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Theoretical Studies on the Photochemical Reactions of 5,7-Dimethoxycoumarin with Adenosine. The Electronic States of 5,7-Dimethoxycoumarin and their Photoadducts

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The chemical reactivity of 5,7-dimethoxycoumarine with adenosine has been calculated by the frontier electron and PPP-CI MO methods. Results suggest that the major reactivity of the 5,7-dimethoxycoumarin is highest at the carbon-4 (position 4), whereas the electrophilic reactivity is generally spread all over the 5,7-dimethoxycoumarin molecule. These results are consistent with the experimental photoaddition reaction products. The small change of bond orders on excitation does not give enough reactivity to triplet states or the efficient intersystem crossing from T_1 to S_0 inhibits photoaddition of 5,7-dimethoxycoumarine to adenosine. Although the relative intensity of the singlet band appears to be considerably higher than the triplet band intensity, its integrated intensity, *i.e.* oscillator strength, is comparable to that of the 5,7-dimethoxycoumarin and adenosine bands.

Introduction

The fluorescence quantum yield of 5,7-dimethoxycoumarin ($\phi_f = 0.65$) is much higher than that of psoralen while the ratio of phosphorescence to fluorescence quantum yields ($\phi_p/\phi_f = 0.05$) is lower than that of psoralen.[1,2] These differences are due to a significant gap between the low lying (π,π^*) and (n,π^*) singlet states in 5,7-dimethoxycoumarin.

The formation of interstrand cross-linking through [2+2] cycloaddition of 3,4-and 4′,5′-double bonds of the psoralens to the 5,6-double bond of the pyrimidine bases, especially thymine, in DNA has been correlated with biological effects of photoexcited psoralens.[3-7]

The photoreaction between psoralens and pyrimidine base can be devided into three distinct steps: (1) formation of a noncovalent complex with pyrimidine base via interacalation of the psoralen between adjacent base pairs (2) photoreaction between the psoralen and a pyrimidine base giving a monoadduct (3,4-or 4′,5′-monoadduct) (3) absorption of a second photon to yield an interstrand cross-link. The interstrand cross links are believed to be largely responsible for the photosensitizing effects of psoralen treatment, although some activity is apparently associated with monoadducts.[8,9]

5,7-Dimethoxycoumarin dimerizes through [2+2] cycloaddition of 3,4-double bond to form a *syn* head to tail dimer on direct irradiation ($\lambda \geq 300$nm) in acetonitrile or benzene solution with a quantum yield of 0.068 via an excited singlet state. In the presence of triplet sensitizers such as benzophenone, an *anti* dimer with a quantum yield of 0.08 is obtained via or through pyrimidine base reaction.[10] The nature of these photoaddition reactions between the excited 5,7-dimethoxycoumarin with adenosine is not clearly understood.

In continuation of our studies on the nature of the photobiological activity of 5,7-demethoxycoumarin,[11,12] electronic states and spectroscopic studies of the photoadducts formed in the photoaddition of 5,7-dimethoxycoumarin with adenosine are carried out in this investigation.

In this paper, we describe the photochemical reactivity of the 5,7-dimethoxycoumarin to adenosine, with the aim of establishing a basis for the photoaddition reaction. The numbering scheme for nonhydrogen atoms is given below for the 5,7-dimethoxycoumarin and adenosine (Figure 1).

Calculations

The electronic structure of the excited states of 5,7-dimethoxycoumarin and adenosine by using a model compound is examined by SCF-MO-CI P-P-P method[13] and the reactivity indices, frontier electron densities and super-

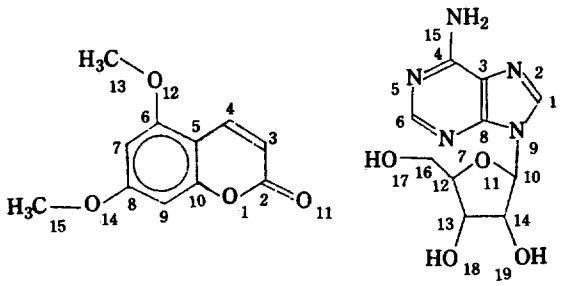

Figure 1. The numbering scheme of 5,7-dimethoxycoumarin and adenosine.

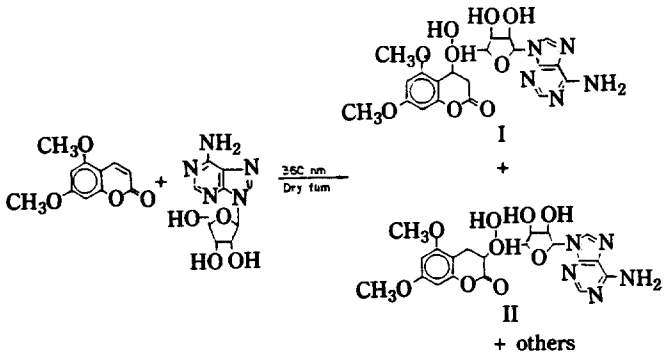

Figure 2. Photoreaction of DMC with adenosine.

