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Quantum Chemical Study on the Cytochrome P-450 catalyzed Hydroxylation of Aromatic Hydrocarbons

Eiji Yukawa, Keiki Kouno, Yukio Ono, and Yo Ueda

Faculty of Pharmaceutical Sciences, Kyushu University[1]

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A quantum chemical method for prediction of the specific bond of an aromatic hydrocarbon at which hydroxylation will occur most easily in liver microsomes is presented.

The interaction energy changes of a binary system composed of an aromatic hydrocarbon and O_2 caused by changes of the mutual spatial arrangement between the hydrocarbon and O_2 were calculated by the CNDO/2 method.

This method was applied to the hydroxylations of naphthalene, anthracene, phenanthrene, acenaphthylene, indene and 1,2-dihydronaphthalene. In all cases, the theoretical predictions were found to coincide very well with the reported experimental results.

Keywords——hydroxylation in liver microsomes; cytochrome P-450; CNDO/2 method; naphthalene; anthracene; phenanthrene; acenaphthylene; indene; 1,2-dihydronaphthalene

Drugs taken into the animal body are metabolized mainly in liver microsomes. The first step of drug metabolism is an oxidation, reduction, or hydrolysis reaction, or some combination of these. Monooxygenase reactions are most frequently observed, and cytochrome P-450 is known to be responsible for a variety of monooxygenase reactions in liver microsomes.

When the substrate is added to the liver microsomes, cytochrome P-450 shows a characteristic substrate-induced difference spectrum in the Soret region. Difference spectra are usually classified into three types, Type I, Type II and modified Type II. Substrates causing the Type I spectrum are known to be oxidized in liver microsomes by the catalytic action of cytochrome P-450. This catalytic reaction is considered to proceed as follows[2]: initially, the ferric cytochrome P-450 interacts with the substrate to form an enzyme-substrate complex, and is then reduced to the ferrous state by the uptake of one electron from the electron transfer components in the system. In the next step, molecular oxygen (O_2) interacts with the reduced cytochrome P-450-substrate complex giving rise to a ternary complex of the reduced cytochrome P-450, O_2 and a substrate molecule. Subsequently, the ternary complex receives a second electron and is degraded into the reaction products through an unidentifiable reaction intermediate. It is presumed that the substrate binds with the protein in the proximity of the heme moiety in the ternary complex and in the reaction intermediate.[3,4]

The catalytic oxidation of drug molecules by cytochrome P-450 takes place at specific atoms or bonds. The ease of oxidation at specific moieties of aromatic hydrocarbons, which are the targets of the present investigation and which belong to the group of substrates showing Type I difference spectra, has hitherto been discussed on the basis of reactivity indices of the free molecules.[5] We considered that the spatial arrangement of a drug molecule in the

1) Location: *Maedashi 3-1-1, Higashi-ku, Fukuoka 812, Japan.*
2) Y. Ishimura, "Cytochrome P-450," ed. by R. Sato and T. Omura, Kodansha Ltd., Tokyo, 1978, pp. 209—227.
3) J.D. Lipscomb and I.C. Gunsalus, *Drug Metab. Dispos.*, **1**, 1 (1973).
4) V. Ullrich and K.H. Schnabel, *Drug Metab. Dispos.*, **1**, 176 (1973).
5) *e.g.*: *a*) E. Boyland and P. Sims, *Biochem. J.*, **84**, 571 (1962); *b*) P. Sims, *Biochem. Pharmacol.*, **19**, 795 (1970); *c*) I.A. Smith, G.D. Berger, P.G. Seybold, and M.P. Serve, *Cancer Res.*, **38**, 2968 (1978); *d*) G.D. Berger, I.A. Smith, P.G. Seybold, and M.P. Serve, *Tetrahedron Lett.*, **1978**, 231.

cytochrome P-450-O_2-drug complex in the monooxygenase reaction must also be important in determining at which atoms or bonds of the molecule the oxidation takes place.

Naphthalene,[6] anthracene,[7] phenanthrene,[5b] acenaphthylene,[8] indene[9] and 1,2-dihydronaphthalene[10] have all been reported to be oxidized to produce limited kinds of dihydro-diol derivatives through the corresponding epoxides in liver microsomes. It is also known that cytochrome P-450 catalyzes only the epoxidation reactions of aromatic hydrocarbons and that the conversion of the epoxide to dihydro-diol is catalyzed by epoxide hydratase. Thus, it was presumed that only limited kinds of specific atoms or bonds of each of the above-mentioned aromatic hydrocarbons can be located in close proximity to O_2 in the ternary intermediate complex of the epoxidation reaction.

