Ortho-localisation Energies for Methyl-1 : 2 benzanthracenes

By Takeshi NAKAJIMA

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Introduction

Various theories have been advanced with a view to examining the hypothesis proposed by Pullman[1] that the carcinogenic activity of the polycyclic hydrocarbons is due to the high π-electron density of the so-called K region (the 3–4 bond, for example, of 1: 2-benzanthracene (B. A.) in Fig. 1). In addition to the electron densities, mobile-bond orders and net free valence values with regard especially to the 3–4 bonds of several methyl-benzanthracenes (M.B.A.) have been calculated rather in the rough approximations by Pullman and Pullman[2], and Daudel and Daudel[3]. Recently, based on the per-

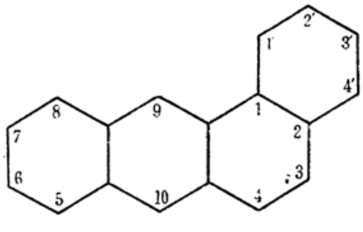

Fig. 1. 1:2-Benzanthracene.

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[1] A. Pullman, *Ann. Chim.*, 2, 5 (1947).

[2] A. Pullman and B. Pullman, *Bull. Soc. Chim. Biol.*, XXXI, 343 (1949).

[3] P. Daudel and R. Daudel, *J. Chem. Phys.*, 16, 639 (1950).

turbation method, Greenwood[4] has made the more rigorous calculations of these quantities. All these quantities as the criteria of the reactivity of a conjugated bond are concerned with the π-electron configuration in the non-reacting ground state.

The other method of approach for the discussion of bond reactivity is the localisation (polarisation) method due originally to Wheland[5] and extended by Brown[6]. According to this method reactivity of a conjugated bond is correlated with the ortho (bond) localisation energy (O.L.E.), defined as the energy required to convert the conjugated bond in question into a double bond. Recently, Pullman, Pullman, and Berthier[7] have calculated O. L. E. for the 3–4 bonds of several M.B.A. and reached the conclusion that the reaction homolytic in nature should occur at the 3–4 bond in contradiction to the conclusion put forward by Greenwood that the reaction should be heterolytic in nature. In virtue of the rough approximation made by Pullman and others[8] in their treatment, however, it seems desirable to carry out an independent calculation of O.L.E. for M.B.A.

Method of Calculation

Let us suppose that the reare two conjugated systems R and S initially separate, and then joined by a bond between atoms r of R and s of S, forming a composite system RS. The delocalisation energy $\Delta\varepsilon(RS)$ across the connecting bond r-s may be defined as the difference between the π-electronic energy of the complete system RS and the sum of the π-electronic energies of the systems R and S taken separately. Formally, then

$$\Delta\varepsilon(RS)=\varepsilon(RS)-\varepsilon(R)-\varepsilon(S). \tag{1}$$

On the other hand, employing the variation method for the orbital interactions between R and S, we can express $\Delta\varepsilon(RS)$ as a function of orbitals and their energies of R and S as follows[9]:

$$\Delta\varepsilon(RS)=2\sum_{i}^{occu}\sum_{j}^{un}\frac{C^2{}_{ir}\,C^2{}_{js}}{\epsilon_i{}^R-\epsilon_j{}^S}\,k^2 +2\sum_{j}^{occu}\sum_{i}^{un}\frac{C^2{}_{js}\,C^2{}_{ir}}{\epsilon_j{}^S-\epsilon_i{}^R}\,k^2 \text{ (in } \beta \text{ units)}, \tag{2}$$

where $\epsilon_i{}^R$ denotes the energy of the ith MO of R, C_{ir} the coefficient of the rth atomic orbital in the ith MO and so on, and k is the resonance integral of r-s bond in β units. Thus, if the MO's and their energies of R and S are known, we can calculate $\Delta\varepsilon(RS)$ without the tedious procedure due to the straightforward application of LCAO MO method for RS.

