[CONTRIBUTION FROM THE SIR JOHN CASS COLLEGE]

Charge Shifts and the Reactions of Conjugated Molecules

BY H. H. GREENWOOD

RECEIVED JULY 29, 1954

The charge shifts implicit in Coulson and Longuet-Higgins' theory of the reactions of conjugated molecules are studied. These suggest bond formation with electrophilic reagents by means of the most tightly bound pair of the π-electron system, a result which contrasts with conventional bonding concepts and with Fukui's hypothesis that the least bound *frontier* electrons are primarily concerned in this role. The charge shifts describe a polarization process associated with a physically satisfactory mechanism and provide a link with Wheland's alternative polarization method.

In a series of recent papers Fukui, *et al.*,[1] have suggested that the pair of π-electrons of importance for bond formation between a conjugated molecule and an attacking electrophilic reagent is the pair occupying the least bound occupied energy level of the π-electron system. These two electrons were termed the frontier electrons. Some time ago the author[2] put forward an alternative opinion that the two electrons occupying the most tightly bound energy level of the π-electron system are the pair concerned in bond formation with an electrophilic reagent. The postulate of Fukui, *et al.*, was based upon molecular orbital calculations which showed that in the unperturbed ground state of conjugated molecules the atom positions most active toward electrophilic reagents are just the positions at which the frontier electron density is greatest. The author's alternative proposal was based upon the implications of the equation

$$\delta\xi = q_r\delta\alpha_r + \frac{1}{2}\pi_{r,r}\delta\alpha_r^2 \qquad (1)$$

due to Coulson and Longuet-Higgins[3] which relates the change $\delta\xi$ in π-electron energy due to a change $\delta\alpha_r$ in coulomb integral at the position r of attack to the charge density q_r and self polarizability $\pi_{r,r}$ at that atom. The change $\delta\alpha_r$ is assumed to represent approximately the effect upon the π-electron system of an ion in the neighborhood of atom r where $\delta\alpha_r$ is negative for electrophilic attack. There appears at first sight to be no contradiction between Fukui's interpretation and that of equation 1 since numerical values of q_r and $\pi_{r,r}$ in the unperturbed ground state predict the same active positions as those deduced from the frontier electron density. This is simply because the physical implications of equation 1 have not, as yet, been fully explored. Associated with the change $\delta\xi$ is a corresponding change in π-electron configuration which represents the spatial distortion due to the polarization of the π-electron system by the electrophilic reagent. The study of the changes in configuration reveals not merely the discrepancy with Fukui's interpretation but also the nature of errors which may arise in interpretations based upon studies of the static distribution of the unperturbed ground state. It emphasizes the need for examination of the relation of this static configuration toward *changes* in configuration. This in itself provides a test of the goodness of equation 1 where, for example, a change in π-electron configuration toward a distribution unfavorable for bond formation at the position of attack would clearly diminish its claim as a suitable criterion.

Charge Shifts in Conjugated Molecules.—The details of the change in π-electron configuration associated with the change $\delta\xi$ of equation 1 can be obtained by solving numerically the corresponding molecular orbital (m.o.) secular equations with $\delta\alpha_r$ negative for electrophilic attack. For this purpose $\delta\alpha_r = k\beta$ where k is a positive number and β the resonance integral is negative, and the simplest m.o. technique, neglecting overlap, is used. Numerical results possess the following features.

(a) The energy levels $\epsilon_j (j = 1, 2 \ldots\ldots n)$ labeled in order with ϵ_1 the lowest, are all lowered. The lowering of ϵ_1 is limited only by the magnitude of $\delta\alpha_r$. The remaining levels are lowered toward limiting values which are those pertaining to the conjugated system obtained by excluding from the original conjugated molecule the position under attack. This we shall call the residual molecule.[4] The level ϵ_2 is lowered toward the lowest level of the residual molecule, ϵ_3 toward the second lowest and so on, with no crossing of levels.

