

suggests that the molecular aggregation is certainly occurring in water environment and a trimerization of the proteolipid protein is likely forming by changing the solvent from chloroform-methanol to water. As we know that the main biological function of the plasma membrane proteolipid protein is the  $K^+$  ion transport, we tried to investigate the  $K^+$  ion effect to the molecular aggregation in aqueous system. Figure 4 shows the polarization plot versus KCl concentration in aqueous system. Polarization value was enhanced linearly as the  $K^+$  ion concentration increases. This result is very interesting in connection with the oligomerization state and  $K^+$  ion transport in the biological membrane. Nonetheless, any conclusive remarks can not be presented at the moment and further study on this subject should be carried out.

Summarizing the fluorescence spectral analysis and quenching experiment, tryptophan environment is more hydrophobic and buried in case of the water soluble form of proteolipid. Fluorescence polarization data present the strong evidence for oligomerization in aqueous system. In addition to the above results, the fact that a hydrophobic interaction is the predominant molecular interaction between the subunits of the proteins is known in general. Upon considering the results and the fact, we can carefully mention about the oligomerization process and state of the proteolipid in water as following. During the formation of the water soluble proteolipid, most of the exposed domain of the protein becomes hydrophilic to maintain the water solubility. But a certain part of the domain keeps the hydrophobic character for the formation of oligomer through the hydrophobic interaction. This hydrophobic domain may contain tryptophan residue or not. Even though tryptophan residue is located in this domain, it is still buried by other subunit and reveal a hydrophobic character after the oligomerization process. However, it is not easy to draw the exact molecular topography of the oligomer and more experimental evidences are required.

**Acknowledgement.** This work was supported by the research grant from the Ministry of Education, Korea, in 1987.

### References

1. G. Sherman and P. T. Folch, *J. Neurochem.*, **17**, 597 (1970).
2. H. Hendrickson, S. Joffe and D. Davidson, *J. Neurochem.*, **19**, 2233 (1972).
3. N. A. Moscarello, J. Gagnon, D. D. Wood, T. Anthony and R. Eppard, *Biochemistry*, **12**, 3402 (1973).
4. V.S. Sapirstein and T.C. Rounds, *Biochemistry*, **22**, 3330 (1983).
5. D. S. Chan and M. B. Lees, *Biochemistry*, **13**, 2704 (1974).
6. Sigrist-Nelson and Azzi, *J. Biol. Chem.*, **254**, 4470 (1979).
7. M. B. Lees, J. D. Sakura, V. S. Sapirstein and W. Cutatolo, *Biochim. Biophys. Acta*, **559**, 209 (1979).
8. D. M. Engleman, R. Henderson, A. D. McLachlan and B. A. Wallace, *Proc. Natl. Acad. Sci., U.S.A.*, **77**, 2023 (1980).
9. M. T. Tosteson and V. S. Sapirstein, *J. Memb. Biol.*, **63**, 77 (1981).
10. O. H. Lowry, N. J. Rosebrough, A. L. Farr and R. J. Randall, *J. Biol. Chem.*, **193**, 265 (1951).
11. G. R. Barlett, *J. Biol. Chem.*, **233**, 466 (1959).
12. T. Azumi and S. P. McGlynn, *J. Chem. Phys.*, **37**, 2413 (1962).
13. R. F. Chen and H. Edelhoch, *Biochemical Fluorescence; concepts*, Volume 2, Marcel Dekker Inc. pp 643 (1976).
14. M. R. Eftink and C. A. Ghiron, *Biochemistry*, **15**, 672 (1976).
15. C. R. Cantor and P. R. Schimmel, *Biophysical Chemistry, Part II*, W. H. Freeman and Comp., pp 465 (1980).