In discussing the effect of a substituent on O.L.E., consider that R denotes a parent molecule, S a substituent, and R' a parent residual molecule for the transition state in which the requisite number of electrons appropriate to a given type of reaction are assumed to be localised at both the ends of the bond of R in question. An expression similar to Eq. (1) may be written for the energy $\varepsilon(R'S)$ of the substituted residual molecule, so that we can immediately derive,

$$\begin{aligned}\text{O.L.E.}&=\varepsilon(R'S)+\varepsilon(=)-\varepsilon(RS)\\ &=\varepsilon(R')+\varepsilon(=)-\varepsilon(R)+\Delta\varepsilon(R'S)-\Delta\varepsilon(RS),\end{aligned} \tag{3}$$

where $\varepsilon(=)$ is the energy of the ethylenic double bond. As we are concerned only with the effect of a substituent with the position of substitution on O.L.E.o f a given molecule, it is convenient to have an expression for the change in O.L.E. ΔO.L.E.$_{\cdot r}$ caused by the substitution at the rth atom. This expression is

$$\Delta\text{O.L.E.}_{\cdot r}=\Delta\varepsilon_r(R'S)-\Delta\varepsilon_r(RS), \tag{3'}$$

With a substituent such as methyl, besides the above considered effect due to delocalisation, the effect due to induction should be taken into account. Induction causes a change in α_r, the coulomb term for atom r to which the substituent is attached. Then, the effect due to induction on O.L.E. is treated by the perturbation method as follows:

$$\Delta\text{O.L.E.}r \text{ due to induction} =(q_r{}'-q_r)\delta\alpha_r+\frac{1}{2}(\pi_{rr}{}'-\pi_{rr})\delta\alpha_r{}^2, \tag{4}$$

where q_r and π_{rr} denote the electron density and self-polarisability of the rth atom respectively and the $'$ refers to the residual molecule.

In calculating O.L.E. for the 3–4 bonds of several M.B.A., consider that R represents the parent molecule, B.A., R' the parent residual molecule, β-phenyl-naphthalene (P.N.), and S the methyl substituent. The MO's and their energies of R, R' and S are calculated by the standard LCAO MO method with overlap omitted. The additional parameters related to the methyl substituent are taken according to Pullman and Pullman[10] as follows:

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4) H. H. Greenwood, *Brit. J. Cancer*, 5, 441 (1951).

5) G. M. Wheland, *J. Am. Chem. Soc.*, **64**, 900 (1942).

6) R. D. Brown, *J. Chem. Soc.*, 1950, 3249 and 1951, 1950, 1955.

7) A. Pullman, B. Pullman, and G. Berthier, *Compt. rend.*, **236**, 2067 (1953).

8) B. Pullman, personal communication; "Dewar's method (*J. Am. Chem. Soc.*, **74**, 3357 (1952)) used in our treatment is erroneous when applied to the calculation of the effect of substituents on O.L.E."

9) T. Nakajima, *Sci. Rep. Tohoku Univ.*, Ser. I. in press.

10) B. Pullman and A. Pullman, "Les Theories Electroniques de la Chimie Organique", 1952, p. 410.

$$\alpha_{H_3}=\alpha-0.2\beta,\qquad \beta_{C\equiv H_3}=2.5\beta,$$
$$\delta\alpha_{C_{aron}}=-0.1\beta,\qquad k=0.7.$$

Result and Discussion

In Table I are given the delocalisation energies $\Delta\varepsilon_r$ produced by methylations in each of the ten possible positions of B.A. containing 20 π-electrons and of P.N. containing 18 π-electrons. Table I lists also the self-polarisabilities π_{rr} of B.A. and P.N. It has been shown by the present author9) that the delocalisation energy per a connecting bond between a given molecule and a given substituent is correlated linearly with π_{rr} of the substituted atom of the molecule. It will be seen that there exists a fairly good correlation of this kind between $\Delta\varepsilon_r$ and π_{rr} in Table I.

TABLE I

DELOCALISATION ENERGIES $\Delta\varepsilon_r$ AND SELF-POLARISABILITIES π_{rr} FOR B.A. AND P.N.

