but F-electronically ground state of an $F_H(OH^-)$ center and the OH^--vibrationally unexcited but F-electronically excited state drastically lowers the crossover barrier from the relaxed excited state to the crossing point of the F center potential curves even in RbCl as illustrated in Figure 2. The unassociated F* center in RbCl is known to have the barrier that is too high to relax nonradiatively *via* crossover.[4,5] The perturbation by tunneling process may even further eliminate the effective potential barrier[15] so that the energy transfer *via* crossover process occurs nearly instantly even at cryogenic temperatures. The almost independence in temperature of the superfast recovery time suggests that the major part of F absorption bleach recovery time is the lattice-vibrational relaxation time rather than the crossover time. It seems that the associated F and OH defects in an $F_H(OH^-)$ center behave, in a sense, much like a supermolecule, in which the energy levels of each component species are no longer independent. The nature of electronic interaction in the energy transfer between the paired defects is electron exchange.

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Theoretical Studies on the Photochemical Reaction of Monofunctional Psoralen Derivatives with Thymine

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Psoralen derivatives has been actively investigated both with regard to their ability to act as dermal photosensitizing agents and as a useful tool for studying the structure and dynamics of nucleic acids.[1,2] Monofunctional derivatives of the psoralen type have two photoreactive sites, the 3,4 and 4',5' double bonds. In the presence of 356 nm light monoadducts with pyrimidine bases are found, *i.e.*, C^4-cycloaddition products involving the 5,6 double bond of pyrimidine bases are formed.[3,4] Moreover DNA cross-links are detected by serveral methods, including the melting and renaturation patten of treated DNA bases.[5] It is assumed that the 3,4 and 4',5' double bonds of monofunctional derivatives of psoralen are both involved in the formation of cross links between pyrimidine bases of opposite DNA base strands. Their Photosensitizing activity has been related to their ability to form a covalent linkage with the pyrimidine bases of DNA upon UV-A irradiation for treatment of several skin diseases.[6]

The photoreactive sites in allopsoralen (AlloPs), carbethoxypsoralen (CEOP) and pyridopsoralen (PyPs) are the 3,4 (pyrone) and 4',5' (furan) bonds. As the 3,4 mono-adduct does not absorb near UV. light, the 4',5' adducts is the intermediate involved in the formation of cross links.[7] Their biological properties have been attributed to their ability to photoreact with nucleic acids. It appears that the genotoxic effects, as well as the therapeutically important antiproliferative effects, are due mainly to their capacity to induce photoconjugation to DNA bases.

We now describe for the postulation and photoadduct of the clinically important monofunctional psoralen with thymine, chosen as a model[8-10] for the pyrimidine base in DNA with which the psoralen derivatives probably bonds. Many efforts have been expended to develop psoralen derivatives which permit only monofunctional photobinding with DNA bases and thereby diminish undesirable side ef-