## Synthesis of an Intermediate for Hirsutene

Jong-Gab Jun\*

*Department of Chemistry, Hallym University, 1 Okchon-Dong, Chunchon 200-702*

Bradford P. Mundy

*Department of Chemistry, Montana State University, Bozeman, MT 59717, U.S.A.*

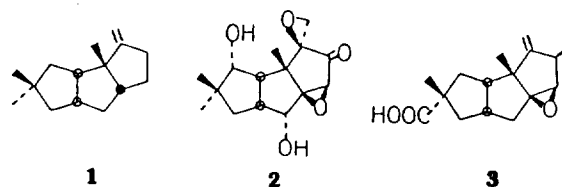
*Received February 13, 1988*

2,7,7-Trimethyl-cis-1,5-dicarboethoxybicyclo[3.3.0]octan-2-ol(**5**) is synthesized as a synthetic intermediate for hirsutene by use of dianion methodology.

### Introduction

Hirsutene(**1**), the biogenetic precursor of coriolin(**2**) and hirsutic acid(**3**), is a tricyclic sesquiterpene hydrocarbon isolated from *Coriolus consers*<sup>1</sup>.

In addition to the synthetic interest elicited by the skeletal features of these terpenoids, there exist a number of remarkable physiological properties associated with the coriolin-type sesquiterpenes.<sup>2</sup> The antibiotic and antitumor

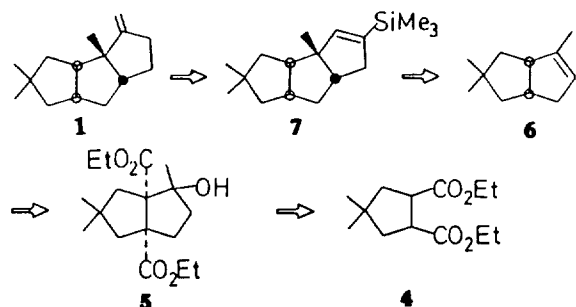


activities of coriolin and hirsutic acid dictate an efficient synthetic approach to these compounds, particularly in view of

their uncertain supply from natural sources.<sup>3</sup> Several interesting syntheses have appeared to date, describing the preparation of coriolin,<sup>4</sup> hirsutic acid<sup>5</sup> and hirsutene.<sup>6</sup>

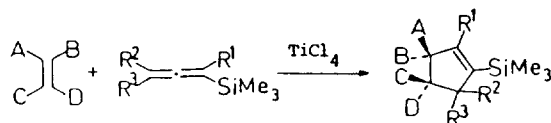
## Results and Discussion

We have been investigating a new method of *cis*-fused ring annulation based on the dianion methodology.<sup>7</sup> From the structure **1**, we can derive a retro-synthetic analysis for surveying the possible route of the dianion chemistry. (Scheme 1).



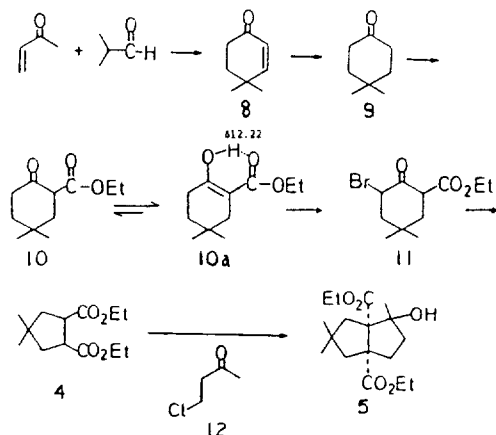
Scheme 1

*Cis*-fused configuration of 2,7,7-trimethyl-*cis*-1,5-dicarboethoxybicyclo[3.3.0]octan-2-ol(**5**) might be a good choice of dianion annulation from the vicinal diester(**4**). Another ring annulation with *cis* stereochemistry from **6** to **7** might be achieved by Danheiser's annulation method.<sup>8</sup> (Scheme 2).



Scheme 2

We decided to make **5** as a possible intermediate for the synthesis of hirsutene. As shown in scheme 3, 4,4-dimethyl-1-cyclohexenone(**8**) is prepared from the aldol condensation of isobutyraldehyde and methyl vinyl ketone with sulfuric acid as a catalyst.<sup>9</sup> Hydrogenation of **8** gave 4,4-dimethylcyclohexanone(**9**) in 96% yield. Carboethoxylation of **9** with ethyl carbonate and sodium hydride produced 2-carboethoxy-4,4-dimethyl-1-cyclohexenol(**10a**) in 68% yield. The <sup>1</sup>H NMR chemical shift at 12.22 ppm indicated the preference for the enol tautomer, **10a**.



