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# Studies of the Absorption Spectra of Some Psoralens

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The $\pi$-$\pi^*$ absorption spectra of some psoralens with skin photosensitizing action were measured in various solvents, up to vacuum ultraviolet region. We found that these compounds exhibit six $\pi$-$\pi^*$ bands within 180—400 nm region and the longest wavelength absorption band of psoralen shows a blue shift with increasing polarity of the solvents. Furthermore, the molecular orbital calculation of the $\pi$-electronic systems of psoralens were carried out by means of the Pariser-Parr-Pople method. The obtained absorption $\pi$-$\pi^*$ bands were assigned on the basis of the calculated results.

**Keywords**——psoralens; photosensitizing agent; absorption spectra; vacuum ultraviolet; solvent effect; MO calculation; Pariser-Parr-Pople method

Psoralens are well known as skin photosensitizing agents as same as coumarins.[2] The photoadditional reaction of psoralens to pyrimidine bases and deoxyribonucleic acid (DNA), and its skin sensitizing activity are studied in detail by Musajo and his co-workers.[3] Since psoralens are photochemically active, it is very important that investigate the electronic spectra of these compounds. There are a few reports of the absorption spectra of psoralens.[4] However, the vacuum ultraviolet (VUV) absorption spectra and the solvent effect of psoralens have never been reported. In this paper, the $\pi$–$\pi^*$ absorption bands of psoralen, 5-methoxypsoralen and 8-methoxypsoralen in various solvents are reported, and the molecular orbital of the $\pi$-electronic system of psoralens have been calculated by means of the Pariser–Parr–Pople (P–P–P) method[5,6] in order to determine the assignments of obtained $\pi$–$\pi^*$ absorption bands.

## Experimental

**Measurements**——The absorption spectra in the ultraviolet region were measured with a Shimazu Double Beam spectrophotometer UV-200, and in the VUV region with a VUV-3 recording spectrophotometer of the Japan Spectroscopic Co., Ltd.

**Materials**——Psoralen, recrystallized from EtOH, mp 164—165° (lit. 163—163.5°),[7] was generausly supplied by Prof. Kiyoshi Hata of Osaka College of Pharmacy. 5-Methoxypsoralen was obtained from commercial bergamot oil and it was recrystallization from EtOH, mp 188—189° (lit. 187.5—188.5°).[8] Commercial product of 8-methoxypsoralen was purified by recrystallization from EtOH–ether, mp 148—149° (lit. 146°).[9] Fig. 1 shows the structure and numbering for psoralen.

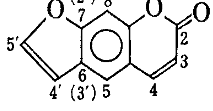

Fig. 1. The Structure and Numbering for Psoralen

**Solvents**——Solvents of commercially available spectrograde were used without further purification. 1,1,1,3,3,3-Hexafluoro-2-propanol (HFP) (Merk Co., Ltd.) was also used without further purification.

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[1] Location: *Yamashiro-cho, Tokushima, 770, Japan.*

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[3] L. Musajo, F. Bordin, G. Caporale, S. Marcianic, and G. Rigatti, *Photochem. Photobiol.*, **6**, 711 (1967); L. Musajo and G. Rodighiero, *ibid.*, **11**, 27 (1970).

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[6] J.A. Pople, *Trans. Faraday Soc.*, **49**, 1375 (1953).

[7] K. Hata and A. Nitta, *Yakugaku Zasshi*, **80**, 742 (1959).

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[9] C. Schöpf and R. Kühne, *Chem. Ber.*, **83**, 390 (1950).

