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Semi-empirical Self-consistent Field Molecular Orbital Calculation of Transition Energy and Oscillator Strength for the Stacked Complexes of Pyrene and 3, 4-Benzopyrene with DNA Bases

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The transition energy and oscillator strength of stacked complexes of pyrene and 3, 4-benzopyrene with DNA bases are calculated using semi-empirical ASMO SCF CI method, and they are compared with those of free pyrene or 3, 4-benzopyrene. Among the assumed stacking models, the intercalation-like one with guanine reproduced well the experimentally observed red shift and decrease of absorption coefficient in DNA aqueous solution, and this result seems to support the intercalation-like stacking of these hydrocarbons with the DNA bases.

Relating to the carcinogenicity of aromatic hydrocarbons, many investigations on the interaction of these compounds with DNA have been carried out,[1-6] and it is known that the hydrocarbons are more soluble in purine bases than in pyrimidine ones,[1] that in native DNA solution, the absorption maxima of 3, 4-benzopyrene and pyrene shift towards longer wavelength by about 10 mμ (334 mμ→344 mμ for pyrene, 383 mμ→395 mμ for 3, 4-benzopyrene). Furthermore, about fifty percent depression of the absorption coefficient has been observed for pyrene.[1] Based on these experimental facts, Boyland and Green,[1] and Liquori *et al.*,[2] have proposed that the hydrocarbons were intercalated between the bases of double-stranded DNA.

On the other hand, Giovanella *et al.*,[7] and Heidelberger[8] showed that hydrocarbon in DNA solution was sedimented or filtered by high-speed centrifugation or millipore filters and insisted that the hydrocarbons were not bound to DNA but existed as an aqueous colloidal suspension. In order to make clear this controversial problem, the present authors, by using the flow dichroism method, have investigated the interaction between DNA and the aromatic hydrocarbons, and have found that hydrocarbons were bound truely to DNA.[9] Interacted hydrocarbons could be extracted with organic solvents, showing that the binding is not covalent.[1,6,9] From the values of dichroism,[9] two types of orientation of hydrocarbons in DNA were found, that is, oriented in parallel or perpendicular with the base planes, and pyrene and 3, 4-benzopyrene were found to belong to the former group. The binding of the hydrocarbons to DNA was strongly inhibited by the presence of proflavine,[6] and this fact, together with the results of the flow dichroism measurements seemed to support the idea that the hydrocarbons were intercalated between DNA bases. However, the possibility of simple insertion, not intercalation-like interaction, may not be denied.

In the study of the interaction between organic dye and DNA, X-ray diffraction measurement has proved to be a powerful tool for clarifying the details of the interaction, and organic dyes have been found to be intercalated between the bases of DNA.[10] But, owing to a small number of interacted hydrocarbons to DNA (about 1/30 and 1/90 nucleotides for pyrene and 3, 4-benzopyrene, respectively),[1] this method is not applicable to the present problem. In these circumstances, the theoretical investigation based on the quantum-mechanical calculation of the complex between the hydrocarbon and DNA bases may be worthy to be done.

In the present paper, we describe the results of calculation on the transition energy and oscillator strength by means of the semi-empirical ASMO SCF Cl method assuming the several models of interaction between the hydrocarbons and purine bases of DNA. It was found that the calculated values for the models of intercalation-like stacking reproduced well the spectroscopic data such as

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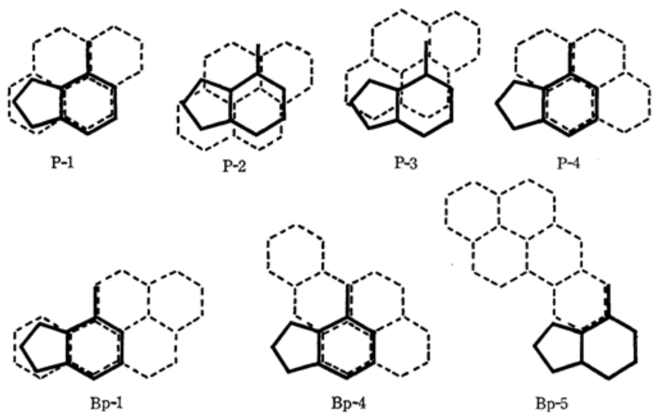

Fig. 1. The postulated models of stacking. Guanine or adenine are indicated by solid lines and pyrene or 3,4-benzopyrene by broken lines.

the red shift of absorption maximum and the large depression of the absorption coefficienet in DNA solution compared with those in aqueous solution or in alcohol, and this supports the intercalation-like interaction between the hydrocarbons and DNA bases. Furthermore, among the DNA bases, adenine and guanine, the latter seemed to be more active site for interaction with the aromatic hydrocarbons.