Scheme 3

Bromination of **10**, followed by Favorskii rearrangement of **11** gave 1,2-dicarboethoxy-4,4-dimethylcyclopentane(**4**) in 67% yield. When 1.5 equivalents of 4-chlorobutane-2-one(**12**) (prepared from hydrochlorination of methyl vinyl ketone) were added to the dianion generated from the vicinal cyclopentane diester **4**, the desired bicyclic alcohol **5** was obtained in 21% yield. This approach to a highly functionalized *cis*-fused bicyclo[3.3.0]octane skeleton leads an easy approach to the related intermediates.

## Experimental

Reported boiling points and melting points are uncorrected. All NMR spectra were recorded on a Bruker 250 MHz FT-NMR using TMS as an internal standard. Mass spectra were obtained by use of a VG MM16 mass spectrometer and accurate mass data were obtained by use of a VG 7070 high resolution mass spectrometer. IR spectra were taken on a Beckmann IR-5 spectrometer. GLC analysis were performed using a Varian Aerograph series 2700 gas chromatograph equipped with 11' x 1/4", 10% OV-17 column. No effort was made to improve the yields.

**4,4-Dimethyl-2-cyclohexenone(8)**. A solution of 27.2 ml(0.30 mole) of isobutyraldehyde and 16.2 ml(0.20 mole) of methyl vinyl ketone was mixed at room temperature with 0.2 ml of concentrated sulfuric acid. The solution was warmed cautiously to 45-50°C and maintained at that temperature by means of occasional cooling with a coldwater bath. (Caution: A violent reaction may result if the temperature is allowed to exceed 65°C). The exothermic reaction subsided within about 1 hour. The solution was then refluxed through a Dean-Stark trap until water removal ceased(ca. 3 hours). Distillation(1.6 mm Hg) of the mixture gave 14.9 g(0.12 mole) of clear liquid at 35-41°C(60% yield).

<sup>1</sup>H NMR(CDCl<sub>3</sub>): δ (ppm) 6.63(1H,d,J=10 Hz), 5.80(1H,d,J=10 Hz), 2.42(2H,t,J=7 Hz) 1.83(2H,t,J=7 Hz), 1.13(6H,s).

<sup>13</sup>C NMR(CDCl<sub>3</sub>): δ (ppm) 199.3(s), 159.6(d), 126.6(d), 35.9(d), 34.2(d), 32.6(s), 27.5(q).

MS: 124(M<sup>+</sup>), 109, 96(base), 82, 81, 77, 67, 53, 41.

HRMS: Calcd for C<sub>8</sub>H<sub>12</sub>O: 124.0888. Observed: 124.0887.

IR(neat): 2933, 1681(α, β-unsaturated C=O), 1464, 1383, 1239, 1125, 805 cm<sup>-1</sup>.

**4,4-Dimethylcyclohexanone(9)**. 6.0 g(0.05 mole) of **8** was dissolved in 40 ml of glacial acetic acid and 0.2 g of 10% palladium on carbon was added. The mixture was shaken overnight under 60 atmosphere of hydrogen. The mixture was filtered twice through florisil, and then poured into a mixture of 200ml of water and 150ml of ether. The acetic acid was neutralized by slow addition of solid sodium bicarbonate. The aqueous layer was separated and washed twice with ether. The ether layers were combined and dried. Concentration gave 6.0 g(0.048 mole) of prism-like needles, mp 37-39°C. Sublimation removed a small amount of residual oil and raised the melting point to 39-41°C(96% yield).

<sup>1</sup>H NMR(CDCl<sub>3</sub>): δ (ppm) 2.31(4H,t,J=7 Hz), 1.63(4H,t,J=7 Hz), 1.06(6H,s).