In order to determine the most stable spatial arrangement of an aromatic hydrocarbon molecule in the ternary complex, one would expect the quantum chemical method to be useful. Since the systems to be calculated in the present investigation are too large for *ab initio* calculations, the CNDO/2 method was considered. In the CNDO/2 method, the attractive interaction is overestimated because many repulsive interactions are neglected, and it is known that this method gives unreliable results particularly in respect of the intermolecular distance when it is used to optimize the mutual spatial arrangement of two molecules interacting with each other; however, the calculated optimum mode of approach of one molecule to another seems to be rather reliable. For example, Inuzuka[11] reported that hydrogen bond energies, bond distances and bond angles were calculated to be larger than, shorter than and nearly equal to the respective experimental values when the mutual spatial arrangements of hydrogen-bonded aldehydes with water were studied by the CNDO/2 method. Silverman[12] reported that the mutual spatial arrangements of stacked dimers of tetrathiafulvalene and tetracyanoquinodimethane optimized by the CNDO/2 method coincided fairly well with those obtained experimentally. In order to obtain further evidence of the applicability of the CNDO/2 method to the present investigation, the mutual spatial arrangement of a plausible transition state in the epoxidation of ethylene with performic acid, which has already been investigated by the *ab initio* method by Plesničar *et al.*,[13] was optimized by the CNDO/2 method. The results showed that the calculated transition state[14] was the same as that obtained by the *ab initio* method. However, all the optimized intermolecular distances were found to be shorter than those obtained by the *ab initio* method. For example, the optimized distance between the carbon atom of ethylene and the oxygen atom of performic acid in the unsymmetrical arrangement was calculated to be 1.6 Å in place of 2.86 Å for the corresponding distance optimized by the *ab initio* method. Judging from these findings, the CNDO/2 method was considered to be applicable in the present investigation, especially in deciding the mode of approach of O_2 to an aromatic hydrocarbon.

As mentioned before, we presumed that the epoxidation reaction would take place most easily at the atom or the bond of an aromatic hydrocarbon located in closest proximity to O_2 in the ternary complex. Therefore, it is necessary to calculate the total energies of various

6) D.M. Jerina, J.W. Daly, D. Witkop, P. Zaltzman-Nirenberg, and S. Udenfriend, *Biochemistry*, **9**, 147 (1970).
7) P. Sims, *Biochem. J.*, **92**, 621 (1964).
8) R.P. Hopkins, C.J.W. Brooks, and L. Young, *Biochem. J.*, **82**, 457 (1962).
9) K.C. Leibman and E. Ortiz, *Mol. Pharmacol.*, **4**, 201 (1968).
10) E. Boyland and P. Sims, *Biochem. J.*, **77**, 175 (1960).
11) K. Inuzuka, *Nippon Kagaku Kaishi*, **1978**, 1118.
12) B.D. Silverman, *J. Chem. Phys.*, **79**, 1614 (1979).
13) B. Plesničar, M. Tasevski, and A. Ažman, *J. Am. Chem. Soc.*, **100**, 743 (1978).
14) The arrangement corresponding to the 1,3-addition mechanism was not included in the calculation, because Dryuk[15] reported that this mechanism can be excluded as a possible mechanism for the epoxidation reaction.
15) V.G. Dryuk, *Tetrahedron*, **32**, 2855 (1976).

mutual spatial arrangements of the three components of the ternary complex in order to find the most stable one. However, even the amino acid residues, which are considered to play important roles in forming the enzyme-substrate complex, cannot be included in the molecular orbital calculations, because the structure of cytochrome P-450 is not yet known. Moreover, the heme moiety of cytochrome P-450 is also too large for calculation. Therefore, a simple model system composed of only O_2 and an aromatic hydrocarbon, which will be called hereafter the binary system, was used in the calculation. The unavoidable shortcomings caused by the use of the CNDO/2 method (the optimized intermolecular distances are unreliable) mean that it is impossible to determine the precise mutual spatial arrangements of components of the system composed of an aromatic hydrocarbon, O_2 and heme. The only thing we can do is to estimate the degree of steric hindrance which may exist between the hydrocarbon and the heme plane. However, this problem was not considered to be too serious in the present investigation, since our aim was only to identify the specific bond of an aromatic hydrocarbon at which the epoxidation reaction should take place most easily.

Results and Discussion

The Method of Investigation

O_2 was brought nearer to the middle points of all kinds of bonds and to all kinds of atoms of each hydrocarbon, and the accompanying change of the interaction energy, which is defined as the energy difference between the total energy of the binary system itself and the sum of the total energies of the two component molecules of the binary system, was calculated by the CNDO/2 method. It can be considered that the smaller the interaction energy(ΔE) is, the more stable the binary system is. For convenience in the molecular orbital calculation, both the approach of O_2 to the middle point of a bond (symmetrical approach) and that to an atom (unsymmetrical approach) were divided into two steps, the A_S and B_S steps and the A_U and B_U steps, respectively.

As the initial process in both the A_S and the A_U steps, a $O_{(1)}$–$O_{(2)}$ bond was placed over the plane of a bond and the adjacent C atom of an aromatic hydrocarbon so as to locate the $O_{(1)}$ atom vertically above the middle point of the bond (M) or the C atom; this plane will be called simply the plane of a double bond, as shown in Figs. 1 and 2.