Stacking Models Adopted in Calculation

In view of the experimental facts described before, purine bases alone were considered in our calculation, and the postulated models for the interacted complex are shown in Fig. 1. Models 1 and 4 are intercalation-like stacking and model 5 is not an intercalation type but a simple insertion. Models 2 and 3 were adopted to see the effects of change in overlap by sliding the hydrocarbon relatively to the bases. In each model the distance between the hydrocarbon and base was taken as 3.36 Å, which is one between the adjacent bases of double-stranded DNA. In order to investigate the dependence on the distance between the hydrocarbon and base, calculation was carried out for pyrene-guanine and pyrene-adenine stacking (model 1) assuming 3 Å distance.

Calculation Procedure

The calculation has been performed according to the semi-empirical SCF LCAO MO method outlined by Pariser, Parr and Pople,[11,12] and the main procedure is the same as that of our previous paper.[13] Namely, one center repulsion integral was obtained from Pariser-Parr approximation and two center repulsion integral from Mataga-Nishimoto one.[14] The values used in this calculation are the same as those in our previous paper.[13] The differential overlaps and the penetration integrals were neglected as is usually done. The core integrals were evaluated according to the Goeppert-Mayer and Sklar potential,[15] and the resonance core integrals were given as follows;

$$\beta_{rs} = (K/2)S_{rs}(I_r + I_s) \tag{1}$$

where S_{rs} is the overlap integral between the rth and sth atomic orbitals and I_r and I_s are the ionization potentials of rth and sth atoms, respectively. This equation was also used in calculating the resonance integrals between the atoms of base and hydrocarbon[16] and $2p\pi$ and $2p\sigma$ type overlap integrals were calculated according to Mulliken's method.[17] Proportional constant K was determined from the resonance integral of carbon atom in benzene, and -0.86 was used throughout the calculation. The oscillator strength of transition was calculated by the equation:

$$f = 1.085 \times 10^{-5} \sigma_{ob} M^2_{ob} \tag{2}$$

where σ_{ob} is the wave number of the transition and M_{ob} is the corresponding transition moment.

After SCF calculation, CI calculation was done, and the matrix element appearing in the calculation were evaluated with the same approximation as that used in the ASMO SCF method by using the above-stated SCF molecular orbitals. The configuration taken into the CI calculation without

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TABLE 1. EXCITED CONFIGURATIONS TAKEN INTO ACCOUNT IN THE CI CALCULATION WITHOUT CHARGE TRANSFER

Model		Transition*
Pyrene		P_8–P_9, P_8–P_{10}, P_8–P_{11}, P_7–P_9
Pyrene-Adenine	1, 2, 3	P_8–P_9, P_8–P_{10}, P_8–P_{11}, P_7–P_9, A_6–A_7, A_6–A_8, A_6–A_9, A_5–A_7
	4	P_8–P_9, P_8–P_{10}, P_7–P_9, P_7–P_{10}, A_6–A_7, A_6–A_8, A_5–A_7, A_5–A_8
Pyrene-Guanine	1, 2, 3, 4	P_8–P_9, P_8–P_{10}, P_8–P_{11}, P_7–P_9, G_7–G_8, G_7–G_9, G_7–G_{10}, G_6–G_8
3, 4-Benzopyrene		B_{10}–B_{11}, B_{10}–B_{12}, B_9–B_{11}, B_{10}–B_{14}
3, 4-Benzopyrene-Adenine	1, 5	B_{10}–B_{11}, B_{10}–B_{12}, B_9–B_{11}, B_{10}–B_{14}, A_6–A_7, A_6–A_8, A_6–A_9, A_5–A_7
	4	B_{10}–B_{11}, B_{10}–B_{12}, B_9–B_{11}, B_{10}–B_{13}, A_6–A_7, A_6–A_8, A_5–A_7, A_5–A_8
3, 4-Benzopyrene-Guanine	1, 4	B_{10}–B_{11}, B_{10}–B_{12}, B_9–B_{11}, B_{10}–B_{13}, G_7–G_8, G_7–G_9, G_7–G_{10}, G_7–G_{11}
	5	B_{10}–B_{11}, B_{10}–B_{12}, B_9–B_{11}, B_{10}–B_{14}, G_7–G_8, G_7–G_9, G_7–G_{10}, G_7–G_{11}

Abbreviation; P: Pyrene, B: 3, 4-Benzopyrene, A: Adenine, G: Guanine

* Numbers of suffix designate the molecular orbitals numbered successively from the lowest orbital.

