

triene, and chloranil were purchased from Aldrich Chemical Company and were used as received. The column chromatography was performed by using Kieselgel 60 (Merck, 70-230 mesh).

Instruments. Infrared spectra were recorded on a Perkin-Elmer 283B Grating Spectrophotometer in KBr pellets or NaCl cells. $^1\text{H-NMR}$ spectra were obtained on a Varian T-60A Spectrometer or Varian FT-80A Spectrometer at 79.542 MHz. Mass spectra were obtained on a Hewlett Packard 5985A GC/MS System using electron impact (EI) method. UV spectra were recorded on a Cary-17 Spectrophotometer.

Irradiation Apparatus. Irradiation was carried out in a Rayonet Photochemical Reactor (The Southern New England Ultraviolet Company) Model RPR-208 equipped with 350 nm UV lamps. The progress of the photoreactions was monitored by pre-coated TLC (silica gel; n-hexane: ethylacetate 4:1 v/v; UV visualization).

Photoreaction of Chloranil with Cyclic Olefins. 500 mg of Chloranil and 2.0 ml of cyclohexene dissolved in 120 ml of dichloromethane was deoxygenated for 30 min by bubbling nitrogen gas and irradiated with 350 nm UV light for 22 hours in a water-cooled reaction vessel. The photoadducts were separated by the column chromatography using n-hexane-ethylacetate (4:1 v/v) as an eluting solvent. 500 mg of chloranil and 2.0 ml of 1,3-cyclohexadiene in 120 ml of dichloromethane was degassed and irradiated for 6 hours in a water-cooled reaction vessel with 350 nm UV light. The excess of diene and dichloromethane were evaporated under reduced pressure. Filtration and recrystallization (chloroform-ethylacetate) yielded a solid(**5**). **5**; m.p., 240°C; UV (methanol), λ_{max} = 308 nm; IR (KBr), 3400 (ν_{OH}), 1207 ($\nu_{\text{C-O}}$), 887 ($\nu_{\text{C=C}}$ for trisubstituted alkene), and 715 cm^{-1} ($\nu_{\text{C-C}}$); $^1\text{H-NMR}$ (80 MHz, acetone- d_6), δ = 8.90 (OH, s), and 3.75 ppm (vinyl proton, s); Mass (EI), m/e = 252 ($\text{M}^+ + 6$, rel. abund. 11.7), 250 ($\text{M}^+ + 4$, 46.7), 248 ($\text{M}^+ + 2$, 100.0). 246 (M^+

$\text{C}_6\text{H}_2\text{O}_2\text{Cl}_4$, 79.0), 217 ($\text{M}^+ \text{CHO}$, C_5HOCl_4 , 2.0), 210 ($\text{M}^+ \text{HCl}$, $\text{C}_5\text{HO}_2\text{Cl}_3$, 12.5), 182 (m/e 217-Cl, C_5HOCl_3 , 18.7), 175 (m/e 210-Cl, $\text{C}_5\text{HO}_2\text{Cl}_2$, 16.7), 147 (m/e 182-HCl, C_5HOCl_2 , 40.0), 111 (m/e 147-HCl, C_5OCl , 16.0), and 87 (m/e 111-C $\equiv$ C, C_5OCl , 53.5). 500 mg of chloranil and 2.2 ml of cycloheptatriene in 120 ml of dichloromethane was degassed for 30 min. by bubbling nitrogen gas and irradiated with 350 nm UV light for 6 hours. The solvent was evaporated in vacuo. Filtration and recrystallization (methanol-n-hexane-dichloromethane) yielded a solid(**5**).

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Theoretical Studies on the Photocycloaddition Reaction of Psoralen with Thymidine

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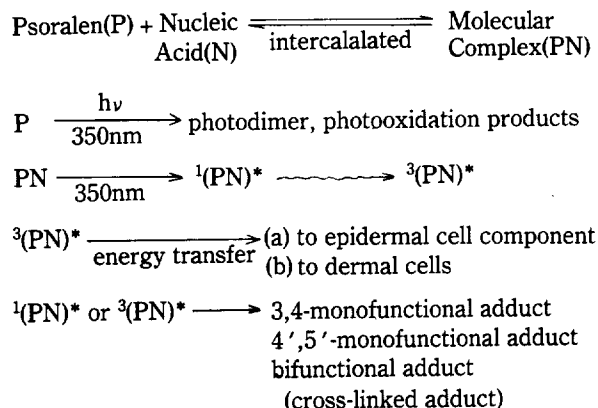
The theoretical studies on the photocycloaddition reaction of 5,7-dimethoxycoumarin and 4',5'-dihydropsoresalen with thymidine were carried out as a model for photosensitizing reaction of psoralen with DNA. The results are in reasonable agreement with experimental observations. The photoadducts between dimethoxycoumarin and thymidine were predicted to be C_4 -cycloadducts through the cycloaddition of 3,4-pyrone double bond of dimethoxycoumarin to 5,6 double bond of thymidine. The major photoadduct of 4',5'-dihydropsoresalen with thymidine has the *anti* head-to-head stereochemistry.