(b) The wave functions are modified so that ψ_1 tends to become increasingly localized around the atom r under attack. Thus using the m.o. (L.C.A.O.) approximation

$$\psi_j = \sum_{r=1}^{n} C_{rj}\phi_r$$

ψ_1 changes so that $C_{r_1} \rightarrow 1$ and $C_{s_1}(S \neq r) \rightarrow 0$. Correspondingly ψ_2 tends toward the wave function describing the lowest level of the residual molecule, ψ_3 toward that describing the second lowest and so on.

(c) The changes in all wave functions are such that the charge distributions for the perturbed ground state, calculated from the formula for the charge density q_s at the s th atom

$$q_s = 2\sum_{j=1}^{n/2} C^2_{sj}$$

in which the lowest levels are occupied by π-electron pairs having coupled spins, show a net flow of π-electron negative charge toward the position r of attack.

There is an obvious consistency in the change in the levels ϵ_2, ϵ_3, etc., and in the corresponding wave functions ψ_2, ψ_3, etc., toward the energy levels and wave functions of the residual molecule. Let us take, for example, the case of attack at atom $r = 1$ of the naphthalene (Fig. 1a) molecule, the residual molecule for which is shown in Fig. 1b.

---

[1] K. Fukui, T. Yonezawa and H. Shingu, *J. Chem. Phys.*, **20**, 722 (1952).

[2] H. H. Greenwood, *ibid.*, **20**, 1653 (1952).

[3] C. A. Coulson and H. C. Longuet-Higgins, *Proc. Roy. Soc.* (*London*), **A192**, 16 (1947).

[4] R. D. Brown, *Quart. Rev.*, **4**, 63 (1952).

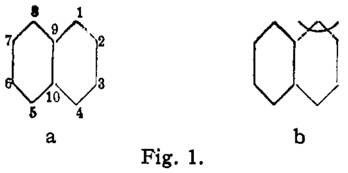

Fig. 1.

Equation 1 implies that the levels ϵ_2 to ϵ_{10} of naphthalene are lowered, with no crossing of levels, toward the nine levels of the residual molecule, whilst the wave functions ψ_2 to ψ_{10} correspondingly change in configuration toward those describing the same nine levels of the residual molecule. The level ϵ_1 is lowered by an extent which depends upon the magnitude of $\delta\alpha_1$ and the wave function ψ_1, becomes increasingly localized round atom 1 in the sense that it tends to become increasingly identified with the atomic orbital ϕ_1. These results mean that the pair of π-electrons occupying the deepest level ϵ_1 tend to become increasingly localized at the atom position 1 of attack. The remaining π-electrons are simultaneously progressively removed from this atom into the region of the residual molecule defined by atoms 2 to 10.

Fortunately it is unnecessary to seek support of these findings in extensive numerical calculations since an explanation can be found in familiar physical and quantum mechanical principles. Thus the net flow of π-electron negative charge into the region under attack, noted in item (c) follows from conventional electrostatics, as indeed does the lowering of the individual energy levels described in (a) which is due to the increased binding produced by the added positive charge represented by the change $\delta\alpha_r$. The change in configuration described in (b) may be explained by appeal to two quantum mechanical principles. Firstly the wave function describing the lowest energy level possesses the same symmetry as the Hamiltonian of the system. Thus if the Hamiltonian is distorted by a lowering of potential in the region under attack, the wave function ψ_1 describing the lowest level will be correspondingly distorted to give a relatively increased amplitude in the same region. The argument can be illustrated in a simple diagram by comparison with the behavior of the lowest level wave function for the particle in a box problem, though it must be emphasized that the comparison is merely utilitarian and not accurate in details.

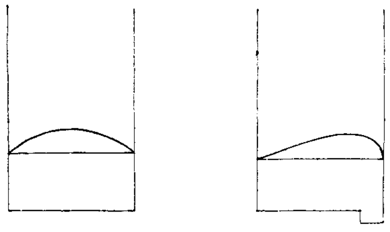
(a) (b)

Fig. 2.