TABLE 2. COMPARISON OF THE CALCULATED TRANSITION ENERGY AND OSCILLATOR STRENGTH OF PYRENE AND 3, 4-BENZOPYRENE WITH EXPERIMENTAL VALUES

Compound	Transition*	Transition energy in eV(mμ)		Oscillator strength	
		Calculated	Experiment**	Calculated	Experiment***
Pyrene	$1 \to 2(8 \to 9)$	3.744(331.1) l	3.717(333.5) l	1.356	0.429
	$1 \to 3(8 \to 10)$	3.832(323.5) s	3.363(371.5) s	0.013	0.003
	$1 \to 4(8 \to 11)$	4.167(297.5)		0.000	
	$1 \to 5(7 \to 9)$	4.652(266.4) s	4.557(272.0) s	1.276	0.503
3, 4-Benzopyrene	$1 \to 2(10 \to 11)$	3.365(368.4)	3.224(384.5)	1.102	0.115
	$1 \to 3(10 \to 12)$	3.486(355.6)	3.076(403.0)	0.004	0.008
	$1 \to 4(10 \to 14)$	4.097(302.5)	4.180(296.5)	0.087	0.264
	$1 \to 5(9 \to 11)$	4.182(296.4)	4.669(265.5)	1.613	0.985

* $1 \to 2$, $1 \to 3, \cdots$ mean the transitions from the ground state (1) to the excited states $(2, 3, \cdots)$.

** Experimental values for transition energy and optical density are taken from Ref. 18.

*** Experimental oscillator strengths are obtained by using the effective wave number limit method (J. R. Platt and H. B. Klevens, *Chem. Revs.*, **41**, 301 (1947)).

Abbreviation: l, long-axis polarized; s, short-axis polarized

charge transfer are shown in Table 1, and charge transfer transitions taken into the CI calculation containing charge transfer are illustrated in Fig. 2 by arrows.

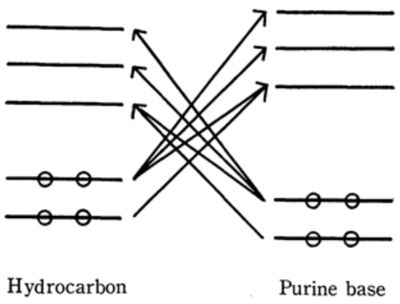

Fig. 2. The charge transfer transitions taken into account in the CI calculation containing charge transfer states.

Results and Discussion

For testing the validity of the results of the calculation, the transition energy and oscillator strength for pyrene and 3, 4-benzopyrene are compared with experimental results obtained by Clar(18) (Table 2). As to the transition energy, an agreement between the calculation and experimental values is good for both compounds, especially for pyrene. A disagreement for pyrene is that the very weak absorption peak which is short-axis polarized has been observed at the longest wavelength at 371.5 mμ,(19) while the calculated transition energy corresponding to this absorption band appeared at the second longest wavelength. Just the same situation appeared in the calculation of Bloor and Brearley,(20) although in a calculation of Nishimoto and Foster,(21) forbidden band appeared at the longest wavelength.

For the case of 3, 4-benzopyrene, assignment of absorption peak is more difficult than the case

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TABLE 3. COMPARISON OF CALCULATED TRANSITION ENERGY AND OSCILLATOR STRENGTH BETWEEN FREE PYRENE AND IT'S STACKED STATES WITH GUANINE AND ADENINE