In Fig. 1, S denotes the projection point of the $O_{(2)}$ atom on the plane of a double bond, r denotes the distance between the $O_{(1)}$ atom and M, $\overline{MP}$ and $\overline{O_{(1)}Q}$ denote the projection line of the $O_{(1)}$–$O_{(2)}$ bond on the plane of the double bond and the straight line drawn in parallel with $\overline{MP}$, respectively, while θ and ϕ denote the angle of intersection between the $O_{(1)}$–$O_{(2)}$ bond axis and $\overline{O_{(1)}Q}$ and that between $\overline{MP}$ and the bond axis[$C_{(i)}$–$C_{(j)}$], respectively. The spatial relationship between the Fe atom of the heme plane and the $O_{(2)}$ atom was drawn arbitrarily. The $O_{(1)}$–$O_{(2)}$ bond was fixed at first so as to make $\overline{MP}$ intersect orthogonally with the $C_{(i)}$–$C_{(j)}$ bond axis; it was also located outside the phenyl ring and made to run parallel with the $O_{(1)}$–$O_{(2)}$ bond axis ($\theta=0°$). Thereafter, θ was changed at intervals of 15° up to 90°.

In Fig. 2, S denotes the projection point of the $O_{(2)}$ atom on the plane of a double bond, r denotes the distance between the $O_{(1)}$ atom and the C atom[$C_{(j)}$], $\overline{C_{(j)}P}$ and $\overline{O_{(1)}Q}$ denote the projection line of the $O_{(1)}$–$O_{(2)}$ bond on the plane of the double bond and the straight line drawn in parallel with $\overline{C_{(j)}P}$, respectively, and θ and ϕ denote the angle of intersection between the $O_{(1)}$–$O_{(2)}$ bond axis and $\overline{O_{(1)}Q}$ and that between the $C_{(i)}$–$C_{(j)}$ bond axis and $\overline{C_{(j)}P}$, respectively. The spatial relationship between the Fe atom of the heme plane and the $O_{(2)}$ atom is drawn arbitrarily. The $O_{(1)}$–$O_{(2)}$ bond was fixed at first so as to make $\overline{C_{(j)}P}$ bisect the angle between two C–C bonds [when the $C_{(j)}$ atom is adjacent to three atoms numbered $i,k,l(i<k<l)$, the $O_{(1)}$–$O_{(2)}$ bond was fixed so as to make $\overline{C_{(j)}P}$ bisect the angle between the two bonds $C_{(j)}$–$C_{(i)}$ and $C_{(j)}$–$C_{(k)}$]; it was also located inside the phenyl ring and made to run

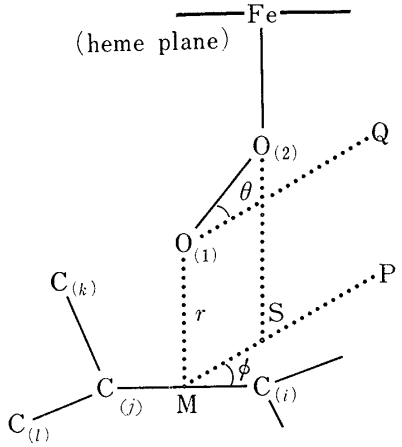

Fig. 1. The Mode of Approach of O_2 to the Middle Point of a C–C Bond (Symmetrical Approach)

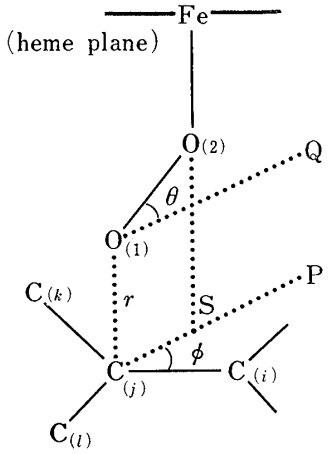

Fig. 2. The Mode of Approach of O_2 to a C Atom (Unsymmetrical Approach)

parallel with the $O_{(1)}$–$O_{(2)}$ bond axis ($\theta = 0°$). Thereafter, θ was changed at intervals of 15° up to 90°.

Thus, seven kinds of initial mutual spatial arrangements of the binary system were considered in both the symmetrical and unsymmetrical approaches.

As the next process in both the A_S and the A_U steps, r was changed in each of the seven arrangements and the interaction energy changes caused by the change of r were calculated by the CNDO/2 method. From the results of these calculations, the optimum pair of θ and r to make the interaction energy of the binary system minimum was selected for the symmetrical and unsymmetrical approaches.

