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A Molecular Orbital Study on the Ternary Complex of Tetranactin, NH_4^+ and SCN^-

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The ternary complex of tetranactin, NH_4^+ and SCN^- was studied from an *ab initio* quantum chemical point of view. When NH_4^+ is inserted into tetranactin, the interaction energy is -109.0 kcal/mol. When SCN^- interacts with the tetranactin-NH_4^+ complex, the interaction energy is -49.4 kcal/mol. This value isalmost entirely due to the electrostatic interaction between SCN^- and NH_4^+. Therefore the interaction energy on ternary complex formation will be over -158.4 kcal/mol. The ternary complex of tetranactin, NH_4^+ and an uncoupler such as picric acid or SF6847 should be similar.

Keywords——molecular orbital; *ab initio*; ternary complex; complex; tetranactin; ammonium ion; structure; inclusion complex; membrane transport; MO

Tetranactin is one of the nonactins, which increase the fluxes of ions across thin lipid membranes.[2] It forms ammonium ion complexes.[3] In another paper,[4] the tetranactin-NH_4^+ complex was studied from a quantum chemical point of view. When the ammonium ion is inserted into tetranactin in a nonpolar solvent, a counter anion such as SCN^- is bound to the tetranactin-NH_4^+ complex.[3] In this note, the ternary complex of tetranactin, NH_4^+ and SCN^- is studied from a quantum chemical point of view.

Method

Molecular orbital calculations have been carried out within the closed-shell LCAO-SCF approximation by the *ab initio* method, using HITAC 8700 and 8800 computers in the Computer Center of the University of Tokyo. *Ab intio* calculations were performed using the GAUSSIAN 70 Program.[5] The basis sets used were STO-3G[6] and 4-31G.[7]

Since data from X-ray diffraction analyses do not give the coordinates of hydrogens, those coordinates were determined by the method given in another paper.[4] The method of energy decomposition analysis was described in other papers.[8]

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Results and Discussion

The ternary complex of tetranactin, NH_4^+ and SCN^- is shown in Fig. 1. When NH_4^+ is inserted into tetranactin, the interaction energy between NH_4^+ and tetranactin was calculated to be -109.0 kcal/mol by using a 4–31G basis set;[4] the tetranactin was replaced by four HCHO molecules and four water molecules.[9] In this note, the interaction energy between the tetranactin-NH_4^+ complex and SCN^- is calculated. In order to cast light on the complex formation between the tetranactin-NH_4^+ complex and SCN^-, the interaction energies illustrated in Fig. 2 were calculated. Since the tetranactin molecule is too large to calculate, only those parts of it influencing complex formation between the tetranactin-NH_4^+ complex and SCN^- were included in the calculations. The molecules used in place of the parts of tetranactin are shown in Fig. 3. The results of the interaction energies between SCN^- and each of these molecules, including NH_4^+, are shown in Table I. The interaction energies originate almost entirely from the electrostatic term, as shown in the columns (1)—(5), and are very close to the interaction energy between NH_4^+ and SCN^- shown in column (6) ("Type II"). The interaction energies between SCN^- and the various parts of tetranactin are described by $\Delta\Delta E_{\text{I-II}}$. $\Delta\Delta E_{\text{I-II}}$ is given by the following equation,