Transition			$P_8 \rightarrow P_9$		$P_8 \rightarrow P_{10}$		$P_7 \rightarrow P_9$	
Model			E in eV(mμ)	f	E in eV(mμ)	f	E in eV(mμ)	f
Pyrene		non CT	3.744(331.1)	1.356	3.832(323.5)	0.013	4.652(266.4)	1.276
Pyrene-Guanine $R=3.36$ Å	1	non CT	3.744(331.1)	0.67	3.992(310.5)	0.002	4.703(263.6)	1.13
		CT	3.730(332.3)	0.40	3.850(321.9)	0.12	4.796(258.4)	1.23
	2	non CT	3.748(330.7)	0.65	3.924(315.9)	0.002	4.671(265.4)	0.97
		CT	3.735(331.9)	0.31	3.872(320.1)	0.28	4.650(266.6)	0.48
	3	non CT	3.715(333.6)	0.64	4.059(305.4)	0.05	4.629(267.8)	0.61
		CT	3.721(333.1)	0.39	3.881(319.4)	0.10	4.652(266.4)	0.35
	4	non CT	3.734(331.9)	0.81	3.850(321.9)	0.02	4.638(267.2)	0.82
		CT	3.728(332.5)	0.71	3.848(322.1)	0.02	4.632(267.6)	0.68
Pyrene-Adenine $R=3.36$ Å	1	non CT	3.766(329.1)	1.12	3.965(312.6)	0.01	4.531(273.6)	0.69
		CT	3.747(330.8)	0.87	3.844(322.5)	0.05	4.546(272.7)	0.40
	2	non CT	3.778(328.1)	1.09	3.874(320.0)	0.01	4.638(267.2)	0.83
		CT	3.762(329.5)	0.90	3.856(321.4)	0.02	4.629(267.8)	0.73
	3	non CT	3.784(327.6)	1.15	3.992(310.5)	0.005	4.570(271.2)	0.73
		CT	3.774(328.4)	0.97	3.842(322.6)	0.07	4.611(268.8)	0.69
	4	non CT	3.769(328.9)	1.16	3.966(312.5)	0.003	4.680(264.9)	1.38
		CT	3.760(329.7)	1.11	3.880(319.5)	0.01	4.715(262.9)	1.57
Pyrene-Guanine $R=3.0$ Å	1	non CT	3.593(345.0)	0.44	4.054(305.7)	0.24	4.732(261.9)	0.96
		CT	3.611(343.3)	0.44	3.953(313.6)	0.40	4.754(260.7)	0.89
Pyrene-Adenine $R=3.0$ Å	1	non CT	3.601(344.2)	0.87	3.848(322.1)	0.05	4.403(281.5)	0.40
		CT	3.513(352.8)	0.36	3.776(328.3)	0.12	4.293(288.7)	0.20

Abbreviation, E: Transition energy, f: Oscillator strength, R: The distance between the planes of the hydrocarbons and DNA bases; non CT or CT indicate that the charge transfer configurations are not or are taken into account in the calculation.

TABLE 4. COMPARISON OF CALCULATED TRANSITION ENERGY AND OSCILLATOR STRENGTH BETWEEN FREE 3,4-BENZOPYRENE AND IT'S STACKED STATES WITH GUANINE OR ADENINE

Transition			$B_{10} \rightarrow B_{11}$		$B_{10} \rightarrow B_{12}$		$B_9 \rightarrow B_{11}$	
Model			E in eV(mμ)	f	E in eV(mμ)	f	E in eV(mμ)	f
3,4-Benzopyrene		non CT	3.365(368.4)	1.10	3.486(355.6)	0.004	4.182(296.4)	1.61
3,4-Benzopyrene-Guanine $R=3.36$ Å	1	non CT	3.282(377.7)	0.65	3.552(349.0)	0.004	4.085(303.4)	1.19
		CT	3.260(380.2)	0.39	3.493(354.9)	0.008	4.137(299.6)	0.41
	4	non CT	3.157(392.6)	0.97	3.350(370.0)	0.06	4.140(299.4)	0.68
		CT	3.136(395.2)	0.82	3.352(369.8)	0.05	4.087(303.3)	1.10
	5	non CT	3.358(369.1)	0.89	3.444(360.0)	0.009	4.153(298.5)	1.39
		CT	3.357(369.2)	0.88	3.437(360.6)	0.006	4.158(298.1)	1.16
3,4-Benzopyrene-Adenine $R=3.36$ Å	1	non CT	3.359(369.0)	0.87	3.541(350.0)	0.15	4.205(294.8)	0.89
		CT	3.310(374.5)	0.80	3.434(360.9)	0.04	4.180(296.5)	0.68
	4	non CT	3.200(387.3)	1.07	3.371(367.7)	0.03	4.144(299.1)	0.59
		CT	3.198(387.6)	1.05	3.332(372.0)	0.006	4.125(300.5)	0.58
	5	non CT	3.364(368.5)	0.99	3.526(351.5)	0.078	4.218(293.9)	1.58
		CT	3.362(368.7)	0.96	3.436(360.7)	0.003	4.125(300.5)	1.94

Abbreviation; B: 3,4-Benzopyrene, others are the same as those of Table 3.

of pyrene, and agreement between the calculated and experimental values is not so good as the case of pyrene. As in the case of pyrene, weak band which is considered to correspond to the observed longest wavelength at 403 mμ appeared at the second wavelength.