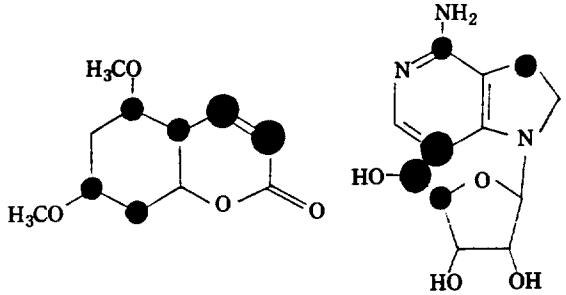

Figure 3. The reactivity maps of 5,7-dimethoxycoumarin and adenosine; FOD>0.12.

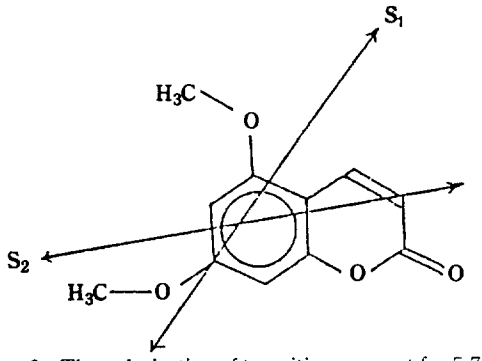

Figure 4. The polarization of transition moment for 5,7-dimethoxycoumarin.

delocalizabilities were calculated by the methods of Fukui *et al.*[14-16] π-Molecular orbital orbital wave functions were obtained within the framework of Hückel approxmations. The two-center electron repulsion integrals of the form(rr/ss) are estimated according to the Magata and Nishimoto formula.[17] The SCF-CI wavefunctions of the molecule can be expressed in terms of the corresponding wave function of "reference" orbitals by using CA method.[18,19]

The electron densities, transition moment directions, energies of excited states, oscillator strength, and bond orders were calculated by the SCF-MO-CI P-P-P method. Semiempirical input parameters for various functional groups are given elsewhere.[20-24]

The oscillator strength is used quantitatively to indicate the relative intensities of various transitions, primarily in the visible, UV, and vacuum UV. The oscillator strength is directly proportional to the intergrated area corresponding to an absorption band.

Oscillator strength of phytochrome were evaluated by using equation

$$f=4.315\times10^{-9}\int\varepsilon(\bar{\nu})\,d\bar{\nu}$$

The symbol $\varepsilon(\bar{\nu})$ is defined as the molar extinction coefficient and has units of $cm^{-1}M^{-1}$. Absorption spectra were resolved by Gaussian curve analysis. Peak areas in the near uv region were determined by multiplying the area under the curve from max of uv region to the longer wavelength region by two. The photoaddition of excited 5,7-dimethoxycoumarin to adenosine is given below. (Figure 2).

Results and Discussion

The photoreaction of 5,7-dimethoxycoumarin only one photochemically reactive functional group (pyrone double bond) with adenosine has been reported as a model reaction in order to elucidate the stereochemistry of photoadducts between psoralen and DNA base.[21] In the frontier molecular orbital approximation, only nucleophile HOMO (−10.0 eV) and electrophile LUMO (−9.3 eV) which are closest in energy are taken into account. The difference in the stabilization energy ΔE for the present case, is used as a measure of the activation energies.

In Figure 3, the chemical reactivity index, frontier electron density, can be used as a measure of the relative reactivity of the various positions of the 5,7-dimethoxycoumarin. It was found that the frontier electron density, fr, is qualified to be an reactivity index. The most reactive position of 5,7-dimethoxycoumarin is predicted at C-4, as both the superdelocalizability (SD_N) and frontier orbital density(FOD) are highest at this position, *i.e.* 0.118 and 1.475 and at C-18of adenosine, *i. e.* 0.2404(FOD), 7.997(SD_N) respectively. The reactivity indices also show its high reactivity at C-3 of 5,7-dimethoxycoumarin, suggesting that the secondary photoadduct is predicted to exhibit a reactivity pattern similar to that of adenosine. In contrast, the electrophilic reactivity is not preferentially localized at a particular position, as reflected by the distribution of the superdelocalizability for electrophilic attack(SD_E), frontier electron density(FED). This prediction has been confirmed experimentally.[23]