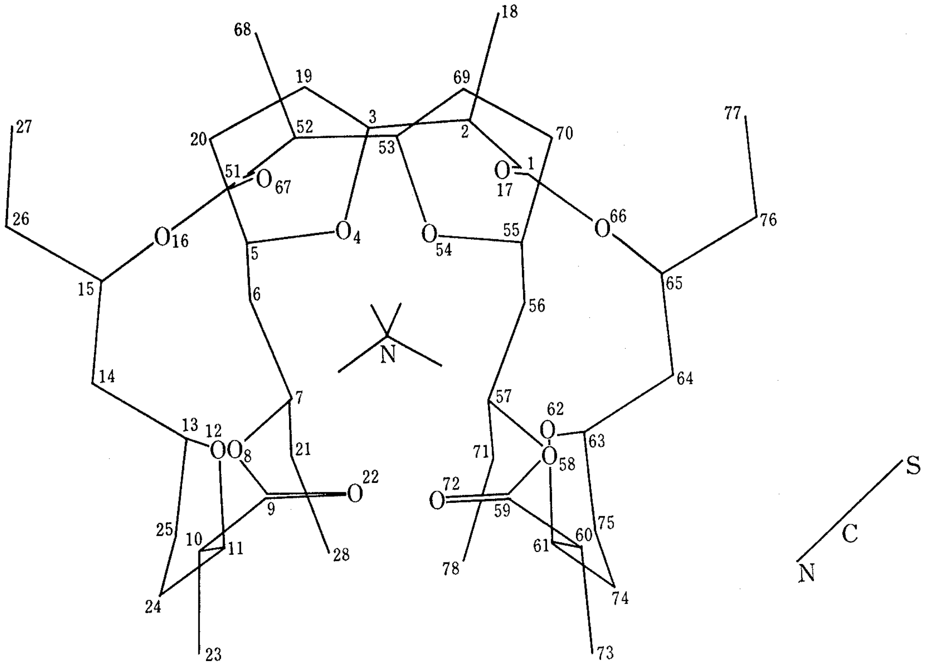

Fig. 1. Structure of the Ternary Complex of the Tetranactin, NH^+ and SCN^-

$$\Delta\Delta E_{\text{I-II}} = \Delta E_{\text{I}} - \Delta E_{\text{II}}$$

The $\Delta\Delta E_{\text{I-II}}$ values for column (1) to (5) were very small. Accordingly, the interaction energy between the tetranactin-NH_4^+ complex and SCN^- is almost entirely due to the interaction energy between NH_4^+ and SCN^-.

Since the electrostatic interaction energy between SCN^- and NH_4^+ was most significant in the complex between SCN^- and the tetranactin-NH_4^+ complex, as shown in Table I, the effects of the ether and carbonyl oxygens on the interaction between NH_4^+ and SCN^- were studied. The results are shown in Table II. The interaction energies between NH_4^+ and

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[9] Molecules other than $HO^{12}H$, $HCHO^{22}$, and NH_4^+ were included as point charges in the SCF calculation. The calculated interaction energy using an STO-3G basis set was -105.8 kcal/mol, taking molecules other than $HO^{12}H$, $HCHO^{22}$ and NH_4^+ as point charges obtained from 4-31G calculations.

each of the various parts of the tetranactin are shown as the Type III interaction in Table I. The interaction energies between the part including the ether oxygen O^{62} and NH_4^+ and between the part including the carbonyl oxygen O^{72} and NH_4^+ were much greater than other interaction energies. Therefore the ether oxygens (O^4, O^{12}, O^{54} and O^{62}) and the carbonyl oxygens (O^{17}, O^{22}, O^{67} and O^{72}) were included in the calculations of the interaction energy between NH_4^+ and SCN^-. When the four ether oxygens (O^4, O^{12}, O^{54} and O^{62}) were included,

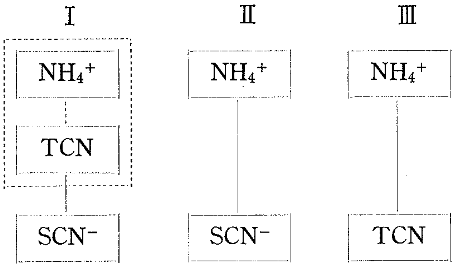

Fig. 2. The Interaction Energies in Ternary Complex Formation of Tetranactin, NH_4^+ and SCN^-

I is the interaction between the tetranactin-NH_4^+ complex and SCN^-. II is the interaction between NH_4^+ and SCN^-. III is the interaction between tetranactin and NH_4^+.

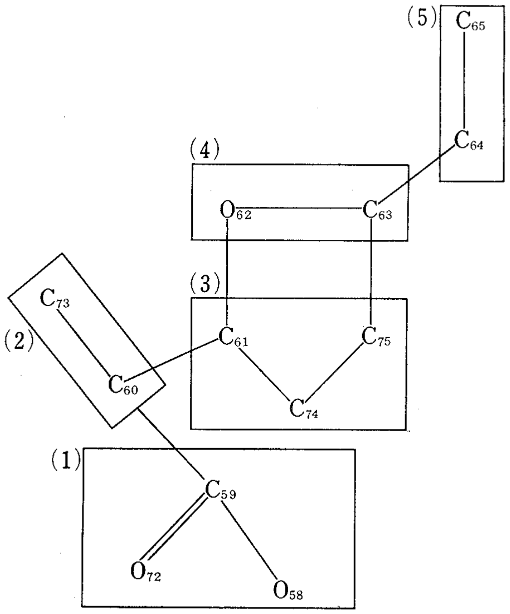

Fig. 3. Various Parts of Tetranactin used in the Calculations for the Complex between the Tetranactin-NH_4^+ Complex and SCN^-

(1) HCOOH was used in place of $-C^{59}O^{72}O^{58}-$.
(2) C_2H_6 was used in place of $-C^{73}H_3C^{60}H\langle$.
(3) C_3H_8 was used in place of $\rangle C^{61}HC^{74}H_2C^{75}H_2-$.
(4) CH_3OH was used in place of $\rangle C^{63}HO^{62}-$.
(5) C_2H_6 was used in place of $\rangle C^{65}HC^{64}H_2-$.