<sup>13</sup>C NMR(CDCl<sub>3</sub>): δ (ppm) 212.0(s), 38.9(d), 37.7(d), 29.7(s), 27.3(q).

MS: 126(M<sup>+</sup>), 111, 83, 71(base), 55, 43.

HRMS: Calcd for C<sub>8</sub>H<sub>14</sub>O: 126.1045. Observed: 126.1049.

IR(KBr): 2933, 1715(C=O) cm<sup>-1</sup>.

**2-Carboethoxy-4,4-dimethyl-1-cyclohexenol(10a).** Into a 250 ml three-necked flask was placed 5.1 g(0.11 mole) of 50% sodium hydride-oil suspension. While under nitrogen, the solid was washed 3 times with dry toluene and 3 times with anhydrous tetrahydrofuran(solvent removed by syringe). A solution of diethyl carbonate(12.1 ml, 0.1 mole) in dry tetrahydrofuran(25 ml) was added dropwise and the stirred mixture was heated to reflux. A solution of **9**(5 g, 0.04 mole) in 10 ml of tetrahydrofuran was slowly added over 45 minutes(fast stirring was required to remove foaming). Heating was continued for 8 hours and the flask was cooled in an ice bath. A solution of acetic acid(40 ml) and saturated brine(50 ml) was slowly added, followed by ether(125 ml) and solid sodium bicarbonate. The layers were separated, and the aqueous phase was extracted with ether(2 × 50 ml). The combined organic layers were washed with brine, dried and evaporated. Distillation(0.63 mm Hg) gave 5.3 g(0.027 mole) of clear, colorless liquid at 74-80°C(68% yield).

$^1\text{H NMR}(\text{CDCl}_3)$ :  $\delta$  (ppm) 12.22(1H,s), 4.18(2H,q,J=7 Hz), 2.26(2H,t,J=7 Hz), 2.00(2H,brs), 1.42(2H,t,J=7 Hz), 1.28(3H,t,J=7 Hz), 0.93(6H,s).

$^{13}\text{C NMR}(\text{CDCl}_3)$ :  $\delta$  (ppm) 172.7(s), 171.0(s), 96.3(s), 60.0(t), 35.9(t), 34.3(t), 28.8(s), 27.7(q), 26.4(t), 14.1(q).

MS: 198( $\text{M}^+$ ), 183, 170, 152, 142(base), 137, 124, 113, 109, 96, 81, 68, 55, 41

HRMS: Calcd for  $\text{C}_{11}\text{H}_{18}\text{O}_3$ : 198.1256. Observed: 198.1251.

IR(neat): 2915(br), 1653, 1616, 1282, 1235, 1205, 1070, 820  $\text{cm}^{-1}$ .

**6-Bromo-2-carboethoxy-4,4-dimethylcyclohexanone(11).** To a solution of 4.2 g(0.021 mole) of the enol ester **10a** in 15 ml of methylene chloride was added dropwise 3.4 g(0.021 mole) of bromine at 0°C and stirred 8 hours at room temperature. The  $\alpha$ -bromo product was isomerized to the  $\gamma$ -bromo by bubbling a stream of moisture through the solution for 1 hour. Excess hydrogen bromide was removed by rinsing with 5% aqueous sodium bicarbonate and water. The organic solvent was dried over anhydrous magnesium sulfate and reduced in volume. The resulting yellow oil(6.1 g) was used directly for the next step.

**1,2-Dicarboethoxy-4,4-dimethylcyclopentane(4).** To a solution of 4 g(0.1 mole) of sodium hydroxide in 25 ml of ethanol and 25 ml of water was added dropwise 6.1 g of crude bromoketo ester **11** at 0°C and stirred for 1.5 hours at 0°C, then reflux for 1 hour. The yellow slurry which resulted was diluted with water, the ethanol evaporated at reduced pressure and then the resulting solution was acidified by adding HCl, extracted with ether, washed with saturated brine, dried over magnesium sulfate and reduced in volume. Distillation(0.67 mm Hg) gave 3.4 g(0.014 mole) of the clear, colorless liquid at 84-90°C(67% yield from **10a**).

