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(22) This does not seem to be due to trace amounts of metal ions impurities contained in CD_3OD, since treated and untreated CD_3OD with disodium EDTA gave essentially the same result.[23]
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(24) So far several dioxetanes have been reported in the cycloaddition of singlet oxygen to aromatic compounds.[25] In contrast to the present case, all of the reported dioxetanes[26] have unusual thermal stability (mp >110 °C). The possibility that some of these dioxetanes may have other structures should not be overlooked.
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Isao Saito,* Seiichi Matsugo, Teruo Matsuura*
Department of Synthetic Chemistry
Faculty of Engineering, Kyoto University
Kyoto 606, Japan
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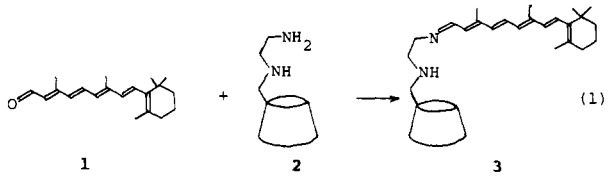
Cyclodextrin Having an Amino Group as a Rhodopsin Model

Sir:

Since the conception of the visual pigment was first provided by Hecht in 1920,[1] physicochemical aspects of the visual process have attracted the attention of many chemists. Although much important information about retinal **1** and rhodopsin (which is composed of retinal and receptor protein, opsin)[2] has been collected in numerous investigations, there still seems to be a serious gap or discrepancy between what is known about retinal itself and what is known about rhodopsin as the actual active pigment in biological systems. Among the significant discrepancies is that the large red shift in the electronic spectrum observed for the Schiff base of retinal bound to opsin has never been reproduced by retinal under any appropriate conditions in aqueous solution and several conflicting explanations for the observed discrepancy have been given.[3,4]

We now report the first successful binding model as an example of our current research using cyclodextrins as the recognition element.[5] We have substituted a ω-aminoethylamino group in place of one of the primary hydroxyl groups of β-cyclodextrin to give a simple binding model of rhodopsin. The resultant diamine, **2**, has a hydrophobic recognition site as well as a carbonyl recognition site to form the corresponding Schiff base. As expected, this host having double recognition sites binds retinal, a hydrophobic aldehyde, very strongly in aqueous solution. With regard to the present model it is interesting to note that the observed λ_{max} of its electronic spectrum is located at 497 nm, in excellent agreement with those of bovine rhodopsin (498 nm) or bovine lumirhodopsin (497 nm) (see Table I and Figure 1).

Thus, the Schiff base **3** was prepared from the reaction between 2 μmol of *all-trans*-retinal (**1**) and 17 μmol of ω-aminoethylamino-β-cyclodextrin (**2**)[6] in 0.5 mL of ethylene glycol at room temperature for 24 h in the dark (eq 1).[7] The corresponding open-chain Schiff bases, ω-retinylidene-*N*-methylethylenediamine (**4**) and ω-retinylidene-*n*-butylamine[8] (**5**)



1 2 3

Table I. Absorption Maxima of Retinal Schiff Bases at 25 °C

Schiff base	solvent	λ_{max} ($\Delta\lambda_{max}$)[a]
3	HO⌒OH	375
3·$(H^+)_2$[b]	HO⌒OH	476
3·$(H^+)_2$[c]	H_2O	497 (+21)
4	MeOH	367
4·$(H^+)_2$[b]	HO⌒OH	470
4·$(H^+)_2$[c]	H_2O	471 (+1)
4·$(H^+)_2$ + β-CD[d]	H_2O	444 (−26)
5[e]	MeOH	366
5·H^+[b]	MeOH	450
5·H^+[c]	H_2O	450 (0)
5·H^+ + β-CD[d]	H_2O	433 (−17)
bovine rhodopsin[f]		498 (cis)
bovine lumirhodopsin[f,g]		497 (trans)