Figure 4 shows the calculated polarization direction of transition moment. The S_1 state in 5,7-dimethoxycoumarin is correlated with the S_2 state of photoadduct *I*, since the S_6 of the latter is most intense and is long-axis polarized. The electron densities and mobile bond orders of 5,7-dimethoxycoumarin in the ground, lowest singlet (π, π^*), and triplet states are shwon in Figure 5. The same trend can be seen that the polarization direction should always favor the increasing

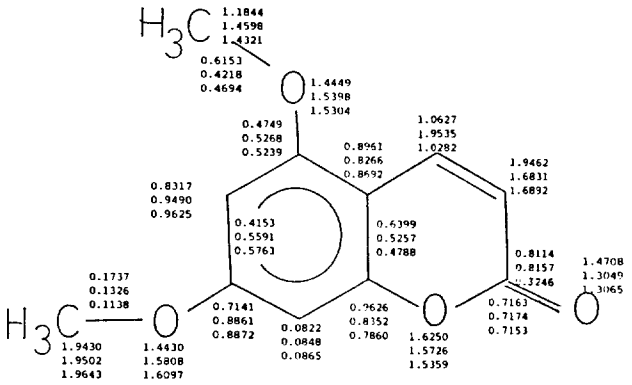

Figure 5. The π-electron density distribution and mobile bond orders, top, middle and bottom numbers at each atom between atoms refer to the ground(S_0), lowest excited singlet(S_1) and triplet (T_1) states, respectively.

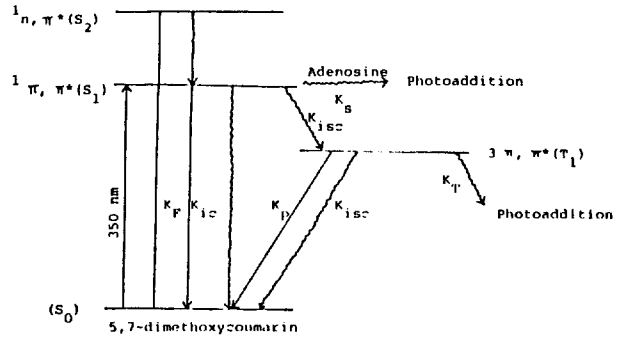

Figure 6. Transitions involved in photoaddition reaction of the excited state.

Table 1. Transition Energies and Oscillator Strengths of 5,7-Dimethoxycoumarin

Transition	state	E(eV)	λ(nm)	F
S_π-S_0	S_1	0.89	1397	0.01
	S_2	2.28	544	0.01
	S_3	3.25	382	0.12
	S_4	4.61	269	0.03
	S_5	6.17	201	0.03
T_π-T_0	T_1	0.95	1309	0.02
	T_2	1.48	838	0.01
	T_3	2.29	543	0.15
	T_4	3.92	316	0.08
	T_5	4.51	275	0.12

electron densities. The π-electron in carbonyl group is in opposite direction compared to ordinary aromatic carbonyls decreasing electron density on oxygen atom upon excitation, especially in the excited singlet state. The mobile bond orders decrease in C=C double bonds in the singlet (π,π^*) state when inductive effect alone is considered while no significant change is observed in C=O bond in 5,7-dimethoxycoumarin.

Figure 6 shows a energy level diagram for 5,7-dimethoxycoumarin. In the absence of bimolecular quenching and photoaddition reaction, the singlet and triplet states are given by the following expressions, respectively.

Table 2. Transition Energies and Oscillator Strengths of Adenosine

Transition	state	E(eV)	λ(nm)	O.S. (F)
S_n-S_0	S_1	0.86	1448	0.24
	S_2	1.63	761	0.05
	S_3	3.52	352	0.36
	S_4	4.70	264	0.39
	S_5	4.83	257	0.17
T_n-T_0	T_1	0.61	2040	0.14
	T_2	0.69	1792	0.47
	T_3	2.50	496	0.32
	T_4	2.99	414	0.22
	T_5	3.84	323	0.01

