electrons (0, 1, or 2) and the coefficient of the rth atomic π-orbital in the jth molecular orbital, respectively, the energy of which is ε_j, and ν is 0, 1 or 2 according as the reagent B is electrophilic, radical and nucleophilic, respectively.

The extent of mutual delocalization of electrons between the pseudo-π-orbital and the initial π-electrons system AX, is represented by

$$\Delta q_h=\sum_{j=1}^{N}\frac{(\nu_j-\nu)C_r{}^{(j)2}}{(\varepsilon_j-\alpha_h)^2}\gamma^2, \qquad (12)$$

where Δq_h is the difference between the total electron density at BX-part in the transition state and the value ν.

The value of α_h is generally understood to be small for an electrophilic reaction and large for a nucleophilic reaction, but this is not necessarily so in the case when the electron delocalization represented by (12) exists. It can easily be shown that Δq_h is always positive for an electrophilic reaction and is negative for a nucleophilic reaction. The delocalization which occurs in an electrophilic substitution from AX to pseudo-π-orbital makes the value of α_h increase and the delocalization from the pseudo-π-orbital to AX in a nucleophilic substitution makes it decrease, and in both the cases the delocalization will cease after the values of integrals in the whole system become self-consistent. Moreover, in heterolytic reactions, the positive or the negative charge in the activated complex distributes over the whole system and never localizes at the orbital ψ_h. In a homolytic reaction, of course, the value of α_h is very close to that of Coulomb integral of the rth atom in the isolated AX molecule. In these circumstances an assumption is made that α_h is always equal to α, the value of Coulomb integral of a carbon atom in benzene. This assumption may have room for improvement in case of modification of the theory in such a way that the self-consistency is satisfied, but it seems rather more concise and useful in the present stage to grasp the essential feature of the mechanism of substitution.

Putting α_h equal to α, the first term in the right side in Equation (11) is always negative, and so it is seen that the hyperconjugation in the transition state decreases the activation energy in a substitution.

V. Relation to the Frontier Electron Theory

Since the σ-part of the activation energy, (8), is a constant if the reagent B and the substituent X are fixed, the relative rate of substitution of a definite type in conjugated molecules by a definite reagent can be measured by the amount of the coefficient of γ^2 in Equation (11). This quantity referred to tentatively as *super-delocalizability* and denoted by S_r, that is

$$S_r=\sum_{j=1}^{N}\frac{(\nu_j-\nu)C_r{}^{(j)2}}{\varepsilon_j-\alpha}\beta, \qquad (13)$$

in which the resonance integral of a C-C bond in benzene, β, is multiplied to make it dimensionless. When ε_j is expressed in the form $\alpha+\lambda_j\beta$,

$$S_r=\sum_{j=1}^{N}\frac{(\nu_j-\nu)C_r{}^{(j)2}}{\lambda_j} \qquad (13)'$$

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* But the change of β_{XR} must be taken into account when the atom X possesses π-electrons or a π-orbital which can conjugate with the π-electrons in A, because a considerable change in the bond AX may occur in the transition state.

[4] C. A. Coulson and H. C. Longuet-Higgins, *Proc. Roy. Soc.*, A **195**, 188 (1948); M. J. S. Dewar, *J. Am. Chem. Soc.*, **74**, 3341 (1952); T. Yonezawa, K. Hayashi, C. Nagata and K. Fukui, *Summary of the Symposium on π-electrons*, Jap. Chem. Soc., p. 26 (1952).

** For a degenerate system a similar equation can easily be derived.

\# When AX is an odd molecule an equation of type of (15) should be used instead of (11).

Then S_r is positive for almost all of the usual compounds, and the greater the value, the more reactive is the rth position of the compound.

When AX is an even molecule and its occupied levels are denoted by 1, 2,......, m and the unoccupied levels by m+1, m+2,......, N, S_r is written in three cases as:

(i) For an electrophilic reaction

$$S_r^{(E)}=2\sum_{j=1}^{m}\frac{C_r^{(j)2}}{\lambda_j},$$

(ii) for a radical reaction

$$S_r^{(R)}=\sum_{j=1}^{m}\frac{C_r^{(j)2}}{\lambda_j}+\sum_{j=m+1}^{N}\frac{C_r^{(j)2}}{(-\lambda_j)},$$