The wave function describing the lowest level (Fig. 2a) is distorted by the well introduced in Fig. 2b to give a relatively increased amplitude in the region of the well. Now the change $\delta\alpha_r$ in coulomb integral at the position of electrophilic attack represents, with $\delta\alpha_r$ negative, a similar local lowering in the potential field. Thus the amplitude of ψ_1 increases at the position of attack and the pair of electrons occupying this orbital is therefore drawn toward the position of attack. Now we appeal to the exclusion principle to account for the progressive removal of all other π-electron pairs from the position of attack. Since, in the absence of excitation, there exists just one orbital ϕ_r associated with the atom r under attack, it follows that the increase in density at this position of the pair of electrons occupying the lowest level, must, in accordance with the exclusion principle, be accompanied by a decrease at the same position of all other π-electron pairs.

Discussion

It is now possible to recognize the discrepancy between the interpretation of equation 1 and the hypothesis that the *frontier* electrons are primarily concerned in bond formation with an electrophilic reagent. For according to the above analysis equation 1 implies that the π-electron pair drawn toward the position of attack during the polarization of the system by an electrophilic reagent is the pair occupying the lowest energy level, and that the remaining π-electron pairs, including the *frontier* electrons, are simultaneously removed from this position. Thus the progressive removal of the frontier electrons from the position of attack during the polarization process of equation 1 denies the hypothesis which links them with bond formation. It must be replaced according to equation 1 by the hypothesis which associates bond formation with the neighboring electrophilic reagent by means of the π-electron pair occupying the lowest level, which for brevity we shall call the π-valence electrons. It is, of course, possible to question the validity of equation 1 in this role, in so far as it represents the effect of a perturbing system outside the conjugated molecule somewhat arbitrarily by a perturbing center within the molecule. The result obtained furthermore conflicts with conventional concepts of bonding which have hitherto associated bond formation during chemical processes with the least bound electrons of the participating systems. Fukui's hypothesis, by contrast, subscribes to these concepts. Yet if we accept the polarization of the π-electron system by the electrophilic reagent then, irrespective of any method of approximation, the charge shifts must take place in accordance with the physical and quantum mechanical principles enumerated above. Thus the polarization process, which must surely form an integral part of the reaction mechanism, precludes the frontier electrons from participating in bond formation at the position of attack.

It is interesting to compare the frontier electron[1] (Fig. 3a) and π-valence electron (Fig. 3b) distributions in the ground state configuration of, for example, anthracene

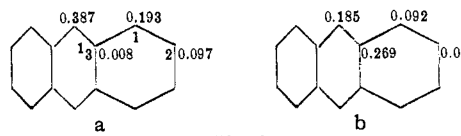

Fig. 3.

The frontier electron density distribution parallels the observed order of reactivity toward electrophilic attack, namely, meso > 1 > 2 which the π-valence electron density fails to do, unless one omits from consideration the high density at the non-perimeter atoms. Yet the ease with which the π-valence electrons are brought to the position of electrophilic attack varies, according to the implications of equation 1, in the order meso > 1 > 2 > 13 for which the self polarizabilities[5] are $\pi_{9,9} = 0.526$, $\pi_{1,1} = 0.454$, $\pi_{2,2} = 0.411$ and $\pi_{13,13} = 0.331$. In general in alternant hydrocarbons the success of the frontier electron density distribution in reflecting the experimental data is paralleled by the failure of the π-valence electron density to do likewise, unless one excludes from consideration the large densities at the non-perimeter atoms as in anthracene. It is clear, therefore, that considerable care must be exercised in the deduction of physical interpretations from correlations between experimental data and static π-electron configurations. It is vital to relate static configurations to changes in configuration, an investigation which advances strong support for equation 1 in preference to the frontier electron concept. Equation 1 also illustrates that in a polarization process the ease of provision of a pair of electrons at the position of attack depends not upon the density of this pair in the unperturbed molecule, but rather upon the total density q_r, or better still, upon the total π-electron configuration. Thus the process concerns both the appearance of a pair at the position of attack and the simultaneous removal of all other π-electron pairs, two complementary processes which cannot be separated. Hence in the unperturbed ground state q_r and $\pi_{r,r}$ are the appropriate criteria and not the density of a particular pair.