In both the B_S and the B_U steps, the two sets of values of θ and r found to be optimum in the A_S and the A_U steps were kept constant, while the $O_{(1)}$–$O_{(2)}$ bond was rotated about the $O_{(1)}$–M axis and about the $O_{(1)}$–$C_{(j)}$ axis clockwise from the viewpoint at the $O_{(1)}$ atom, respectively. These rotations correspond to changes of the angle ϕ. The angle ϕ was defined as 0° when the $O_{(1)}$–$O_{(2)}$ bond is placed so as to locate the point S on the C–C bond axis and on the same side as the C atom of the bond bearing the largest number with respect of the point M and the $C_{(j)}$ atom, respectively. The interaction energy change caused by the change of ϕ was calculated by the CNDO/2 method. From the results of this calculation, the optimum values of ϕ were selected in both the B_S and the B_U steps.

Interaction energies of all mutual spatial arrangements of the binary system optimized for both symmetrical and unsymmetrical approaches of O_2 to all kinds of bonds and atoms were compared, and the arrangement having the smallest interaction energy was selected as the most stable mutual spatial arrangement of the binary system.

Lastly, the spatial relationship between the aromatic hydrocarbon molecule and the heme plane was examined geometrically. In this examination, the Fe–$O_{(2)}$ bond length and the Fe–$O_{(2)}$–$O_{(1)}$ bond angle were assumed to be 1.75 Å and 135° from the literature[16] and the intermolecular distance (r_{C-O}) between the hydrocarbon and O_2 of the binary system having the most stable mutual spatial arrangement was used, even though this distance must be considerably shorter than that in the ternary complex. If it can be concluded that O_2 can approach the hydrocarbon without suffering steric hindrance by this examination, such an approach should actually be possible in liver microsomes.

If epoxidation is going to take place at a C–C bond of an aromatic hydrocarbon, this bond is expected to become weaker than the same bond of the same molecule in the free state, and

16) J.P. Collmann, R.R. Gangne, C.A. Reed, T.R. Halbert, G. Lang, and W.T. Robinson, *J. Am. Chem. Soc.*, **97**, 1427 (1975).

the $O_{(1)}$–$O_{(2)}$ bond is also expected to become weaker. Now the resonance energy of a bond is known to correlate closely with the bond energy.[17] Therefore, the resonance energy changes of both a C–C bond of an aromatic hydrocarbon ($\Delta E^{R}_{C\text{-}C}$) and the $O_{(1)}$–$O_{(2)}$ bond ($\Delta E^{R}_{O\text{-}O}$) caused by the approach of O_2 to the hydrocarbon were calculated.

Naphthalene

Naphthalene has four kinds of double bonds, exemplified by $C_{(8a)}$–$C_{(4a)}$, $C_{(8a)}$–$C_{(1)}$, $C_{(1)}$–$C_{(2)}$ and $C_{(2)}$–$C_{(3)}$, and three kinds of carbon atoms, exemplified by $C_{(8a)}$, $C_{(1)}$ and $C_{(2)}$. Figs. 3 and 4 show the interaction energy changes of the binary system composed of naphthalene and O_2 caused by the A_S and the A_U steps of approach of O_2 when the angles (θ) are 15°, 30° and 45°. The binary system having other angles (θ) was found to be definitely less stable than in the cases shown in these figures. Among the cases shown, the following pairs of θ

