

Ab Initio Study on the Psoralen(I)

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The electronic structure of photosensitizing psoralens has been investigated by the *ab initio* calculations. The photocycloaddition reaction of 8-methoxypsoralen with thymine is studied as a model for the photosensitizing reaction of psoralen with DNA bases. The photocycloadduct was inferred to be a C4-cycloaddition product with the stereochemistry of *Syn, H-H, Syn, H-T* formed through [2+2] addition reaction between the 3,4-double bonds of 8-methoxypsoralen and 5,6-double bond of thymine base.

key words : Ab initio, C4-cycloaddition, 8-methoxypsoralen

Naturally occurring and synthesized psoralen derivatives are photosensitizers of UVA especially from 320nm to 400nm, a range at which cellular nucleic acids and proteins are weakly absorbing if any at all. Because of their photosensitizing properties, these compounds have been used in the photochemotherapy of psoriasis and vitiligo.[1-3]

Psoralens have two different photoreactive sites 3,4 -and 4', 5'- double bonds ; therefore, two types of monoadducts, that is 3,4- and 4',5'- monoadducts, can be formed by the C4- photocycloaddition with 5,6-double bond of a pyrimidine base of DNA.[4]

Recently, many studies have shown the semiempirical calculations can yield useful information for predicting the overall sequence of the photochemical reaction between psoralen and pyrimidine base. However, no calculation is reported for 8-methoxypsoralen(8-MOP) and thymine(TME) so far.

In this work, the model which we chose included 8-methoxypsoralen and was centered with the thymine in the form of *Syn H to H*, and *Syn H to T* structure. The optimized geometry was assumed according to the photochemical reaction between psoralen and thymine We believed that our molecular complex was enough for calculation since previous work,[5, 6] and our recent paper have gotten the reliable results with the molecular complex.[7-9]

The geometries of 8-methoxypsoralen was optimized starting from the probable bond angles, bond length and dihedral angles by *ab initio* calculation. Bond length alternation in the calculated structures is observed in the pyrone ring bonds not common to the results of 6-31G for possible photocycloadducts of 8-methoxypsoralen(8-MOP) with thymine(TME) are shown in Figure 1.

Major monoadducts was calculated to be a C4-cycloaddition

product formed between 5,6-double bond of thymine and 3,4-double bond of 8-MOP with stereochemistry. In all cases, rotations about the photocycloadducts were investigated in order to locate the lowest energy conformation.

Two types of photocycloadducts have been proposed; (1) *Syn Head to Head*, 8-MOP(3,4) <> TME(5,6); (2). *Syn Head to Tail*, 8-MOP(3,4) <> TME(5,6)

The calculated results can provide some constructive information for photocycloadduct synthesis.[11-13]

The 8-MOP in which the most reactive site, the 3,4 double bond(1.35Å, singlet, 1.37Å, triplet) reaction site of the 8-MOP is open for a photobinding with the 5,6 double bond of TME.

No ground state charge transfer complex is formed between

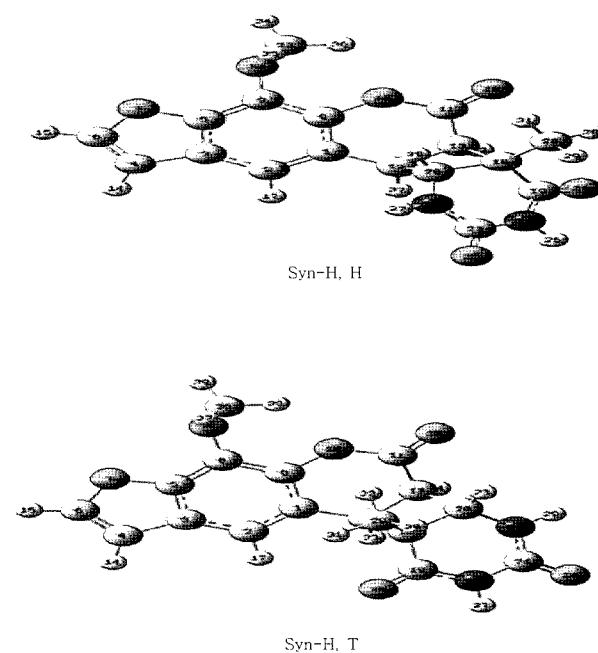


Figure 1. Photocycloadducts of 8-MOP with TME by HF/6-31G.

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Received Aug. 10, 2005 Accepted Oct. 20, 2005

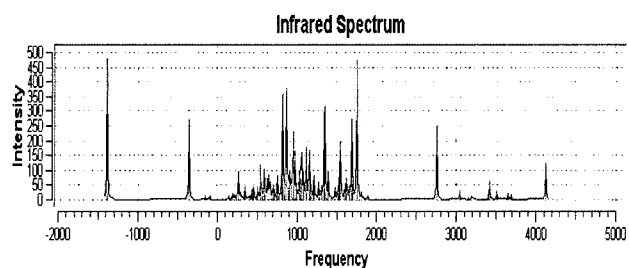


Figure 2. IR Spectrum of 8-MOP \langle TME (Syn-H,H) at Singlet State by HF/6-31G.

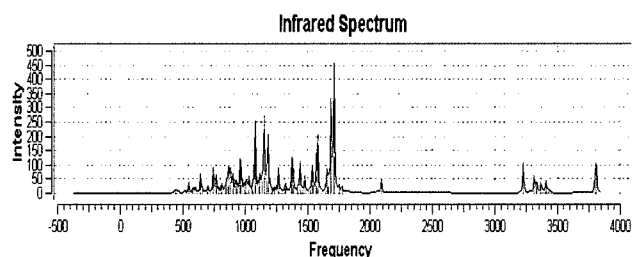


Figure 3. IR Spectrum of 8-MOP \langle TME (Syn-H, T) at Singlet State by HF/6-31G.

8-MOP and thymine since the absorption spectra of the mixture are exactly the sum of two individual spectra of 8-MOP and thymine. The fluorescence of 8-MOP is not quenched by thymine even though the concentration of thymine is increased up to 100 fold molar excess to 8-MOP. Therefore, no exciplex is formed between 8-MOP and thymine in contrast to 8-MOP-TME. TME quenches the fluorescence of 8-MOP, but not very efficiency ($k_q \cdot \tau = 1.2$) [14]

The I.R. spectrum of the 8-methoxypsoralen and thymine is depicted in Figure 2,3.

The observed frequencies and intensities are compared the values calculated at the HF/6-31G level for photocycloadducts.

Electron-donating substituents, such as methoxy as in 8-MOP groups will raise the ${}^1(n, \pi^*)$ state and thus enhance the photoreaction by way of the singlet state due to a weakening the vibronic interaction between the ${}^1(n, \pi^*)$ and ${}^1(\pi, \pi^*)$ states. Kanne et al. isolated a pair of cis-syn 4',5'-monoadducts of 8-MOP to thymidine as a major adducts from the photoreaction of 8-MOP with high molecular weight, double stranded DNA.[15]

ACKNOWLEDGMENT

This work was supported by research funds of Chonbuk

National University. One of the authors(KJH) is grateful to JongHyeok Kim for computation.

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4. Pienta, N. J. (1988) Amines, Thiols and Thioethers, Heteroaromatic Electron Donors, in *Photoinduced Electron Transfer*. Part C, Ed by Fox, M. A and Chanon, M, Elsevier, New York.

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