**Molecular Orbital Calculations**——The computation was performed on a FACOM 230 computer. The MO calculations were carried out by P-P-P method. The MO calculations of psoralen and 8-methoxypsoralen, and various carbonyl compounds have been reported by P.S. Song and his co-workers,[4] and Kuboyama and his co-workers[10] respectively. In this paper, integral values used were determined by reference to their reports. These values are listed in Table I. In this table, the suffix letters C, =O and –O– denote the carbon, carbonyl oxygen and etheral oxygen atoms respectively. $U$ denotes the one-center core integral. $U_C$ denotes the $U$ of carbon atom. $U_C^{=O}$ and $U_C^{-O-}$ denote the $U_C$ of C=O and C–O– groups respectively. $\beta_{C-C}$, $\beta_{C=C}$, $\beta_{C\doteq C}$, $\beta_{C=O}$, and $\beta_{C-O-}$ denote the two-center core integrals of C–C single, C=C double, benzene ring, C=O carbonyl, and C–O– etheral bonds respectively. The electronic repulsion integrals were calculated using the Nishimoto-Mataga formula.[11] In the configuration interaction (CI) calculation, the thirty lowest singly-excited configurations were included.

Table I. Electronic Intergral Values (eV) used for the MO Calculation

| | |
|---|---|
| A) One-center core integrals | |
| $U_C$ | −9.50 |
| $U_C^{=O}$ | −10.00 |
| $U_C^{-O-}$ | −9.50 |
| $U_{=O}$ | −14.00 |
| $U_{-O-}$ | −27.00 |
| B) Two-center core integrals | |
| $\beta_{C-C}$ | −2.00 |
| $\beta_{C=C}$ | −2.50 |
| $\beta_{C\doteq C}$ | −2.30 |
| $\beta_{C=O}$ | −3.00 |
| $\beta_{C-O-}$ | −1.80 |
| C) Electronic repulsion integrals Nishimoto-Mataga method | |

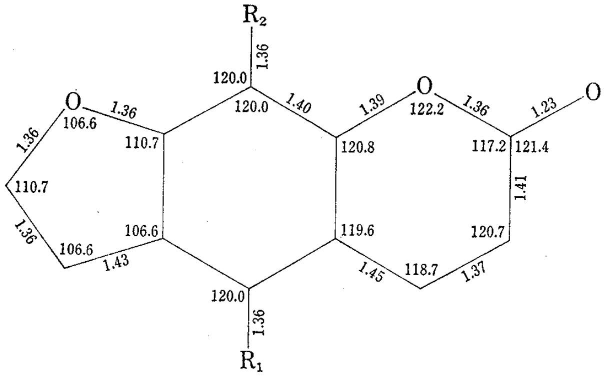

Fig. 2. Bond Lengths (Å) and Bond Angles (°) of Psoralens

Psoralen $R_1=R_2=H$.
5-Methoxypsoralen $R_1=OCH_3$ $R_2=H$.
8-Methoxypsoralen $R_1=H$ $R_2=OCH_3$.

The molecular structure of psoralen has not yet been elucidated. Psoralen is considered to take the planar structure. The dimensions of psoralen, 5-methoxypsoralen, and 8-methoxypsoralen were assumed considering from the molecular structures of coumarin,[12] furan,[13] and anisole.[14] Those assumed dimensions are shown in Fig. 2. All the bond lengths of the benzene rings in psoralens were assumed to be 1.4 Å, while its bond angles were assumed to be 120°. The calculated excitation energies ($E$) and oscillator strength ($f$) are shown in Table III, along with the observed results in cyclohexane and HFP solutions. The second colum of this table indicates the numbering of the magnitude of excitation energies and the data on the heigher excitated states with small $f$-values have been omitted.

## Results and Discussion

### Solvent Effect

The absorption spectra of psoralen, 8-methoxypsoralen and 5-methoxypsoralen in various solvents are shown in Figs. 3—5 respectively (besides shown in the figures, the absorption spectra in carbontetrachloride and benzene solutions were also measured). The position and molar absorption coefficient ($\varepsilon$) of the absorption maxima ($\lambda_{max}$) of main bands and shoulders in these spectra are given in Table II. The spectra of VUV region were only measured in HFP solution owing to limited solubility of psoralens to measurable solvents. From the $\varepsilon$

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[10] *a*) A. Kuboyama, S. Matsuzaki, H. Takagi, and H. Arano, *Bull. Chem. Soc. Jpn.*, **47**, 1604 (1974); *b*) A. Kuboyama, F. Kobayashi, and S. Morokuma, *ibid.*, **48**, 2145 (1975); *c*) A. Kuboyama and H. Arano, *ibid.*, **49**, 1401 (1976); *d*) A. Kuboyama, Y. Sato, and H. Arano, *ibid.*, **49**, 3685 (1976).