$^1\text{H NMR}(\text{CDCl}_3)$ :  $\delta$  (ppm) 4.12(4H,q,J=7 Hz), 3.25(2H,m), 1.85(2H,m), 1.66(2H,m), 1.23(6H,t,J=7 Hz), 1.02(6H,s).

$^{13}\text{C NMR}(\text{CDCl}_3)$ :  $\delta$  (ppm) 174.4(s), 60.1(t), 46.3(d), 44.1(t), 38.9(s), 28.6(q), 13.8(q).

MS: 242( $\text{M}^+$ ), 227, 197, 196, 168, 153, 139, 123, 95(base), 81, 67, 55, 41.

HRMS: Calcd for  $\text{C}_{13}\text{H}_{22}\text{O}_4$ : 242.1517. Observed: 242.1512.

IR(neat): 2933, 1724(C=O), 1176, 1035  $\text{cm}^{-1}$ .

**4-Chlorobutan-2-one(12).** A methylene chloride solution of 20 g(0.28 mole) of methyl vinyl ketone was stirred at 0°C while 10.2 g of gaseous HCl were bubbled into the flask

at a rate such that little or no HCl was detected by wet litmus paper at the exit port of the reaction flask. The reaction was deemed complete when HCl was evidenced above the reaction(ca. 2 hours). The reaction was worked up by transferring the methylene chloride solution to a separatory funnel and rinsing repeatedly with saturated sodium bicarbonate solution. If this rinse procedure was omitted, the distilled product became highly colored and rapidly polymerized. After removal of the methylene chloride in vacuo, the reddish residue was distilled(40-41°C at 18 mm Hg) to provide 23.7 g(0.224 mole) of colorless liquid(80% yield).

$^1\text{H NMR}(\text{CDCl}_3)$ :  $\delta$  (ppm) 3.71(2H,t,J=6.5 Hz), 2.90(2H,t,J=6.5 Hz), 2.18(3H,s).

$^{13}\text{C NMR}(\text{CDCl}_3)$ :  $\delta$  (ppm) 204.8(s), 45.5(t), 38.0(t), 30.0(q).

MS: 108( $\text{M}^+ + 2$ ), 106( $\text{M}^+$ ), 91, 71, 63, 43(base).

HRMS: Calcd for  $\text{C}_4\text{H}_7\text{OCl}$ : 106.0185. Observed: 106.0189.

IR(neat): 1718(C=O), 1368, 1163, 727, 649  $\text{cm}^{-1}$ .

**2,7,7-Trimethyl-cis-1,5-dicarboethoxybicyclo[3.3.0]octan-2-ol(5).** A solution of 2.5 equivalents of lithium diisopropylamide in 50 ml of dry tetrahydrofuran was stirred while cooled to -78°C and 0.70 g(0.0029 mole) of the diester **4** was added slowly via syringe under nitrogen. After stirring 30 minutes, 0.46 g(1.5 eq.) of **12** was added at -78°C. The reaction was then stirred for 24 hours at room temperature and quenched by cautiously adding 10% aqueous HCl solution, extracted with ether, washed with saturated brine and then dried over magnesium sulfate. This gave 0.89 g of an orange syrup which was passed through a silica gel column (5 cm × 45 cm, 9:1 hexane:ethyl acetate) to provide 0.19 g(0.0061 mole) of the product(21% yield).

$^1\text{H NMR}(\text{CDCl}_3)$ :  $\delta$  (ppm) 4.09(2H,q,J=7 Hz), 4.07(2H,q,J=7 Hz), 2.9-1.4(9H,m), 1.51(3H,s), 1.24(3H,t,J=7 Hz), 1.21(3H,t,J=7 Hz), 1.09(3H,s), 1.04(3H,s).