Table I. The Interaction Energies in kcal/mol and the Results of Energy Decomposition Analyses between SCN^- and Each of the Various Molecules used in Place of Parts of Tetranactin, Including NH_4^+, using an STO-3G Basis Set

Type		Various parts of tetranactin					
		(1)	(2)	(3)	(4)	(5)	(6)[a]
I	ΔE[b]	−49.1	−48.8	−49.8	−50.0	−48.6	−47.0
	ES	−48.4	−48.4	−48.6	−49.6	−47.6	
	EX	−0.0	3.7	2.4	0.0	1.4	
	PL	−0.6	−1.6	−1.6	−0.4	−1.0	
	$\Delta\Delta E$ (I−II)	−2.1	−1.9	−2.8	−3.1	−1.7	—
Ⅲ	ΔE	−3.6	−0.9	−1.5	−24.0	−0.6	—

(1): $HC^{59}O^{72}O^{58}H+SCN^-$, (2): $H_3C^{73}C^{60}H_3+SCN^-$, (3): $H_3C^{61}C^{74}H_2C^{75}H_3+SCN^-$, (4): $HO^{62}C^{63}H_3+SCN^-$, (5): $H_3C^{64}C^{65}H_3+SCN^-$, (6): SCN^-.

a) Since (6) is the interaction between NH_4 and SCN^-, it is called "Type II."

b) ΔE is the interaction energy between two molecules, and can be broken up into ES, EX, PL, CT and MIX. ES is the electrostatic interaction, EX is the exchange repulsion, PL is the polarization energy, CT is the charge transfer, and MIX is the coupling energy.

Table II. The Interaction Energies in kcal/mol between SCN^- and Part of the Tetranactin-NH_4^+ Complex Using a 4-31G Basis Set

	SCN^-			
	NH_4^+	$\sum_i^4 HO^iH^{a)}+NH_4^+$	$\sum_m^4 HCHO^{m\,b)}+NH_4^+$	$\sum_i^4 HO^iH+\sum_m^4 HCHO^m+NH_4^+$
ΔE	−47.5	−45.9[c]	−50.7[d]	−49.4[e]

a) The i's are 4, 12, 54 and 62 in Fig. 1.

b) The m's are 17, 22, 67 and 72 in Fig. 1.

c) Molecules other than $HO^{12}H$ and NH_4^+ were placed in the SCF calculation as point charges.

d) Molecules other than $HCHO^{22}$ and NH_4^+ were placed in the SCF calculation as point charges.

e) Molecules other than $HO^{12}H$, $HCHO^{22}$ and NH_4^+ were placed in the SCF caluculation as point charges.

the interaction energy was calculated to be −45.9 kcal/mol. Since the interaction energy between NH_4^+ and SCN^- was −47.5 kcal/mol, the effects of these ether oxygens were very small. Even when the four carbonyl oxygens (O^{17}, O^{22}, O^{67} and O^{72}) were included, the effects were still very small. Accordingly, the interaction energy between SCN^- and the tetranactin-NH_4^+ complex is almost entirely due to the direct electrostatic interaction between NH_4^+ and SCN^-.

When NH_4^+ is inserted into tetranactin, the interaction energy between NH_4^+ and the tetranactin model was −109.0 kcal/mol.[4] Since the interaction energy between SCN^- and the tetranactin-NH_4^+ complex model was −49.4 kcal/mol in Table II, the interaction energy on ternary complex formation will be over −158.4 kcal/mol. Therefore the enthalpy of ternary complex formation in a nonpolar solvent will be over −158.4 kcal/mol.

Ternary complexes among tetranactin, NH_4^+ and an uncoupler such as picric acid or SF6847 have been reported.[10] The factors involved in the formation of these ternary complexes should be similar to those discussed here.

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A New Synthesis of Pyrimido[4,5-*b*]quinoline-2,4(1*H*,3*H*)diones (5-Deazaalloxazines) by Oxidative Cyclization of Aryl-bis(6-amino-1,3-dimethyluracil-5-yl)-methanes with Diethyl Azodicarboxylate

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Treatment of aryl-bis(6-amino-1,3-dimethyluracil-5-yl)methanes, which were prepared by the condensation of 6-amino-1,3-dimethyluracil with aryl aldehydes, with diethyl azodicarboxylate in the presence of sulfolane led to the formation of the corresponding 1,3-dimethylpyrimido[4,5-*b*]quinoline-2,4(1*H*,3*H*)diones (1,3-dimethyl-5-deazaalloxazines).

Keywords——5-deazaalloxazine; pyrimido[4,5-*b*]quinoline; oxidative cyclization; diethyl azodicarboxylate; bis(6-amino-1,3-dimethyluracil-5-yl)methane

Diethyl azodicarboxylate (DAD) is a strong hydrogen acceptor and has been shown to be a useful reagent for the syntheses of various heterocycles.[2] The present paper describes a new synthesis of 1,3-dimethylpyrimido[4,5-*b*]quinoline-2,4(1*H*,3*H*)diones (1,3-dimethyl-5-deazaalloxazines) by the oxidative cyclization of aryl-bis(6-amino-1,3-dimethyluracil-5-yl)-methanes with DAD. Previously it was reported that the treatment of 6-anilino-1,3-dimethyluracils with dimethylformamide dimethylacetal afforded the corresponding 1,3-dimethylpyrimido[4,5-*b*]quinoline-2,4(1*H*,3*H*)diones (1,3-dimethyl-5-deazaalloxazines).[3] Although this

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