Finally the details of the polarization process provide a link between the two methods of approximation used for the description of the reactions of conjugated molecules, namely, the method of equation 1 and the alternative transition state method of Wheland.[6] The numerical correlation observed hitherto is now consolidated by the obvious physical connection indicated by the change in electron configuration implicit in (1) toward that used in Wheland's method. Numerically the π-valence electron density in benzene, for example, increases at the position of attack from 0.333 in the ground state to 1,378 for the change in coulomb integral $\delta\alpha_r = 2\beta$, a change which has been used to represent the effect of the neutral oxygen atom in a conjugated molecule[4,7] and which, therefore, does not appear to be excessive as a representation of the effect due to the net positive charge carried by a neighboring electrophilic reagent. Thus the π-valence electron density achieves a high degree of localization at the position of attack for a relatively small perturbation.

Nucleophilic reactions can be considered in exactly the same way as for electrophilic. The details of the charge shifts are less interesting since the whole system of π-electrons is removed from the position of attack, as in an analogous classical problem. Nevertheless the charge shifts take place in accordance with the physical and quantum mechanical principles enumerated earlier.

(5) H. C. Longuet-Higgins and C. A. Coulson, *J. Chem. Soc.*, 971 (1949).

(6) G. W. Wheland, THIS JOURNAL, **64**, 900 (1942).

(7) G. W. Wheland and L. Pauling, *ibid.*, **57**, 2086 (1935).

ALDGATE, LONDON, ENGLAND

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

Equilibrium Constants of the Reaction between Sulfite and Oxidized Glutathione

BY W. STRICKS, I. M. KOLTHOFF AND R. C. KAPOOR

RECEIVED OCTOBER 16, 1954

The reversible reactions between sulfite or bisulfite with oxidized glutathione (GSSG + $SO_3^{=}$ $\rightleftarrows$ GS^- + $GSSO_3^-$, GSSG + HSO_3^- $\rightleftarrows$ GSH + $GSSO_3^-$) have been studied quantitatively in the *p*H range 12.4 to 5.2. From the results, four equilibrium constants for the reactions involving $SO_3^{=}$ and the various charge types of oxidized and reduced glutathione and glutathione sulfonate and one constant for the reaction of one charge type with HSO_3^- have been calculated. The heat of reaction was estimated from the values of the equilibrium constants at 12 and 25°. The results were compared with data for the analogous reactions between sulfite with cystine and with dithiodiglycolic acid.

In the course of investigations on the reactivity of disulfide groups in proteins and peptides it appeared of interest to study in a quantitative way the reaction between oxidized glutathione and sulfite and to compare the results with the data previously reported[1] for the analogous reactions of sulfite and cystine and dithiodiglycolic acid.

The reaction between oxidized glutathione (GSSG) and sulfite was studied at various *p*H and temperatures. Equilibrium constants and the heat of reaction have been calculated from results obtained by the polarographic method of analysis.

Materials.—Oxidized glutathione was prepared from glutathione in the reduced state by a method described in a previous paper.[2] Sodium sulfite was a C.P. reagent grade Merck product. All the other chemicals were C.P. reagent grade products.

Stock solutions of oxidized glutathione were 0.02 *M* in GSSG. The stock solutions were analyzed for GSSG by the polarographic method[2] and also by amperometric mercurimetric titration at the dropping mercury electrode as indicator electrode.[3] Stock solutions of sulfite were prepared with air-free water and were 0.2 to 0.5 *M* in sodium sulfite. They were analyzed for sulfite iodometrically. Only freshly prepared sulfite solutions were used.

---

(1) W. Stricks and I. M. Kolthoff, THIS JOURNAL, **73**, 4569 (1951).

(2) W. Stricks and I. M. Kolthoff, *ibid.*, **74**, 4646 (1952).

(3) W. Stricks, I. M. Kolthoff and N. Tanaka, *Anal. Chem.*, **26**, 299 (1954).