Introduction

The photosensitization activity of psoralens is generally

correlated to their photoreactivity with pyrimidine bases in DNA. On irradiation with near UV light, the intercalated psoralen molecule can successively photoreact with two pyri-

midine bases causing a crosslinkage between separated strands of DNA through the following mechanism.^{1,4}

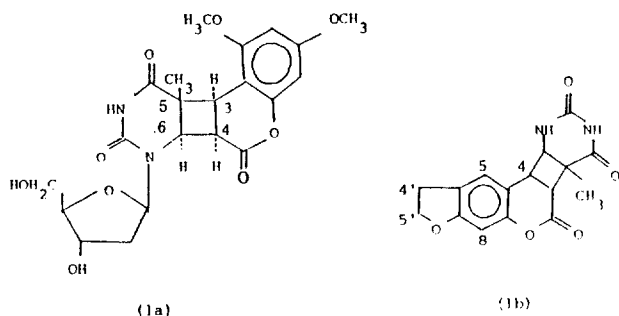


The cross-linkage is caused by the formation of cyclobutane adducts, which are produced by photoreactions of the psoralen 3,4-pyrone and 4',5',-furan double bonds of two pyrimidine bases.^{5,6} The molecular orbital calculations predict that the triplet excited state is the better candidate for the cycloaddition reaction than the singlet excited state. This prediction is consistent with the experimental finding that the oxygen and paramagnetic ions quench the photoreaction between psoralen and thymine.^{7,8}

In this paper, we report the results of MO calculations in which the charge transfer interaction to form molecular complexes between the compounds is the first step of the photocycloaddition reaction between 5,7-dimethoxycoumarin (5,7-DMC) or 4',5'-dihydropsoresalen (DHP) and pyrimidine bases.

Calculations

In the hypothetical molecular complexes, the chemical reactivity index can be used as a measure of the relative reactivity index of the various position of the photocycloaddition. It is postulated that the photocycloaddition of thymine to the excited psoralens may yield the following adducts. The numbering scheme for nonhydrogen atoms is shown for the 5,7-dimethoxycoumarin-thymidine (5,7-DMP) (1a) and 4',5'-dihydropsoresalen-thymine (1b).



The charge transfer interactions are emphasized in the calculation. The parameters in the calculations were obtained from EHT-spd and PPP-CI methods using programs distributed by QCPE.^{9,10} Charge transfer quantities were calculated both for the 5,7-DMC and pyrimidine bases and for their complexed forms.

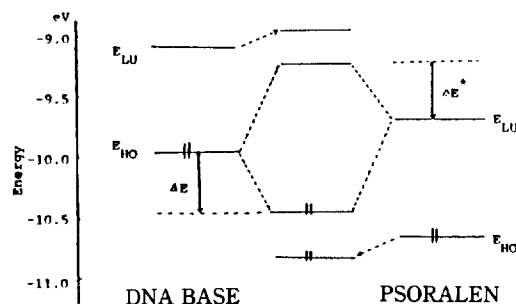


Figure 1. The interaction of a donor DNA base with an acceptor, psoralen.

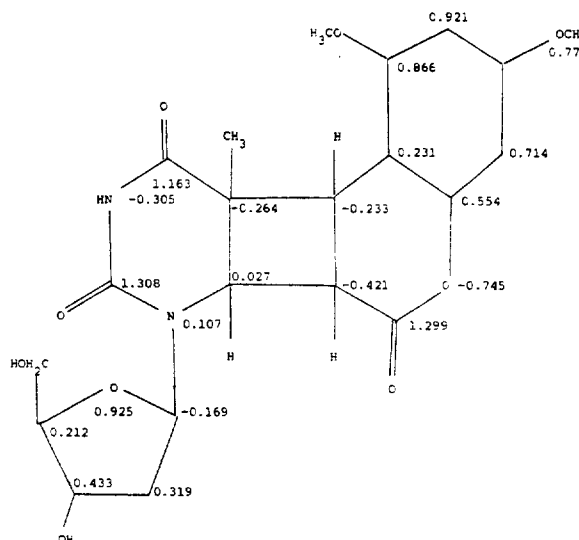


Figure 2. Net charges of 5,7-DMC <-> Thd.