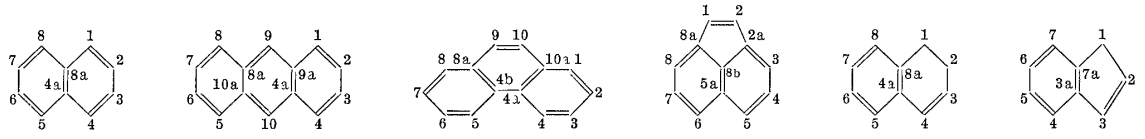

Chart 1

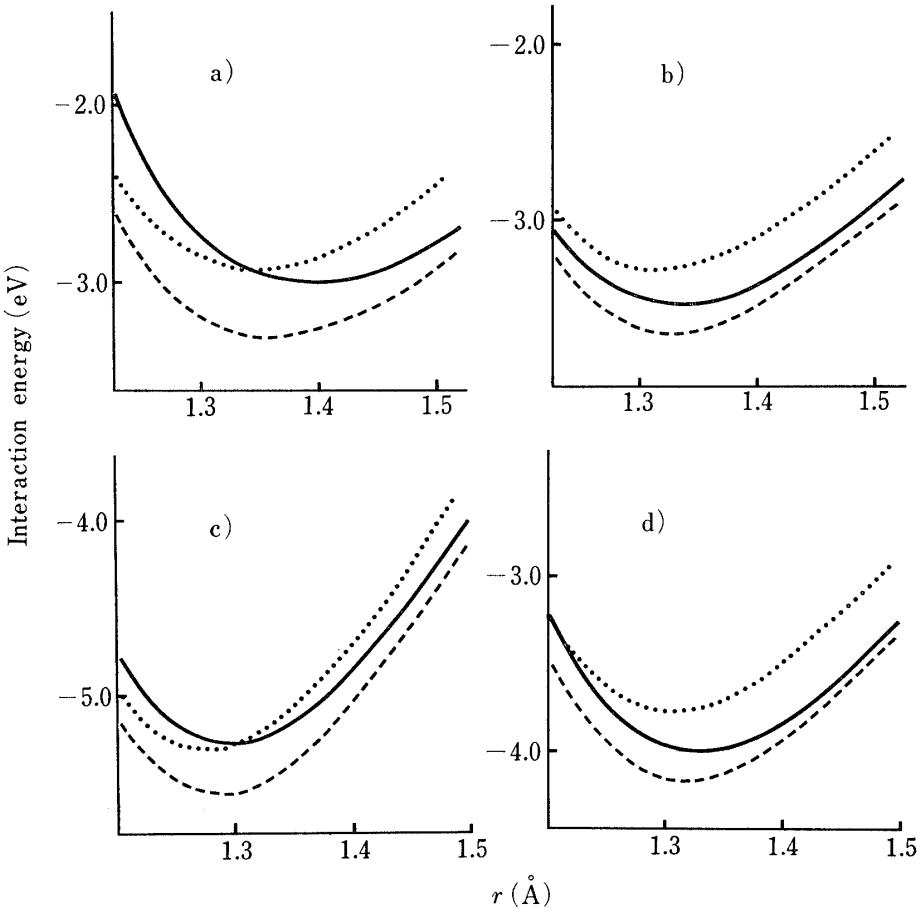

Fig. 3. Interaction Energy Changes due to the Change of r when O_2 was brought nearer to the Middle Points of the following Bonds of Naphthalene: a) the $C_{(8a)}$–$C_{(4a)}$ Bond; b) the $C_{(8a)}$–$C_{(1)}$ Bond; c) the $C_{(1)}$–$C_{(2)}$ Bond; d) the $C_{(2)}$–$C_{(3)}$ Bond

——: θ=15°, ----: θ=30°, ····: θ=45°.

17) H. Fischer and H. Kollmar, *Theoret. Chim. Acta* (Berl.), **16**, 163 (1970).

and r were found to be optimum: 30° −1.35 Å[$C_{(8a)}$–$C_{(4a)}$], 30° −1.33 Å[$C_{(8a)}$–$C_{(1)}$], 30° −1.30 Å[$C_{(1)}$–$C_{(2)}$], 30° −1.33 Å[$C_{(2)}$–$C_{(3)}$], 30° −1.58 Å[$C_{(8a)}$], 30° −1.53 Å[$C_{(1)}$] and 30° −1.53 Å[$C_{(2)}$].

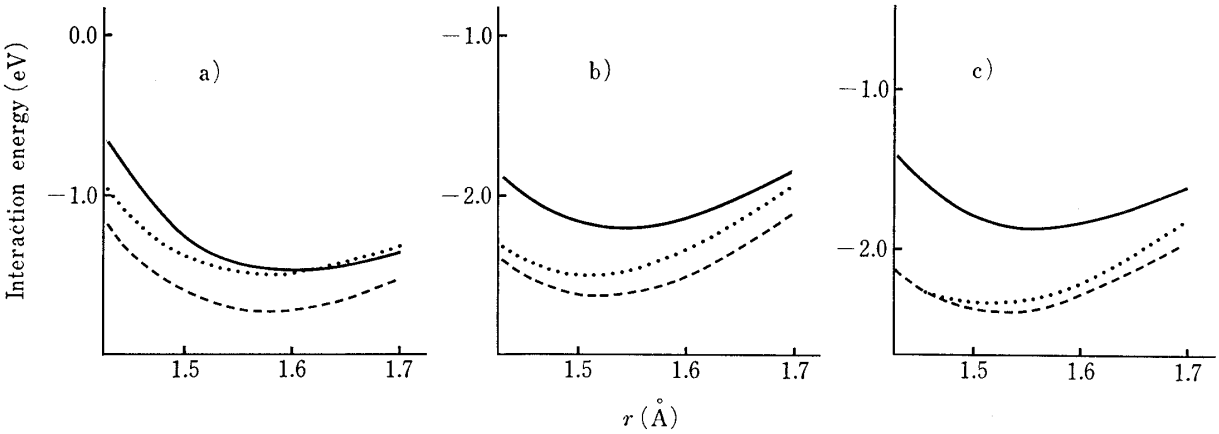

Fig. 4. Interaction Energy Changes due to the Change of r when O_2 was brought nearer to the following C Atoms of Naphthalene: a) the $C_{(8a)}$ Atom; b) the $C_{(1)}$ Atom; c) the $C_{(2)}$ Atom
——: θ=15°, – – –: θ=30°, ····: θ=45°.