[11] K. Nishimoto and M. Mataga, *Z. Phys. Chem.* (*N.F.*), **12**, 335 (1957).

[12] R.M. Myasnikova, T.S. Davydova, and V.I. Simonov, *Sov. Phys. Crystallogr.*, **18**, 454 (1974).

[13] B. Bak, D. Christensen, W.B. Dixon, L. Nygaard, J. Rastrup-Anderson, and M. Schottlaender, *J. Mol. Spectr.*, **9**, 124 (1962).

[14] H.M. Seip and R. Seip, *Acta. Chem. Scand.*, **27**, 4024 (1973).

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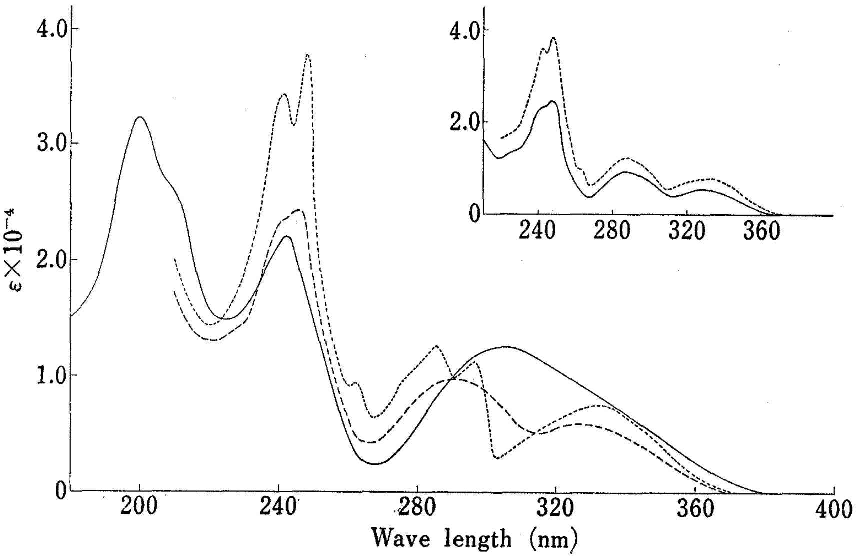

Fig. 3. Absorption Spectra of Psoralen in Various Solvents

——: HFP, ——: MeOH, ------: cyclohexane.
Inserted graph, ——: acetonitrile, ------: dioxane.

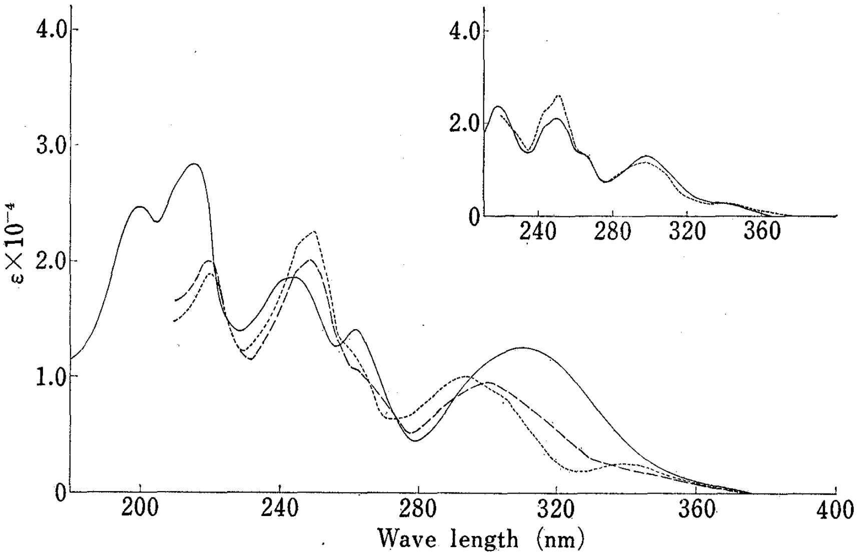

Fig. 4. Absorption Spectra of 8-Methoxypsoralen in Various Solvents

——: HFP, ——: MeOH, ------: cyclohexane.
Inserted graph, ——: acetonitrile, ------: dioxane.

values in Table II, it is clear that the all absorption bands have arisen from the $\pi$–$\pi^*$ transition. It was not possible to identify any n-$\pi^*$ bands.