(iii) for a nucleophilic reaction

$$S_r^{(N)}=2\sum_{j=m+1}^{N}\frac{C_r^{(j)2}}{(-\lambda_j)}. \tag{14}$$

Since, in many compounds especially in large molecules, λ_m and λ_{m+1} are considerably small compared with the other λ's, the magnitude of S_r is determined predominantly by the term whose j is m+1 or m. $S_r^{(E)}$ is large when $2\ C_r^{(m)2}$, i.e. the electron density at the rth atom in the highest occupied orbital, is large, and $S_r^{(N)}$ is large when $2C_r^{(m+12)}$, i.e. the electron density at the rth atom in the lowest vacant orbital, is large. In a radical substitution $S_r^{(R)}$ is large when $C_r^{(m)2}+C_r^{(m+1)2}$ is large, so far as λ_m is approximately equal to $(-\lambda_{m+1})$.

When AX is a neutral odd molecule, in which the mth orbital is partly occupied and its energy is approximately equal to α, the perturbation theory for a degenerate system is available. The π-activation energies are obtained as:

(i) For an electrophilic reaction.

$$\varDelta E_\pi=|C_r^{(m)}|\gamma+S_r^{(E)}\frac{\gamma_2}{\beta},$$

$$S_r^{(E)}=2\sum_{j=1}^{m-1}\frac{C_r^{(j)2}}{\lambda_j}\sim2\frac{C_r^{(m-1)2}}{\lambda_{m-1}}$$

(ii) For a radical reaction

$$\varDelta E_\pi=2|C_r^{(m)}|\gamma+S_r^{(R)}\frac{\gamma^2}{\beta}+(\alpha-\alpha_B)\sim2|C_r^{(m)}|\gamma,$$
$$+(\alpha-\alpha_B)$$

$$S_r^{(R)}=\sum_{j=1}^{m-1}\frac{C_r^{(j)2}}{\lambda_j}+\sum_{j=m+1}^{N}\frac{C_r^{(j)2}}{(-\lambda_j)},$$

and in this case the first order perturbation term is dominant,

(iii) For a nucleophilic reaction

$$\varDelta E_\pi=|C_r^{(m)}|\gamma+S_r^{(N)}\frac{\gamma^2}{\beta}+2(\alpha-\alpha_B),$$

$$S_r^{(N)}=2\sum_{j=m+1}^{N}\frac{C_r^{(m+1)2}}{(-\lambda_j)}\sim2\frac{C_r^{(m+1)2}}{(-\lambda_{m+1})}, \tag{15}$$

The orbital which determines dominantly the value of S_r in each type of reaction is the same as the *frontier orbitals* which have previously been pointed out by the present authors as playing an important role in the course of reaction. Thus the frontier electron theory is deduced naturally.

If $\varDelta E_\pi$ is calculated in the case of naphthalene, as an example, by solving Equation (10) directly without using the perturbation theory, it can be shown that $|\varDelta E_\pi|$ of α-position is always larger than that of β-position for any value of γ, and the circumstances are entirely the same concerning 1 and 2 positions in butadiene. The conclusion obtained in the present paper, therefore, never depends on the assumption that the value of γ in (10) is so small that the perturbation method may be used for solving Equation (10).

IV. Summary

A theory concerning the mechanism of substitution in conjugated molecules is stated. The energy of the whole system is divided into σ- and π-parts. When certain relations hold between some integrals of σ-electrons, the σ-part of the energy of the system has a maximum in the process of the reaction, by which the transition state is defined. In the transition state a hyperconjugation may take place between the initial π-electron system and the pseudo-π-orbital in the vicinity of the reaction center. By means of the perturbation method, the π-part of the energy of the system involving the pseudo-π-orbital is obtained. The perturbation energy is always negative and by the magnitude of its absolute value, the reactivity of conjugated molecules can be discussed in a definite type of reaction with a definite reagent. From an approximate expression of this perturbation energy, the frontier electron theory is derived, which has previously been proposed by the present authors, whose coincidence with chemical experiences has already been ascertained. The mechanism stated above, therefore may supply us with a key to grasp a feature of the transition state and at the same time may present us with a physical meaning of the frontier electron theory.

The authors wish to express their heartfelt gratitudes to Professor R.S. Mulliken and to Professor C. A. Coulson for their suggestive discussions on the present problem at the International Conference of Theoretical Physics in Japan, September 1953.

Financial support for this work has been received in part from GAFSR, (1953–59168), Education Ministry, Japanese Government.

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