Figures 5 and 6 show the interaction energy changes of the binary system caused by the B_S and the B_U steps of approach of O_2. The magnitudes of the interaction energies of the binary system optimized for approach of O_2 to all four kinds of double bonds and three kinds of carbon atoms of naphthalene are shown in Table I. It can be concluded that when O_2 was brought nearer to the middle point of the $C_{(1)}$–$C_{(2)}$ bond so as to make the angles (θ and ϕ) equal to 30° and 90°, respectively, the binary system is most stable. Other modes of approach of O_2 to the naphthalene molecule seem improbable. The intermolecular distance

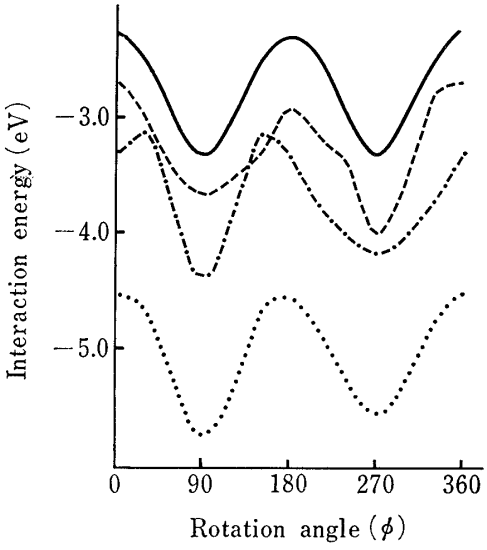

Fig. 5. Interaction Energy Change due to Rotation of the $O_{(1)}$–$O_{(2)}$ Bond about the $O_{(1)}$–M Axis in the Case of Naphthalene

——: the $C_{(8a)}$–$C_{(4a)}$ bond,
– – –: the $C_{(8a)}$–$C_{(1)}$ bond,
····: the $C_{(1)}$–$C_{(2)}$ bond,
–·–·: the $C_{(2)}$–$C_{(3)}$ bond.

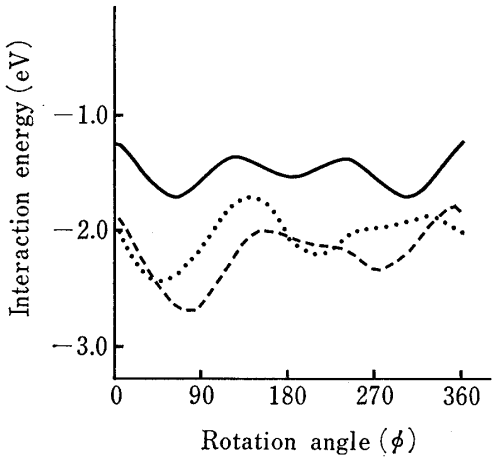

Fig. 6. Interaction Energy Change Due to Rotation of the $O_{(1)}$–$O_{(2)}$ Bond about the $O_{(1)}$–$C_{(j)}$ Axis in the Case of Naphthalene

——: the $C_{(8a)}$ atom,
– – –: the $C_{(1)}$ atom,
····: the $C_{(2)}$ atom.

Table I. Results for Naphthalene

Bond or atom	Interaction energy (eV)	$\Delta E^{R}_{C\text{-}C}$ (eV)	$\Delta E^{R}_{O\text{-}O}$ (eV)	$r_{C\text{-}O(1)}$ (Å)	ϕ (°)
$C_{(8a)}$–$C_{(4a)}$	−3.34	4.59	7.03	1.52	90
$C_{(8a)}$–$C_{(1)}$	−4.00	4.93	7.17	1.50	270
$C_{(1)}$–$C_{(2)}$	−5.76	6.81	8.47	1.48	90
$C_{(2)}$–$C_{(3)}$	−4.36	5.11	7.58	1.50	90
$C_{(8a)}$	−1.73		3.70	1.58	180
$C_{(1)}$	−2.70		4.56	1.50	285
$C_{(2)}$	−2.43		4.20	1.53	45

($r_{C\text{-}O(1)}$) between the two component molecules of the binary system was found to be 1.48 Å when the mutual spatial arrangement of the system was optimized. This distance is very close to the interatomic distance of the covalent C–O bond, and is considered to be improper as the intermolecular distance between naphthalene and O_2 in the ternary complex. However, the mode of approach of O_2 to the naphthalene molecule is expected to be reasonably reliable, as discussed previously.

In order to estimate the degree of steric hindrance between the naphthalene molecule and the heme plane, their mutual spatial arrangement was examined geometrically. In this examination, an intermolecular distance ($r_{C\text{-}O}$) of 1.48 Å between naphthalene and $O_{(1)}$ was used. The results indicated that O_2 can approach naphthalene without suffering steric hindrance. Thus, judging from the results mentioned above, the epoxidation of naphthalene is predicted to take place at its $C_{(1)}$–$C_{(2)}$ bond. Naphthalene is known to be converted in liver microsomes to the 1,2-dihydro-diol derivative and to 1-naphthol through the 1,2-dihydro-1,2-epoxide derivative. Thus, the theoretical prediction presented in this paper coincides very well with the experimental results.