**Psoralen**——As may be seen in Fig. 3 and Table II, psoralen in solution appears to have six distinct $\pi$–$\pi^*$ bands. These absorption bands are situated near 330 (band A), 290 (band B), 260 (band C), 250 (band D),[4] 210 (band E), and 200 nm (band F) respectively. Band A which have a moderated absorption intensity is broad, but this band was not observed in HFP solution. Furthermore, band A tentes to show a blue shift with increasing polarity of the solvent. Since the $\pi$–$\pi^*$ bands of longer wavelength region generally show a red shift with increasing polarity of the solvent,[15] the above mentioned fact is noteworthy. Similar phenomenon is found in

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15) A. Kuboyama, *Bunko Kenkyu*, **20**, 14 (1971).

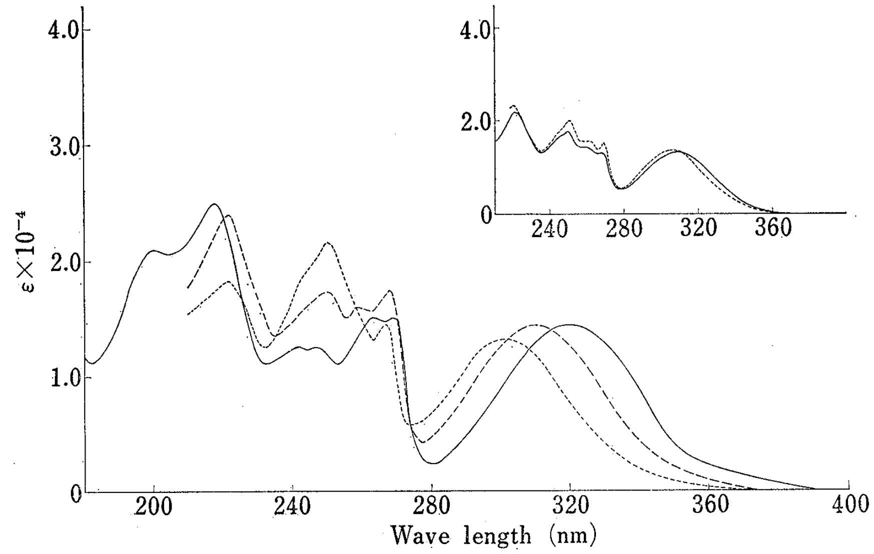

Fig. 5. Absorpttion Spectra of 5-Methoxypsoralen in Various Solvents

——: HFP, ----: MeOH, ------: cyclohexane.
Inserted graph, ——: acetonitrile, ------: dioxane.