B.A.			P.N.		
r	$\Delta\varepsilon_r$ (in β units)	$\pi_{rr}\times\beta$	r	$\Delta\varepsilon_r$ (in β units)	$\pi_{rr}\times\beta$
10	0.16023	0.513	9	0.15820	0.480
9	0.15901	0.495	8	0.15498	0.447
5	0.15528	0.452	5	0.15454	0.441
8	0.15511	0.449	10	0.15422	0.439
4′	0.15439	0.439	1′	0.15309	0.425
1′	0.15340	0.429	3′	0.15139	0.412
7	0.15111	0.410	6	0.15093	0.408
2′	0.15111	0.410	7	0.15063	0.405
6	0.15098	0.409	2′	0.14971	0.396
3′	0.15051	0.404	4′	0.14971	0.396

ΔO.L.E.$_{\cdot r}$ are calculated by taking account merely of the delocalisation effect from Eq. (3). The contribution due to the inductive effect is ignored because in Eq. (4) the first term vanishes as the electron density is unity at every position of B.A. and P.N. and the actual values of the second term are very small. ΔO.L.E.$_{\cdot r}$ thus calculated are compared with $\pi_{rr}'-\pi_{rr}$ in Table II. The linear correlations seen between $\Delta\varepsilon_r$ and π_{rr} in Table I and between ΔO.L.E.$_{\cdot r}$ and $\pi_{rr}'-\pi_{rr}$ in Table II lead to the conclusion that in discussing the effect of the substituent, the delocalisation effect may be replaced effectively by a virtual inductive effect by the suitable choice of the value of $\delta\alpha_r$ in Eq. (4), in which, in this case, only the second term is effective.

TABLE II

HOMOLYTIC ΔO.L.E.$_{\cdot r}$, DIFFERENCES IN SELF-POLARISABILITIES $\pi_{rr}'-\pi_{rr}$, AND RELATIVE CHANGES IN BOND ORDER δp_{3-4}

r	ΔO.L.E.$_{\cdot r}$ (in β units)	$(\pi_{rr}'-\pi_{rr})\times\beta$	δp_{3-4}
3′	0.00088	0.008	0.0007
	0.00000	0.000	0.0000
6	−0.00005	−0.001	−0.0002
8	−0.00013	−0.002	−0.0002
1′	−0.00031	−0.004	−0.0005
7	−0.00048	−0.005	−0.0016
5	−0.00074	−0.011	−0.0023
9	−0.00081	−0.015	−0.0021
2′	−0.00140	−0.014	−0.0050
4′	−0.00468	−0.043	−0.0092
10	−0.00601	−0.074	−0.0175

Brown6) has shown that it is possible to correlate bond order with O.L.E., suggesting that bond order also should be a useful index of bond reactivity. The relative changes in mobile order δp_{3-4} of the 3–4 bond of B.A. caused by methylations have been calculated by Greenwood4) and are arranged also in Table II. Considering that Greenwood's calculations have been made by taking account merely of the inductive effect by the second order perturbation method, it is remarkable that there exists a close parallelism between ΔO.L.E.$_{\cdot r}$ and δp_{3-4} as seen in Table II. This parallelism is a further evidence of the above deduction that the delocalisation effect may be replaced effectively by a virtual inductive effect.

It is clear that we cannot correlate decrease in O.L.E. of the 3–4 bond of M.B.A. with the experimentally determined increase in the rate of addition of OsO_4 to the 3–4 bond11), since an increase in reactivity consequent upon methylation is in fact accompanied by an increase in O.L.E. (except the methylation at 3′-position). It has been established by Brown5) that O.L.E. provides a very satisfactory interpretation of the relative reactivities of conjugated bonds toward bond reagents such as OsO_4 for a system of alternant hydrocarbons. As we have seen, in the case of substituted hydrocarbons, however, this correlation no longer holds. Agreeing to Greenwood's suggestion deduced from the decrease in δp_{3-4} this suggests that although for alternant hydrocarbons OsO_4 may react by a largely homolytic mechanism, the reactions for substituted hydrocarbons may be not homolytic but heterolytic in nature.

At this point we must distinguish two types of bond localisation as in the case of atom localisation. In the homolytic and heterolytic (electrophilic or nucleophilic) atom localisations, 1 and 2 or 0 π-electrons respectively are assumed to be localised at the site of reaction. By analogy with this we assume that in the homolytic and heterolytic bond localisations 2 and 4 or 0 π-electrons respectively are localised at the reaction sites of the bond in question. Thus, O.L.E. so far considered is that for the homolytic type of bond localisation.