$^{13}\text{C NMR}(\text{CDCl}_3)$ :  $\delta$  (ppm) 178.9(s), 173.8(s), 83.1(s), 73.0(s), 63.6(s), 61.4(t), 60.6(t), 50.5(t), 49.7(t), 40.5(t), 36.9(s), 36.8(t), 32.7(q), 31.2(q), 23.7(q), 14.0(q), 13.9(q).

MS: 312( $\text{M}^+$ ), 266, 241, 221, 195(base), 167, 149, 121, 107, 93, 79, 65, 43.

HRMS: Calcd for  $\text{C}_{17}\text{H}_{28}\text{O}_5$ : 312.1936. Observed: 312.1938.

IR(neat): 3333(-OH), 2924, 1712(C=O), 1684(C=O), 1368, 1277, 1212, 1186, 1026, 911, 730  $\text{cm}^{-1}$ .

## References

1. S. Nozoe, J. Furukawa, U. Sankawa, and S. Shibata, *Tetrahedron Lett.*, **17**, 195 (1976).
2. R. D. Little and G. W. Muller, *J. Am. Chem. Soc.*, **101**, 7129 (1979).
3. P. T. Lansbury, N. Y. Wang, and J. E. Rhodes, *Tetrahedron Lett.*, **20**, 1982 (1979).
4. S. Danishefsky, R. Zamboni, M. Kahn, and S. J. Etheredge, *J. Am. Chem. Soc.*, **102**, 2097 (1980).
5. B. M. Trost, C. D. Shuey, F. DiNimo, Jr, and S. S. McElvain, *J. Am. Chem. Soc.*, **101**, 1284 (1979).
6. (a) R. L. Funk and G. L. Bolton, *J. Org. Chem.*, **49**, 5021 (1984); (b) P. A. Wender and J. J. Howbert, *Tetrahedron Lett.*, **23**, 3983 (1982); (c) R. D. Little and G. W. Muller, *J. Am. Chem. Soc.*, **103**, 2744 (1981); (d) T. Hudlicky, T. M. Kutchan, S. R. Wilson, and D. T. Mao, *J. Am. Chem. Soc.*,

- 102, 6351 (1980); (e) K. Tatsuta, K. Akimoto, and M. Kinoshita, *J. Am. Chem. Soc.*, **101**, 6118 (1979).
7. (a) J. -G. Jun and B. P. Mundy, *Bull. Korean Chem. Soc.*, **8**, 489 (1987); (b) J. -G. Jun and B. P. Mundy, *Bull. Korean Chem. Soc.*, **8**, 310 (1987); (c) D. Wilkening and B. P. Mundy, *Synth. Commun.*, **14**, 227 (1984).
8. (a) R. L. Danheiser, C. A. Kwasigroch, and Y. -M. Tsai, *J. Am. Chem. Soc.*, **107**, 7233 (1985); (b) R. L. Danheiser and D. M. Fink, *Tetrahedron Lett.*, **26**, 2513 (1985).
9. M. E. Flaugh, T. A. Crowell, and D. S. Farlow, *J. Org. Chem.*, **45**, 5399 (1980).

## Medium Effect on the Formation of Ion-Pair between Methylene Blue and Tetraphenylborate in Dilute Solutions

Eui Wha Moon, Beom-Gyu Lee, and Kang-Jin Kim \*

Department of Chemistry, Korea University, Seoul 136-701

Received February 22, 1988

The hydrophobic interaction leading to the formation of ion-pair between MB<sup>+</sup> and TPB<sup>-</sup> was investigated spectroscopically by varying the medium with the addition of 1,4-dioxane or urea. Beyond 0.01 mole fraction of 1,4-dioxane in water or above 2.0M urea the ion-pair appeared to be completely dissociated into individual ions. The ion-pair was not observed in common organic solvents and the absorption maxima of MB<sup>+</sup> were correlated relatively well with the  $\pi^*$ -scale.