Table II. Absorption Spectral Data of Psoralens

| Compound | Solvent | $\lambda_{max}$ nm ($\varepsilon$) | | | | | |
|---|---|---|---|---|---|---|---|
| | | Band A | Band B | Band C | Band D | Band E | Band F |
| Psoralen | Cyclohexane | 332(7520) | 275( 9340)$^{s}$<br>285(12600)<br>296(11160) | 262( 9320) | 241(34000)<br>248(37760) | | |
| | Dioxane | 331(7800) | 286(12640) | 262( 8750) | 242(36000)<br>248(38300) | | |
| | $CCl_4$ | 331(5590) | 287( 9180)<br>297( 8020) | | | | |
| | Benzene | 331(6020) | 287( 9430)<br>298( 8570) | | | | |
| | MeOH | 326(5750) | 290( 9800) | | 242(23360)$^{s}$<br>246(24260) | | |
| | Acetonitrile | 327(5500) | 288( 9300) | | 242(23200)$^{s}$<br>247(24360) | | |
| | HFP | | 304(12760) | | 242(22000) | 210(26070)$^{s}$ | 200(32200) |
| 8-Methoxypsoralen | Cyclohexane | 340(2320) | 293(10000)<br>305( 8200)$^{s}$ | 265(10400)$^{s}$ | 245(21600)<br>250(22520) | 220(18600) | |
| | Dioxane | 340(2650) | 295(11200) | 265(13500) | 244(23000)$^{s}$<br>250(25620) | | |
| | $CCl_4$ | 340(2540) | 297(10460) | | | | |
| | Benzene | 340(2590) | 297(11400) | | | | |
| | MeOH | | 300( 9200) | 264(11150)$^{s}$ | 244(18600)$^{s}$<br>249(20000) | 220(20000) | |
| | Acetonitrile | | 297(12000) | 264(12900)$^{s}$ | 243(24250)$^{s}$<br>249(26000) | 219(23740) | |
| | HFP | | 310(12600) | 263(14160) | 243(18720) | 216(28380) | 200(24660) |
| 5-Methoxypsoralen | Cyclohexane | | 301(13200) | 267(14400) | 242(18120)$^{s}$<br>250(21600) | 222(18000) | |
| | Dioxane | | 305(14000) | 260(15830)<br>268(15530) | 244(18250)$^{s}$<br>250(20110) | | |
| | $CCl_4$ | | 306(12600) | | | | |
| | Benzene | | 306(11430) | | | | |
| | MeOH | | 310(14400) | 259(15900)<br>268(17420) | 242(15460)$^{s}$<br>250(17300) | 222(24000) | |
| | Acetonitrile | | 306(13600) | 258(15330)<br>268(16140) | 243(15680)$^{s}$<br>250(17700) | 222(22050) | |
| | HFP | | 320(14400) | 263(15200)<br>269(15000) | 242(12400)<br>247(12500) | 218(24500) | 200(21000) |

s: shoulder.

coumarin.[16] In band B with a strong absorption intensity, the fine structure was observed in cyclohexane, carbon tetrachloride, and benzene solutions, but no fine structure in dioxane, MeOH, and acetonitrile solutions. It was found that band B tentes to show a red shift with increasing polarity of the solvent. This red shift is markedly large in HFP solution. In addition, the absorption maximum of band B in MeOH solution (290 nm) is in longer wavelength region than that in acetonitrile solution (287 nm). From this fact, it may be considered that a effect of hydrogen bonding is larger than that of electrostatic force on a red shift of band B. Psoralen exhibits one broad band which locates near 300 nm in HFP solution. This fact may be considered to be the result of the blue shift of band A and the red shift of band B, duing to the very strong hydrogen bonding between psoralen and HFP. Band C in cyclohexane and dioxane solutions appears as a weak absorption band and a shoulder on the longer wavelength side of band D respectively, but this band was not observed in other

TABLE III. The Calculated and Observed Values of the Excitation Energies ($E$), Oscillator Strength ($f$), and Band Names