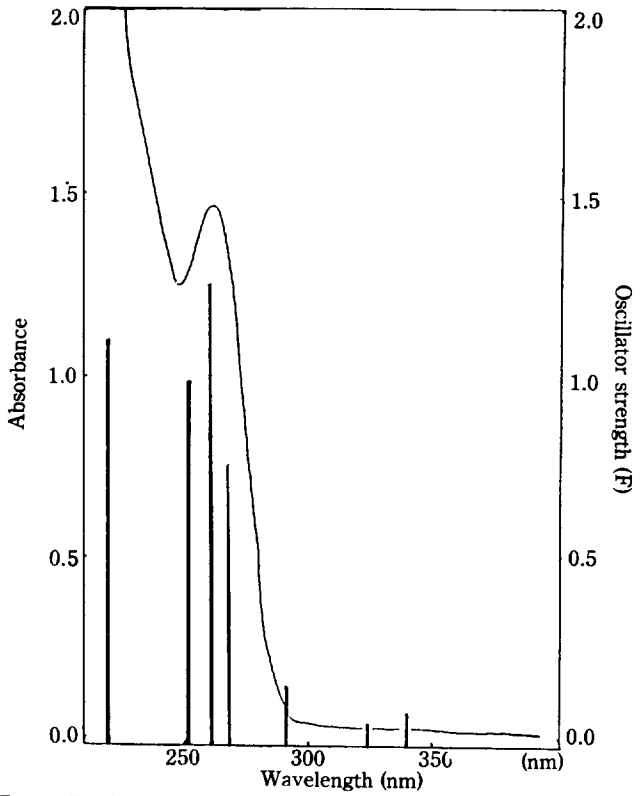

Figure 7. Calculated absorption spectrum of photoadduct I by PPP-SCF-CI. (—experimental, —calculated).

$$T_s=1/(K_F+K_{ic}+K_{isc}),\quad T_t=1/(K_{isc}+K_p)\simeq 1/K_{isc}$$

Most of the organic photochemical processes start from the lowest excited singlet and triplet states in condensed phase.[23] It is, therefore, one of the most important things in photochemistry to study the nature of these states. Unlike a thermal reaction, photoreations proceed with the excited states of limited lifetimes. Usually the longer the lifetime, the more reactive is the excited state, because the steady state concentration of the reacting state species is higher. It is therefore not suprising that only 5,7-dimethoxycoumarin, among coumarin derivatives, photoreacts with a pyrimidine base via the singlet excited state with a relatively long lifetime.[24]

The results of the calculation for singlet-singlet and

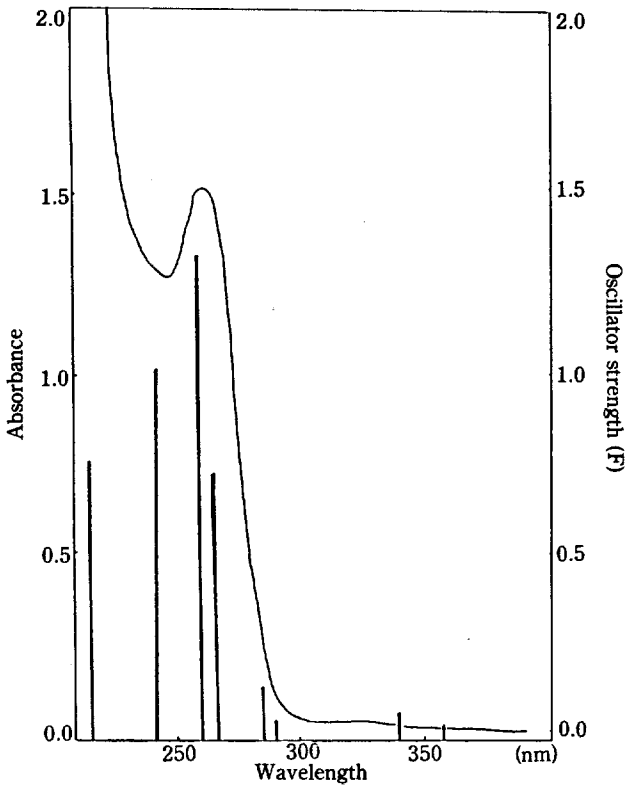

Figure 8. Calculated adsorption spectrum of photoadduct II by PPP-SCF-CI. (—experimental, —calculated).

singlet-triplet transition energies, oscillator strength, are summarized in Table 1, 2. The calculated and experimental absorption spectra of the isolated photoadduct I and II are similar to each other and 325 nm band (λ_{max} of dimethoxycoumarin) is absent. The UV spectra are exactly the sum of spectra of adenosine and 5,7-dimethoxycoumarin showing λ_{max} at 260 nm which is λ_{max} adenosine.[25]

Two photoadducts of 5,7-dimethoxycoumarin with adenosine as can be seen by comparing Figure 7 with 8. The calculated transition energies are reasonably good agreement with the experimental measurements. These photoadducts were not split short wavelength UV light, and show λ_{max} at 260 nm which is the same as that of adenosine. On the basis of the above results, we now summarized the theoretical calculations of the photoadducts that adenosine remains unchanged, photobinding of dimethoxycoumarin occurs to adenosine through covalent bond formation between C-3(for photoadduct I) and C-4(photoadduct II) of the pyrone ring of dimethoxycoumarin and ribose C-5′ of adenosine. Although the relative intensity of the singlet band appears to be considerably higher than the triplet band intensity, its oscillator strength.

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