With regard to the oscillator strength, an agreement between the calculation and experimental results is not so good as in the case of transition energy, but in general, MO calculation is known to give too large oscillator strengths than the experimental values. In view of this fact, the agreement between calculation and experiment is not so bad in the case of pyrene. For 3,4-benzopyrene, an agreement between the calculation and experiment is not satisfactory, especially for the transitions at 3.224 eV and 4.18 eV. This point might be improved by considering more configuration interactions.

As was stated before, red shift due to the solubilization of pyrene and 3, 4-benzopyrene in DNA aqueous solution have been observed at 334 mμ and 384 mμ, respectively. These absorption peaks correspond to the calculated transitions of 8→9 of pyrene and 10→11 of 3, 4-benzopyrene respectively (Table 2), and the comparisons are made for these transitions between the isolated state and stacked ones in Tables 3 and 4. However, for the comparison, other transitions are indicated together.

It has been demonstrated experimentally that aromatic hydrocarbons are more soluble in purine bases than in pyrimidine ones, indicating that the binding affinity of formers is larger than that of latters. However, no definite information has been obtained as to which is larger between guanine and adenine in binding capacity with aromatic hydrocarbons. As is seen in Table 3, transition energies in $P_8 \rightarrow P_9$, for all models of pyrene-adenine stacking at the distance 3.36 Å are larger than that of free pyrene. This contradicts the fact that the absorption maximum at 334 mμ of pyrene in aqueous solution shifts to the longer wavelength (343 mμ) in DNA aqueous solution. On the other hand, if charge transfer configuration were taken into consideration, calculated transition energy of $P_8 \rightarrow P_9$ transition, for all models of pyrene-guanine stacking at distance 3.36 Å are smaller than that of free pyrene consisting with experiments, although the shifts are far smaller than the experimentally observed one.

The oscillator strength of pyrene has been known to be decreased by fifty per cent or more in DNA aqueous solution compared with in water.[1] Calculated oscillator strength decreased greatly in the pyrene-guanine stacking, whereas far less decreases are seen in the case of pyrene-adenine stacking. From this result, together with the change in transition energy by stacking, it may be supposed that guanine moiety is preferable site for binding with pyrene.

The transition energy and oscillator strengths for benzopyrene-purine bases stacked models are shown in Table 4. The degree of red shift for model 5 which is simple insertion, is extremely small and it is difficult to explain the experimentally observed red shift of 10 mμ. On the other hand, red shift of 10—30 mμ are calculated at the transition, $B_{10} \rightarrow B_{11}$ of models 1 and 4 for benzopyrene-guanine and benzopyrene-adenine stacking. As far as the transition energy is concerned, therefore, intercalation-like stacking models agree with experimental result than the simple insertion model.

It is noteworthy that the charge transfer configurations contribute to bring about the decrease of transition energy in almost all models, especially the effects are remarkable in the cases of model 1 of benzopyrene-guanine, or models 1 and 2 of pyrene-guanine stacking. This might suggest that the charge transfer force is involved in the binding between DNA bases and pyrene or 3, 4-benzopyrene.

In all cases, the calculated absorption coefficients for the stacked states are smaller than that of free hydrocarbons. The amounts of decrease depend on the stacked molecules, model of stacking, and charge transfer configuration: thus, guanine or pyrene is more effective than adenine or 3, 4-benzopyrene, and decrease is more remarkable in model 1 or 2 than the other stacking models. No definite value have been observed experimentally as to the decrease of absorption coefficient of 3, 4-benzopyrene when it interacted with DNA, though some decrease have been expected. It is noteworthy that in the case of 3, 4-benzopyrene, model 1 with guanine gave the especially large amount of decrease.

As is seen in Table 3, both of the transition energy and oscillator strength vary greatly with the change of the distance between the stacked molecules. If we take the model 1 for pyrene-purine bases stacking as an example, the transition energy and oscillator strength decrease remarkably by varying the distance from 3.36 Å to 3.0 Å. In order to reproduce the experimental value of red shift, the distance between the stacked molecules must be smaller in the case of pyrene than the case of 3, 4-benzopyrene, hence it could be supposed that pyrene is intercalated into narrower space than 3, 4-benzopyrene.

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