| Compound | No. | Calcd. | | Band name | Obsd. | | | |
|---|---|---|---|---|---|---|---|---|
| | | $E$(eV) | $f$ | | $E_1$(eV)[a] | $f_1$[a] | $E_2$(eV)[b] | $f_2$[b] |
| Psoralen | 1 | 3.813 | 0.143 | A | 3.8 | 0.25 | | |
| | 2 | 4.221 | 0.100 | B | 4.2<br>4.4<br>4.5 | 0.35 | | |
| | 3 | 4.639 | 0.512 | C | 4.7 | $\sim$0.07 | | |
| | 4 | 4.891 | 1.175 | D | 5.0 | 1.37 | 5.1 | 0.88 |
| | 5 | 5.287 | 0.015 | | | | | |
| | 6 | 5.650 | 0.035 | | | | | |
| | 7 | 5.901 | 0.302 | E | | | 5.9 | 2.10 |
| | 8 | 6.307 | 0.186 | F | | | 6.2 | |
| | 10 | 6.117 | 0.215 | | | | | |
| | 12 | 6.453 | 0.126 | | | | | |
| 8-Methoxypsoralen | 1 | 3.602 | 0.029 | A | 3.7 | 0.07 | | |
| | 2 | 4.040 | 0.121 | B | 4.2 | 0.33 | | |
| | 3 | 4.431 | 1.016 | | | | | |
| | 4 | 4.782 | 0.286 | C | 4.7 | $\sim$0.17 | | |
| | 5 | 5.027 | 0.447 | D | 5.0 | 0.72 | 5.1 | 0.67 |
| | 6 | 5.420 | 0.041 | | | | | |
| | 7 | 5.612 | 0.119 | E | | | 5.7 | $\sim$1.00 |
| | 8 | 5.695 | 0.071 | | | | | |
| | 9 | 5.820 | 0.159 | F | | | 6.2 | $\sim$1.05 |
| | 10 | 5.989 | 0.190 | | | | | |
| | 11 | 6.116 | 0.103 | | | | | |
| | 12 | 6.219 | 0.361 | | | | | |
| 5-Methoxypsoralen | 1 | 3.705 | 0.055 | A | | | | |
| | 2 | 3.963 | 0.285 | B | 4.1 | 0.57 | | |
| | 3 | 4.417 | 0.806 | | | | | |
| | 4 | 4.807 | 0.405 | C | 4.6 | 0.14 | | |
| | 5 | 5.057 | 0.369 | D | 5.0<br>5.1 | 0.72 | 5.0<br>5.1 | 0.37 |
| | 6 | 5.358 | 0.252 | E | | | 5.7 | $\sim$0.97 |
| | 7 | 5.631 | 0.021 | | | | | |
| | 8 | 5.802 | 0.090 | | | | | |
| | 9 | 5.857 | 0.112 | F | | | 6.2 | $\sim$0.86 |
| | 10 | 5.937 | 0.113 | | | | | |
| | 12 | 6.328 | 0.257 | | | | | |

a) For cyclohexane solution.
b) For HFP solution.

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[16] T. Nakabayashi, *Yakugaku Zasshi*, **74**, 901 (1954).

solvents. This may be considered to be the result that band C is hidden by the strong band D. As, in hydrogen bonding solvents of 5-methoxypsoralen, the absorption band corresponding to band C appears as main band, this band seems to be separate band. The absorption intensity of band D is very strong and its absorption maximum is little shifted by change of the solvents. It is noteworthy that the $\varepsilon$ values of this band in cyclohexane and dioxane solutions are remarkably strong comparing with those in other solvents. It has been also found in the absorption band near 220 nm of chromone that its absorption intensity drastically changes by the solvents.[17,18] However, the mechanism have been not clear at the present stage. Band E and F appear near 210 nm as a shoulder, and 200 nm as a main band with a very strong absorption intensity respectively.

From the correspondence of the experimental with theoretical results, the obtained $\pi$–$\pi^*$ band, apart from band F, reasonably assigned as shown in Table III. However, as for band F, the assignment based on the calculated results was not clear. The assignment of bands in the UV region (band A—D) agree with those made by P.S. Song *et al.*[4]

**8-Methoxypsoralen**——The absorption spectral pattern of 8-methoxypsoralen in solution is similar to that of psoralen, namely this compound exhibits six $\pi$–$\pi^*$ absorption bands which have the absorption maxima near 340, 300, 265, 250, 220,[4] and 200 nm respectively (Fig. 4). The names of these bands are listed in Table I. Although band A with a moderate absorption intensity appears in nonpolar solvents, it is not obvious in polar solvents. Therefore the effect of the solvent on the absorption maximum of band A was not obtained. Band B shows a red shift with increasing polarity of the solvent. Band A disappears in HFP solution and the absorption maximum of band B in MeOH solution is situated in longer wavelength than that of acetonitrile solution. These phenomenons may be interpreted in term of the marked red shift of band B duing to the hydrogen bonding between 8-methoxypsoralen and solvents, as same as psoralen. Band C appears as a weak absorption band near 263 nm in HFP solution, but in other solvents as shoulders. In addition, the absorption maximum of this band seems to be little changes by the solvents. The absorption intensity of band D is stronger in nonpolar solvents than in polar solvents, and the position of band D and E in HFP which is very strong proton donor is situated in shorter wavelength region than those in other solvents.