The resonance energy changes, $\Delta E^{R}_{C\text{-}C}$ and $\Delta E^{R}_{O\text{-}O}$, are also shown in Table I. Table I indicates that both $\Delta E^{R}_{C\text{-}C}$ and $\Delta E^{R}_{O\text{-}O}$ have the largest values when O_2 is brought nearer to the $C_{(1)}$–$C_{(2)}$ bond. This result provides further support for epoxidation of naphthalene at the $C_{(1)}$–$C_{(2)}$ bond in preference to other C–C bonds.

Anthracene, Phenanthrene, Acenaphthylene, Indene and 1,2-Dihydronaphthalene

The conjugated systems of these compounds can be considered to resemble that of naphthalene very closely. Since in the case of naphthalene, the unsymmetrical approach of O_2 was found to be definitely unfavorable, the unsymmetrical approach of O_2 to these hydrocarbons was excluded from the calculation.

Since none of the results of investigations of these hydrocarbons had any unusual features in comparison with the results for naphthalene, the results will only be described briefly. The final results of the symmetrical approach of O_2 to C–C bonds of these hydrocarbons are shown in Tables II—VI. In all cases, the most stable mutual spatial arrangements of the binary systems of these hydrocarbons were examined geometrically to determine the degree of steric hindrances between the hydrocarbons and the heme plane. It was found that in all cases O_2 can approach the hydrocarbons without steric hindrance. Therefore, it may be theoretically predicted that anthracene, phenanthrene, acenaphthylene, indene and 1,2-dihydronaphthalene will be converted to epoxides in liver microsomes most easily at the $C_{(1)}$–$C_{(2)}$, the $C_{(9)}$–$C_{(10)}$, the $C_{(1)}$–$C_{(2)}$, the $C_{(2)}$–$C_{(3)}$ and the $C_{(3)}$–$C_{(4)}$ bonds, respectively. Every one of these theoretical predictions coincides very well with the corresponding reported experimental result.

The values of $\Delta E^{R}_{C\text{-}C}$ and $\Delta E^{R}_{O\text{-}O}$ for these hydrocarbons provide further support for the predictions mentioned above.

Table II. Results for Anthracene[a)]

Bond	Interaction energy (eV)	$\Delta E^{R}_{C\text{-}C}$ (eV)	$\Delta E^{R}_{O\text{-}O}$ (eV)	$r_{C\text{-}O(1)}$ (Å)	ϕ (°)
$C_{(9a)}$–$C_{(4a)}$	−3.06	4.01	6.47	1.55	270
$C_{(9a)}$–$C_{(9)}$	−4.91	5.92	7.92	1.48	90
$C_{(9a)}$–$C_{(1)}$	−3.82	4.51	6.67	1.52	270
$C_{(1)}$–$C_{(2)}$	−6.01	7.03	8.56	1.48	90
$C_{(2)}$–$C_{(3)}$	−4.15	4.94	7.50	1.50	90

a) In all cases the optimum value of θ was found to be 30°.

Table III. Results for Phenanthrene[a)]

Bond	Interaction energy (eV)	$\Delta E^{R}_{C\text{-}C}$ (eV)	$\Delta E^{R}_{O\text{-}O}$ (eV)	$r_{C\text{-}O(1)}$ (Å)	ϕ (°)
$C_{(9)}$–$C_{(10)}$	−6.35	7.41	8.75	1.48	90
$C_{(10)}$–$C_{(10a)}$	−3.45	4.34	6.70	1.52	90
$C_{(10a)}$–$C_{(1)}$	−4.26	5.13	7.40	1.50	270
$C_{(1)}$–$C_{(2)}$	−5.55	6.59	8.37	1.48	90
$C_{(2)}$–$C_{(3)}$	−4.63	5.73	8.07	1.48	90
$C_{(3)}$–$C_{(4)}$	−5.52	6.57	8.37	1.48	90
$C_{(4)}$–$C_{(4a)}$	−4.34	5.23	7.43	1.50	90
$C_{(4a)}$–$C_{(10a)}$	−3.75	4.81	7.18	1.52	90
$C_{(4a)}$–$C_{(4b)}$	−2.98	3.75	6.01	1.55	90

a) In all cases the optimum value of θ was found to be 30°.

Table IV. Results for Acenaphthylene[a)]

Bond	Interaction energy (eV)	$\Delta E^{R}_{C\text{-}C}$ (eV)	$\Delta E^{R}_{O\text{-}O}$ (eV)	$r_{C\text{-}O(1)}$ (Å)	ϕ (°)
$C_{(1)}$–$C_{(2)}$	−6.54	8.49	8.95	1.46	90
$C_{(2)}$–$C_{(2a)}$	−2.88	3.45	5.70	1.56	270
$C_{(2a)}$–$C_{(3)}$	−5.49	6.60	8.37	1.48	90
$C_{(3)}$–$C_{(4)}$	−4.50	5.21	7.57	1.50	90
$C_{(4)}$–$C_{(5)}$	−5.76	6.76	8.39	1.48	90
$C_{(5)}$–$C_{(5a)}$	−4.04	4.99	7.04	1.50	90
$C_{(5a)}$–$C_{(8b)}$	−3.61	4.78	7.34	1.52	90
$C_{(8b)}$–$C_{(2a)}$	−3.84	4.67	6.96	1.52	270

a) In all cases the optimum value of θ was found to be 30°.