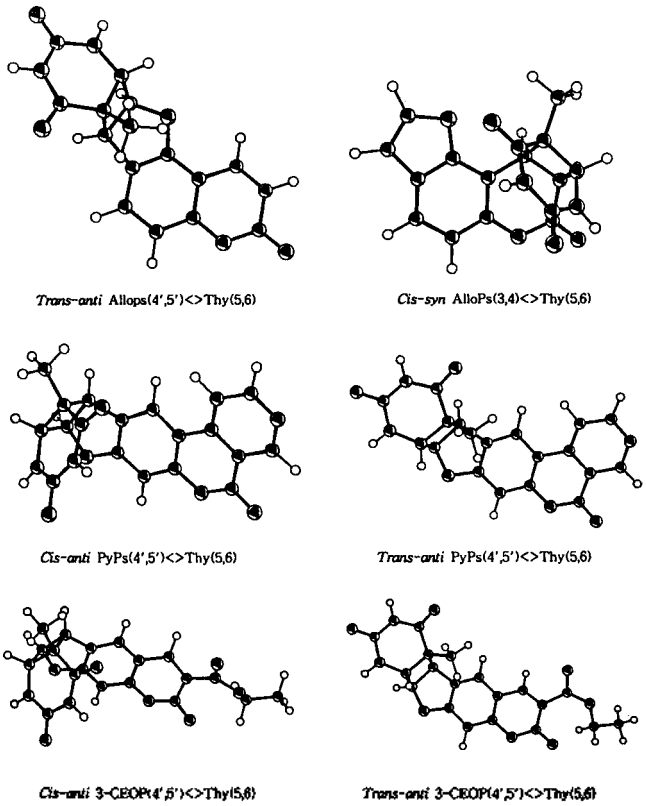

Figure 1. Stereo ORTEP drawing of molecular configuration for photoadducts.

fects.

The geometries of monofunctional derivatives was optimized starting from the probable bond angles, bond length and dihedral angles by PM3-UHF calculation. Bond length alternation in the calculated structures is observed in the pyrone ring bonds not common to the results of semiempirical calculation for possible photocycloadducts of monofunctional psoralen with thymine are shown in Table 1, and Figure 1. In all cases, rotations about the photocycloadducts were investigated in order to locate the lowest energy conformation.

Three types of photoadducts have been proposed; (1) *cis-anti* AlloPs(3,4)<>Thy(5,6); (2) *trans-syn* 3-CEOP(4',5')<> Thy(5,6); (3) *cis-anti* PyPs(4',5')<>Thy(5,6). The calculated heat of formation and the interaction energies in Table 1. refer to the stable conformer for possible photochemical interaction energies are calculated from the monofunctional psoralen of excited state and thymine of ground state. The photoadducts was inferred to be a C_4-cycloaddition product with the stereochemistry of *cis-anti* AlloPs (3,4), *trans-syn* 3-CEOP (4',5') and *cis-anti* PyPs (4',5') formed through [2+ 2] addition reacton between the 5,6-double bond of thymine.

The interaction energy determined from the PM3 calculation appears to be significantly higher in the case of 3-carbethoxy psoralen derivatives, increasing in the order:

3-CEOP(4',5')<>(5,6)Thy > AlloPs(3,4)<>(5,6)Thy > PyPs (4',5')<>(5,6)Thy

Table 1. The calculated heat of formation and interaction energies by PM3-CI-UHF calculation (in kcal/mol)

Formation	E_{total}	$E_{torsion}$	E_{strain}	$\triangle H_f$
AlloPs(3,4)<>Thy(5,6)				
cis-anti	25.949	21.160	19.619	- 198.201
cis-syn	25.965	21.226	19.635	- 198.196
trans-anti	26.507	21.293	20.177	- 197.751
trans-syn	28.041	22.449	21.711	- 196.179
AlloPs(4',5')<>Thy(5,6)				
cis-anti	31.907	28.538	23.317	- 191.271
cis-syn	32.675	28.539	24.085	- 190.444
trans-anti	32.771	28.221	24.181	- 190.363
trans-syn	33.584	27.993	24.994	- 189.543
3-CEOP(4',5')<>Thy(5,6)				
cis-anti	48.702	33.206	34.192	- 273.266
cis-syn	48.212	32.295	33.702	- 273.820
trans-anti	48.572	32.879	34.062	- 273.483
trans-syn	46.702	33.399	32.192	- 274.959
PyPs(4',5')<>Thy(5,6)				
cis-anti	45.749	38.439	37.159	- 189.690
cis-syn	46.315	37.871	37.725	- 189.648
trans-anti	46.555	38.436	37.965	- 189.068
trans-syn	47.348	38.546	38.758	- 188.407

These 3-carbethoxypsoralen reacts as a best monofunctional compound. The 3-CEOP in which the most reactive site, the 3,4 double bond of the psoralen molecule is blocked by a 3-carbethoxy group. Thus in principle only the 4',5' double bond reaction site of the molecule is open for a photobinding with the 5,6 double bond of pyrimidine bases.

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