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11) G. M. Badger, *J. Chem. Soc.*, **1950**, 456.

Next the heterolytic (electrophilic) O.L.E. for several M.B.A. will be calculated. For the calculation of heterolytic O.L.E. the inductive effect contributes much because the electron density at every atom of the parent residual molecule which, in this case, is P.N. with two π-electrons lost is not necessarily unity. The contribution due to induction is calculated by Eq. (4) in which, in this case, the first term is effective and the second term is ignored. Then, for the heterolytic (electrophilic) bond localisation Eq. (4) may be rewritten as follows:

$$\Delta\text{O.L.E.}_r \text{ due to induction} = (q_r'-q_r)\delta\alpha_r = -q_r^f\,\delta\alpha_r, \qquad (5)$$

where q_r^f denotes the electron density in the frontier orbital (the highest occupied orbital) of P.N.12).

From the results given in Table III we can notice the following points. (1) There exists a close parallelism between the heterolytic ΔO.L.E.$_r$ due to delocalisation and induction, so that the resultant sum is closely correlated with q_r^f. This suggests that heterolytic ΔO.L.E.$_r$ may be calculated effectively by taking account merely of the virtual induction by the suitable choice of the value of $\delta\chi_r$ in Eq. (5). (2) Except with regard to the 4′-position, both the delocalisation and inductive effect decrease heterolytic O.L.E.; for details, the former lowers relatively the energy of the transition state and the latter raises that of the ground state. (3) We can correlate the decrease in heterolytic O.L.E. with the experimentally determined increase in the rates of addition of OsO_4 to the 3–4 bond though the experimental data are not sufficient. (4) The changes in heterolytic O.L.E. with the position of substitution are remarkable compared with those in homolytic O.L.E.

Table III lists also the relative carcinogenic powers of M.B.A13). It may be seen that there exists a satisfactory correlation between heterolytic O.L.E. and the activity especially with regard to M.B.A. substituted in the angular ring and at the 9-position. In this respect, it should be remembered that the especially high electron densities for 2′- and 4′-M.B.A. which are inactive and the relatively low density for 9-M.B.A. which is highly active have provided the results in direct contradiction to the attempt to correlate the electron density of the 3–4 bond of M.B.A. with the activity4),9).

TABLE III

HETEROLYTIC ΔO.L.E.$_r$, RATE CONSTANTS OF ADDITION OF OsO_4, 10^3K AND CARCINOGENIC ACTIVITIES

r	ΔO.L.E.$_r$ (in β units)			10^3K	carcinogenic activity
	due to delocalisation	due to induction	total		
9	0.04301	0.04169	0.08470	0.96	++
8	0.03137	0.02996	0.06133		+
5	0.02400	0.02353	0.04753		++
10	0.02089	0.02559	0.04648	0.91	+++
6	0.01689	0.01611	0.03300	0.64	+
3′	0.01248	0.01104	0.02352		0
1′	0.00788	0.00780	0.01568		0
7	0.00653	0.00667	0.01320		+
2′	−0.00048	0.00088	0.00040		0
	0.00000	0.00000	0.00000	0.48	0
4′	−0.00376	0.00088	−0.00288		0

Summary

(1) The effects of the methyl substituent on O.L.E. for the 3–4 bond of B.A. have been calculated. The effect may be discussed by the perturbation method taking account of the virtual inductive effect through the suitable choice of the value of $\delta\alpha$ of the substituted position.

(2) The homolytic and heterolytic O.L.E. were defined. The former predicts the bond reactivity only for a system of alternant hydrocarbons. With substituted hydrocarbons the latter should be used as a criterion of bond reactivity.

(3) The heterolytic O.L.E. for the 3–4 bonds of several M.B.A. have been successfully correlated with the experimental evidences on rates of addition of OsO_4 and the carcinogenic activities.

(4) The method of calculation of the effect of the methyl substituent on O.L.E. used in the present note may be applicable, with due caution, to other substituents in general.

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

13) G. M. Badger, *Brit. J. Cancer.*, **2**, 309 (1949).

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Department of Chemistry, Faculty of Science, Tōhoku University, Sendai