[a] Spectral shift of λ_{max} from that of each protonated species in methanol or ethylene glycol. [b] Excess of HCl was added. [c] At pH 1.16 in the aqueous HCl solution. [d] At pH 1.16 in the aqueous HCl solution, β-cyclodextrin, 2×10^{-2} mol/L. [e] I. Suzuki and Y. Kito, *Photochem. Photobiol.*, **15**, 275 (1972). [f] R. G. Mathews, R. Hubloard, P. K. Brown, and G. Wald, *J. Gen. Physiol.*, **47**, 215 (1963). [g] Lumirhodopsin is considered to contain *all-trans*-retinal as the chromophore. See ref 2f.

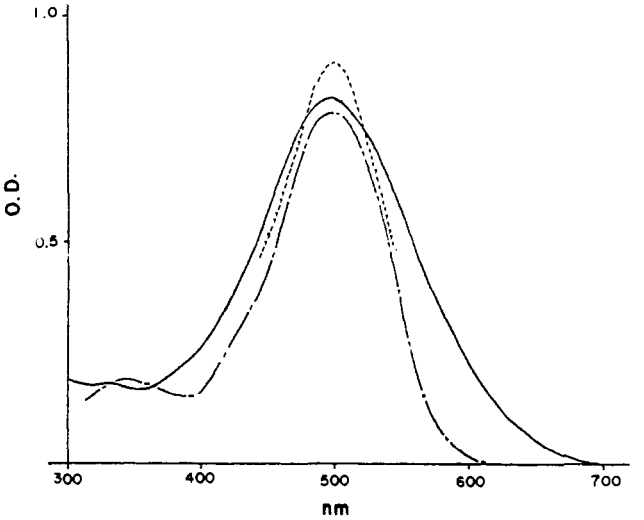
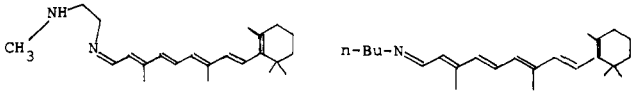


Figure 1. Electronic spectra of **3**·$(H^+)_2$ (—) at pH 1.16 in the aqueous HCl solution and bovin rhodopsin (- - -) and lumirhodopsin (- - - -) (G. Wald, J. Durell, and R. C. C. St. George, *Science*, **111**, 179 (1950)). Concentrations of all compounds are 2×10^{-5} M.

were also prepared by a similar procedure.

All of these Schiff bases, **3**–**5**, showed electronic spectra with "normal" λ_{max} at ~370 nm in methanol or ethylene glycol. In aqueous solution at pH 1, **4** and **5** were completely protonated



4 5

and their λ_{max}'s shifted to longer wavelength, independently of the solvent (water, methanol, or ethylene glycol). However, **3** behaved quite uniquely in aqueous solution at pH 1, although, on protonation in ethylene glycol, a red shift of a similar order of magnitude to that seen for **4**·$(H^+)_2$ was observed.[9] It is very

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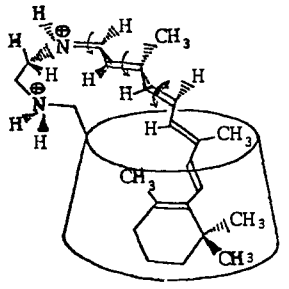

Figure 2. Schematic representation of plausible binding of retinal moiety of **3**·$(H^+)_2$ based on CPK model.

important to note that in aqueous solution, **3**·$(H^+)_2$ showed a further red shift from 476 (in ethylene glycol) to 497 nm; the latter wavelength is practically the same as those of native rhodopsins (see Table I). This significant red shift can not be interpreted by the simple binding of the chromophore in a hydrophobic cavity, since, on the contrary, **4**·$(H^+)_2$ or **5**·(H^+) showed a substantial *blue shift* in the hydrophobic cavity of unsubstituted β-cyclodextrin (−26 and −17 nm, respectively). Therefore, this significant and unique red shift (21 + 26 = 47 nm or 53 nm from **4**·$(H^+)_2$·β-CD to **3**·$(H^+)_2$) caused by covalent combination of the CO recognition site and the hydrophobic binding site is neither due to a solvent effect nor to simple binding in a hydrophobic cavity.