Results and Discussion

The photocycloaddition reaction between 3,4-pyrone double bond of dimethoxycoumarin and 5,6-double bond of thymidine on irradiation with 350 nm UV light can produce four different C₄-cyclobutane stereoisomers theoretically; *syn* head-to-head, *syn* head-to-tail, *anti* head-to-head, and *anti* head-to-tail. Furthermore, total of sixteen different stereoisomers are possible because of the 1'-asymmetric carbon in thymidine and because of the chirality in the cyclobutane ring of photoadducts. The photoreaction of 5,7-dimethoxycoumarin with only one photochemically reactive functional group (pyrone double bond) with thymidine has been reported as a model reaction in order to elucidate the stereochemistry of photoadducts between psoralen and DNA.¹¹

In the frontier molecular orbital approximation, only the nucleophile HOMO and electrophile LUMO 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, which is schematically illustrated in Figure 1. The possible stereoisomers of photocycloaddition reaction are shown in Figure 2 and Figure 3. The most reactive position is predicted to be C-3, C-4, C-5 and the net negative charge is highest at these positions, *i.e.* -0.233, -0.421, and -0.264, respectively. This prediction has been confirmed experimentally.¹² In the photoreaction of 5,7-DMC with thymidine, 3,4-monoadducts and 4',5'-monoadducts were formed. It was also found that the negative

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Partial Reduction of Nitriles to Aldehydes by Thexylbromoborane-Methyl Sulfide†

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A systematic study of the partial reduction of nitriles to the corresponding aldehydes with thexylbromoborane-methyl sulfide ($\text{ThxBHBr}\cdot\text{SMe}_2$) under practical conditions has been carried out. The yields of aldehydes are good in the aliphatic series. However, the yields of aromatic series vary with substituents and ring itself.

The conversion of carboxylic acid derivatives, such as acid chlorides¹, esters², amides³, and nitriles⁴, to the corresponding aldehydes is a very important synthetic route. Among them, the partial reduction of nitriles to aldehydes by reducing agents is one of the widely-used methods for such transformations. Diisobutylaluminum hydride⁵ and lithium triethoxyaluminumhydride⁶ are considered as the major metal hydride reducing agent for this purpose. Very recently, Yoon and his coworkers reported that diethyldihydroaluminate achieves the partial reduction of aliphatic nitriles to aldehydes in the presence of diethylaluminum 2,6-di-*t*-butylphenoxide as a Lewis acid in high yields⁷.

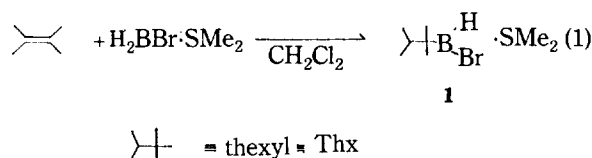
In the course of a systematic study of the reducing characteristics of thexylbromoborane-methyl sulfide⁸, we have found that this reagent possesses the ability to reduce nitriles to aldehydes efficiently, even though this reagent appeared to be a mild reducing agent.

Therefore, we decided to study systematically such reduction in the hope of establishing a practical means.

Results and Discussion

The reagent, thexylbromoborane-methyl sulfide (1), is

readily prepared by hydroborating 2,3-dimethyl-2-butene with monobromoborane-methyl sulfide in methylene chloride (eq 1). Monobromoborane-methyl sulfide is easily prepared by treating borane-methyl sulfide with a half equiv of bromine in carbon disulfide.



Thexylbromoborane-methyl sulfide is a much milder and hence more selective reducing agent than thexylchloroborane-methyl sulfide⁹. Thus, the reagent tolerates many organic functionalities, *viz.*, esters, acid chlorides, epoxides, halides and nitro compounds. Besides, the most interesting feature of this reagent is its reluctance to hydroborate double bonds even at room temperature. The chloro-derivative readily hydroborates double bonds. However, the reagent attacks the triple bond of both aliphatic and aromatic nitriles readily and the aldehyde intermediate thus formed are relatively inert to the second attack of reagent. This suggested the possibility of achieving a synthesis of aldehydes from nitriles, even in the presence of other readily reducible groups.

† Dedicated to Professor Nung Min Yoon on the occasion of his 60th birthday.