Table V. Results for Indene[a)]

Bond	Interaction energy (eV)	$\Delta E^{R}_{C\text{-}C}$ (eV)	$\Delta E^{R}_{O\text{-}O}$ (eV)	$r_{C\text{-}O(1)}$ (Å)	ϕ (°)
$C_{(2)}$–$C_{(3)}$	−6.46	8.64	9.06	1.46	90
$C_{(3)}$–$C_{(3a)}$	−2.59	3.62	5.67	1.56	90
$C_{(3a)}$–$C_{(4)}$	−4.74	6.00	8.11	1.48	90
$C_{(4)}$–$C_{(5)}$	−5.13	6.23	8.20	1.48	90
$C_{(5)}$–$C_{(6)}$	−5.00	6.07	8.15	1.48	90
$C_{(6)}$–$C_{(7)}$	−5.05	6.18	8.21	1.48	90
$C_{(7)}$–$C_{(7a)}$	−4.87	6.09	8.15	1.48	90
$C_{(7a)}$–$C_{(3a)}$	−4.39	5.43	7.62	1.50	270

a) In all cases the optimum value of θ was found to be 30°.

Table VI. Results for 1,2-Dihydronaphthalene[a)]

Bond	Interaction energy (eV)	$\Delta E^{R}_{C\text{-}C}$ (eV)	$\Delta E^{R}_{O\text{-}O}$ (eV)	$r_{C\text{-}O(1)}$ (Å)	ϕ (°)
$C_{(3)}$–$C_{(4)}$	−6.58	8.73	9.25	1.46	90
$C_{(4)}$–$C_{(4a)}$	−2.53	3.66	5.51	1.56	90
$C_{(4a)}$–$C_{(5)}$	−4.72	6.00	8.10	1.48	90
$C_{(5)}$–$C_{(6)}$	−5.11	6.23	8.18	1.48	90
$C_{(6)}$–$C_{(7)}$	−5.01	6.07	8.15	1.48	90
$C_{(7)}$–$C_{(8)}$	−5.06	6.19	8.20	1.48	90
$C_{(8)}$–$C_{(8a)}$	−4.84	6.11	8.12	1.48	90
$C_{(8a)}$–$C_{(4a)}$	−4.50	5.87	8.01	1.48	270

a) In all cases the optimum value of θ was found to be 30°.

Calculations

All calculations were carried out on a FACOM M-190 computer at the Computation Center of Kyushu University.

The following values for bond angles of acenaphthylene, indene and 1,2-dihydronaphthalene were based on the X-ray crystallographic analysis data for acenaphthene [18] and cyclopentadiene,[19] and on the electron diffraction data for cyclohexadiene.[20] Acenaphthylene: $\angle C_{(8b)}C_{(8a)}C_{(1)}$, 98.2°; $\angle C_{(2)}C_{(1)}C_{(8a)}$, 111.8°. Indene: $\angle C_{(3)}C_{(3a)}C_{(7a)}$, 111°; $\angle C_{(3a)}C_{(7a)}C_{(1)}$, 105°; $\angle C_{(7a)}C_{(1)}C_{(2)}$, 105.7°; $\angle C_{(1)}C_{(2)}C_{(3)}$, 108.2°; $\angle C_{(2)}C_{(3)}C_{(3a)}$, 110.1°. 1,2-Dihydronaphthalene: $\angle C_{(4)}C_{(4a)}C_{(8a)}$, 122°; $\angle C_{(4a)}C_{(8a)}C_{(1)}$, 122°; $\angle C_{(8a)}C_{(1)}C_{(2)}$, 114.2°; $\angle C_{(1)}C_{(2)}C_{(3)}$, 118.7°; $\angle C_{(2)}C_{(3)}C_{(4)}$, 118.7°; $\angle C_{(3)}C_{(4)}C_{(4a)}$, 122.2°.

Values for all other bond angles and for all bond lengths were taken from the literature.[21]

18) H.W.W. Ehrlich, *Acta Cryst.*, **10**, 699 (1957).
19) G. Liebling and R.E. Marsh, *Acta Cryst.*, **19**, 202 (1965).
20) H. Oberhammer and S.H. Bauer, *J. Am. Chem. Soc.*, **91**, 10 (1969).
21) J.A. Pople and D.L. Beveridge, "Approximate Molecular Orbital Theory," McGraw-Hill, New York, N.Y., 1970.