In the literature, there are many mechanisms postulated to interpret the unique and remarkable red shift,[10] which can, in principle, be arranged into the following three categories: (a) the effect of the large polarizability of the microenvironment, most probably of aromatic amino acid residue(s) in opsin's binding site;[11] (b) the abnormally large electrostatic effect of the appropriately located counteranion and/or the additional anion or cation along the surface of the binding site of opsin[12] upon the protonated Schiff base; (c) the possible twist or distortion of the retinal moiety caused by the tight binding by opsin.[2f,13]

Since **3**·$(H^+)_2$ (Figure 2) is located in a very similar electrostatic and/or microenvironment to **4**·$(H^+)_2$ + β-CD, the remarkable red shift observed for **3**·$(H^+)_2$ (+53–47 nm) can not be attributable to the electrostatic or microenvironmental effects alone, but rather to a unique combination of these effects, or these effects including the twist mechanism[14] seem to be operating. Apparently, the electrostatic mechanism is operating as is seen from the comparison of **5**·H^+ with **4**·$(H^+)_2$ (+21 nm). The present model study is a very suggestive one which should lead to further insights into the rhodopsin mechanism, and additional model studies are now underway.

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Iwao Tabushi,* Yasuhisa Kuroda, Kazuhiro Shimokawa
Department of Synthetic Chemistry
Kyoto University, Yoshida, Kyoto 606, Japan

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The Iron(II) "Homologous Cap" Porphyrin. A Novel Dioxygen Binder

Sir:

As part of our current research program in the area of synthetic oxygen carriers, we have been investigating the base and dioxygen binding of the iron and cobalt "cap" and "homologous cap" porphyrins.[1-4] We report here some experimental results concerning Fe(HmCap)(1-MeIm) which show that the complex is capable of *weakly* binding a second molecule of 1-MeIm and that the complex so formed can bind dioxygen reversibly *without* displacing the weakly bound 1-MeIm ligand. In an accompanying communication, comparisons between the Cap and HmCap systems are made.

The $HmCapH_2$ was prepared in a similar manner to that described for the normal cap porphyrin.[1] The reaction of $HmCapH_2$ with anhydrous ferrous chloride in refluxing THF under dry nitrogen gave Fe(HmCap)Cl: UV $\lambda_{max}(CHCl_3)$ 425, 510, 560 (sh), 590 (sh). Benzene or toluene solutions of the iron(III) porphyrin were reduced using aqueous sodium dithionite[5] to give Fe(HmCap), λ_{max}(toluene) 542 nm. The presence of bands in the infrared spectra of the iron–dioxygen adducts attributable to $\nu_{^{16}O_2}$ and $\nu_{^{18}O_2}$ confirms that oxygenation has occurred.[6]

Figure 1A shows the spectral changes which occurred during the titration of a toluene solution of Fe(HmCap) with a 0.0566 M 1-MeIm solution in toluene. The observed changes are due primarily to the equilibrium

$$\text{Fe(HmCap)} + \text{1-MeIm} \overset{K^B}{\rightleftharpoons} \text{Fe(HmCap)(1-MeIm)} \quad (1)$$

and a value for log K^B (23 °C) of 3.31 ± 0.05 was obtained. If this titration was followed by one using neat 1-MeIm, the spectral changes shown in Figure 1B were observed and these changes are associated with the equilibrium

$$\text{Fe(HmCap)(1-MeIm)} + \text{1-MeIm} \overset{K_B{}^B}{\rightleftharpoons} \text{Fe(HmCap)(1-MeIm)}_2 \quad (2)$$

for which log $K_B{}^B$ (23 °C) = 0.77. Consistent with this inter-

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