The obtained $\pi$–$\pi^*$ bands of 8-methoxypsoralen were assigned on the basis of the MO calculation as shown in Table III. As will be shown in this table, band B and F could not be clearly assigned. The assignments of the bands A, C, D, and E agree with those made by P.S. Song *et al.*[4]

**5-Methoxypsoralen**——As will be clear from Fig. 5, 5-methoxypsoralen exhibits one absorption band with a strong absorption intensity near 300 nm in any solvents, differing from psoralen and 8-methoxypsoralen. As this band is very broad, its absorption band may be composed of two $\pi$–$\pi^*$ bands. Comparing with the $\pi$–$\pi^*$ bands of psoralen and 8-methoxypsoralen, it is considered that this broad band corresponds to the overlapped band of band A and B of these compounds. As the $\varepsilon$ value of band B is larger than that of band A as observed in psoralen and 8-methoxypsoralen, the absorption maximum of this overlapped band may be chiefly due to band B. Therefore, 5-methoxypsoralen in solutions appears to have six $\pi$–$\pi^*$ bands. These bands were named as is shown in Table III. Band B shows a red shift with increasing polarity of the solvent, and this shift is markedly large in hydrogen bonding solvents such as MeOH and HFP. In HFP solution, band C appears as a distinct main absorption band near 265 nm and its position is not hardly affected by the solvents. From this fact, it is clear that this band is a $\pi$–$\pi^*$ band differing from band D. Band D, E and F appear near 250, 220 and 200 nm respectively. The absorption intensity of band D

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17) P.J.F. Griffiths and G.P. Ellis, *Spectrochim. Acta.*, **28A**, 707 (1972).

18) A. Kuboyama, personal communication.

decrease with changing the solvents from cyclohexane to HFP, while the absorption maxima of band D and E in HFP solution are situated in shorter wavelength region than those in other solvents.

The assignment of observed absorption bands based on the MO calculation is shown in Table III, but band B and F could not be clearly assigned. Although we could not experimentally observe band A, because it is hidden by band B, from the calculated results it may be expected that this band exist near 335 nm.

### Effect of Methoxy Group

When a methoxy group is introduced into the 5- or 8-positions of psoralen, band A—E shift towards longer wavelength region. Particulary this red shift is remarkably large in band B of 5-methoxypsoralen, and this is considered to be one of the reason that 5-methoxypsoralen only exhibits one broad absorption band near 300 nm in any solvents. The absorption intensity of band F is stronger than that of band E in psoralen, but its intensity become to be reversed in methoxypsoralens. Since, as for the red shift of band A, the correspondence between the experimental and theoretical results is excellent, the MO calculation of various methoxypsoralens were carried out to obtained the information involved in the effect of methoxy group on the position of the longest wavelength absorption band. From the calculated results (Table IV), it may be expected that the longest wavelength absorption band of 4-methoxypsoralen shifts toward shorter wavelength region, and other methoxypsoralens shift toward longer wavelength region. As a $\pi$–$\pi^*$ band, in general, shows a red shift by substitution of electron donating group,[15] the above mentioned blue shift (calculated result) of 4-methoxypsoralen is noteworthy. Such a fact has been already found in methyl-$\alpha$-naphtoquinone.[10a]

TABLE IV. The Calculated Excitation Energies ($E$) of the Longest Wavelength $\pi$-$\pi^*$ Bands of Psoralen and its Methoxy-derivatives

| Compound | $E$(eV) | $\Delta E$(eV)[a] |
|---|---|---|
| Psoralen | 3.813 | |
| 3-Methoxypsoralen | 3.742 | −0.071 |
| 4-Methoxypsoralen | 3.844 | +0.031 |
| 5-Methoxypsoralen | 3.705 | −0.108 |
| 8-Methoxypsoralen | 3.602 | −0.211 |
| 4′-Methoxypsoralen | 3.661 | −0.152 |
| 5′-Methoxypsoralen | 3.668 | −0.145 |

[a] The values which the $E$ of psoralen is substrated from that of methoxypsoralens.

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