### Introduction

The visible absorption spectra of aqueous solution containing methylene blue cation (MB<sup>+</sup>) and tetraphenylborate anion (TPB<sup>-</sup>) show spectral changes, especially at long wavelengths presumably due to the aggregation of MB<sup>+</sup> and TPB<sup>-</sup>.<sup>1</sup> The new absorption behavior could be clearly differentiated from the well-studied metachromatic effects in methylene blue both in solutions of pure MB<sup>+</sup> of varying concentrations and in systems where the dye is adsorbed on solid surfaces. They consist of a shift of the long wavelength peak to a shorter wavelength. The metachromacy of aqueous MB<sup>+</sup> solutions can be related to the formation of dimer, (MB<sup>+</sup>)<sub>2</sub>.<sup>2</sup>

Since both the cation and the anion are large, univalent, and poorly hydrated, the water structure forces the two ions to form an ion-pair, MB-TPB, to minimize their disturbance to itself and maximize the water-water bonding.<sup>3</sup> The opposite charges on the anion and cation facilitate the association. The ion-pairs can be associated further to produce double ion-pairs again by the water structure as suggested recently.<sup>4</sup> The tendency of water molecules to self-associate should be responsible for the ion-pairing. Therefore, the factors which could modify this tendency should be likely to influence the formation of ion-pairs.

For the purpose of elucidating the nature of ion-pair formation, in this paper the absorption and fluorescence emission behaviors of MB<sup>+</sup> and TPB<sup>-</sup> mixed solutions are reported by varying the composition of the medium with the addition of 1,4-dioxane and urea. The addition 1,4-dioxane into water decrease the dielectric constant of medium whereas urea increases it. In addition, the effects of replacing MB<sup>+</sup> with other cationic dyes having similar structure and of changing water with common organic solvents were investigated.

### Experimental

**Chemicals.** Methylene blue, thionine, and toluidine blue

(all from Merck, GR) were used as cationic sources, MB<sup>+</sup>, Thio<sup>+</sup>, and TB<sup>+</sup>, respectively. Sodium tetraphenylborate (MCR, GR) as a source of boron complex anion, TPB<sup>-</sup>, was dissolved in distilled water and stored in a polyethylene bottle to prevent contamination from glasswares containing boron. N-methylformamide (NMF), N-methylpropionamide (NMP), dimethylformamide (DMF), and 1,4-dioxane, from Fluka, 1,2-dichloroethane (DCE), formamide, and pyridine, from Junsei, and dimethylsulfoxide (DMSO), acetonitrile, CH<sub>2</sub>Cl<sub>2</sub> and alcohols used from Aldrich Co. were all reagent grade. For all solutions the concentrations of MB<sup>+</sup> and TPB<sup>-</sup> were 1.0 × 10<sup>-6</sup>M and 1.0 × 10<sup>-5</sup>M, respectively.

**Methods.** Visible spectra were made on a Cary 17D spectrophotometer. Fluorescence excitation and emission spectra were recorded on a Hitachi 650-60 spectrofluorimeter. All solutions containing MB<sup>+</sup> were stored in polyethylene bottles wrapped with aluminum foil to minimize the photodecomposition of MB<sup>+</sup>. Measurements were made at room temperature.

### Results and Discussion

Figure 1 shows the absorption spectra of 1.0 × 10<sup>-6</sup>M MB<sup>+</sup> in water (a) and in methanol (b), and of mixed solutions of 1.0 × 10<sup>-6</sup>M MB<sup>+</sup> and 1.0 × 10<sup>-5</sup>M TPB<sup>-</sup> in water (c) and methanol (d). The mixed solution in water reveals a broad absorption spectrum in comparison with other spectra. Particularly, it has a considerable absorbance around 710 nm and there exists a significant contribution near 623 nm in the light of the decrease in absorbance of MB<sup>+</sup> at the absorption maximum, 666 nm. The species responsible for the spectral change that is present only in the mixed aqueous solution was attributed to the aggregation of MB-TPB ion-pairs.<sup>1,4</sup>

Since both monovalent MB<sup>+</sup> and TPB<sup>-</sup>, large and hydrophobic, contribute to tightening up their surrounding water, there would be a tendency for the water structure to force these ions into a single cavity in order to minimize disturbance of the water structure.<sup>3</sup> The tendency of water mole-