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CATALYTIC EFFECTS OF Mg^{2+} ION ON ELECTRON TRANSFER REACTIONS OF PHOTO-EXCITED FLAVIN ANALOGUES (3-METHYL-10-PHENYL-5-DEAZA-ISOALLOXAZINES AND 3-METHYL-10-PHENYLISOALLOXAZINE) WITH METHYL AND METHOXY SUBSTITUTED BENZENES

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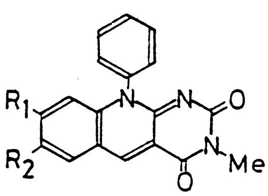
The Mg^{2+} ion acts as an efficient catalyst for the electron transfer reactions of photo-excited flavin analogues (3-methyl-10-phenyl-5-deazaisoalloxazines and 3-methyl-10-phenylisoalloxazine) with methyl and methoxy substituted benzenes in acetonitrile. The catalytic effect of Mg^{2+} ion is caused by the complex formation between flavin analogues and Mg^{2+} ion.

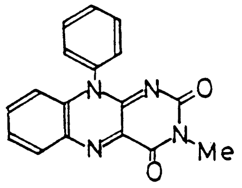
The discovery of 5-deazaflavin containing carbon in place of nitrogen at the 5-position of flavins as a naturally occurring cofactor in various bacteria[1)] has provoked considerable interest in both thermal[2)] and photochemical[3,4)] redox reactions involving the modified flavins. On the other hand, model compounds of metalloflavin have recently been developed in relation to the important function of metalloflavin chelates in biological redox reactions.[5)] However, no interaction between 5-deazaflavins and metal ions is known. Moreover, no catalytic effect of metal ions in photoredox reactions involving flavins as well as 5-deazaflavins has so far been reported.

We wish to report herein the formation of 1 : 1 complexes between flavin analogues and Mg^{2+} ion, showing remarkable enhancement in the rate of electron transfer reactions of photo-excited flavin analogues with methyl and methoxy substituted benzenes.



		R_1	R_2
1a	:	H	H
1b	:	Cl	H
1c	:	H	NO_2

Flavin analogues (3-methyl-10-phenyl-5-deazaisoalloxazines: **1a**-**c**, 3-methyl-10-phenylisoalloxazine: **2**) were prepared according to the literatures.[6)] The electronic spectra of **1a**-**c** and **2** in dry acetonitrile (MeCN) were significantly affected by the addition of $Mg(ClO_4)_2$; the absorption bands of **1a**-**c** and **2** in the absence of Mg^{2+} ion (λ_{max} = 403, 404, 401, and 439 nm, respectively) were blue-shifted in the presence of 0.10 mol dm^{-3} Mg^{2+} ion (λ_{max} = 388, 388, 387, and 424 nm, respectively). Similar blue-shifts were observed for the fluorescence spectra of **1a**-**c** and **2** by the addition of Mg^{2+} ion. Examinations of the dependences of the absorbances of **1a**-**c** and **2** in the λ = 380 - 430 nm region on the Mg^{2+} concentration showed the formation of 1 : 1 complexes between the flavin analogues Fl and Mg^{2+} ion (Eq. 1). Such a complex formation



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$$\mathrm{Fl} + \mathrm{Mg}^{2+} \overset{K}{\rightleftharpoons} [\mathrm{Fl}\ \mathrm{Mg}^{2+}] \qquad (1)$$

has not been observed between Fl and $NaClO_4$. The formation constants K of the Mg^{2+} complexes with **1a**-**c** and **2** have been determined by the spectrophotometric method described previously[7] as 1.1 x 10^3, 6.4 x 10^2, 1.8 x 10^2, and 1.7 x 10^2 mol^{-1} dm^3, respectively, in MeCN at 298 K. The K values decreased by the addition of H_2O to dry MeCN, probably because of the hydration of Mg^{2+} ion.[8]

The singlet excited state of a flavin analogue (3-methyl-5-deazaisoalloxazine) is known to be quenched by methyl and methoxy substituted benzenes being electron donors D (Eq. 2).[4] In the present case as well,

$$\mathrm{Fl}^{*} + \mathrm{D} \longrightarrow \mathrm{Fl}^{\overline{\cdot}} + \mathrm{D}^{\overset{+}{\cdot}} \qquad (2)$$

the fluorescence of **1a**-**c** as well as **2** was quenched by methyl and methoxy substituted benzenes. The quenching constants K_q of **1a**-**c** and **2** with the electron donors D have been determined from the Stern-Volmer equation $I_0/I = 1 + K_q[D]$, where I_0 and I are the fluorescence intensities of **1a**-**c** and **2** in the absence and presence of a quencher D, respectively. The logarithms of the K_q values of **1a**, **1b**, and **2** in the absence of Mg^{2+} ion are plotted against the oxidation peak potentials of the donors E^p_{ox}[9], as shown by the open circles in Fig. 1, which exhibits a typical dependence of log K_q on E^p_{ox} for electron transfer processes,[10] *i.e.* as E^p_{ox} decreases, log K_q increases to reach a constant value which may be diffusion-limited. A similar result was obtained for **1c**.

Although the reduction potentials E^0_{red} of **1a**-**c** and **2** cannot be obtained precisely by the electrochemical methods because of the low solubilities of **1a**-**c** and **2** in MeCN, the relative values of

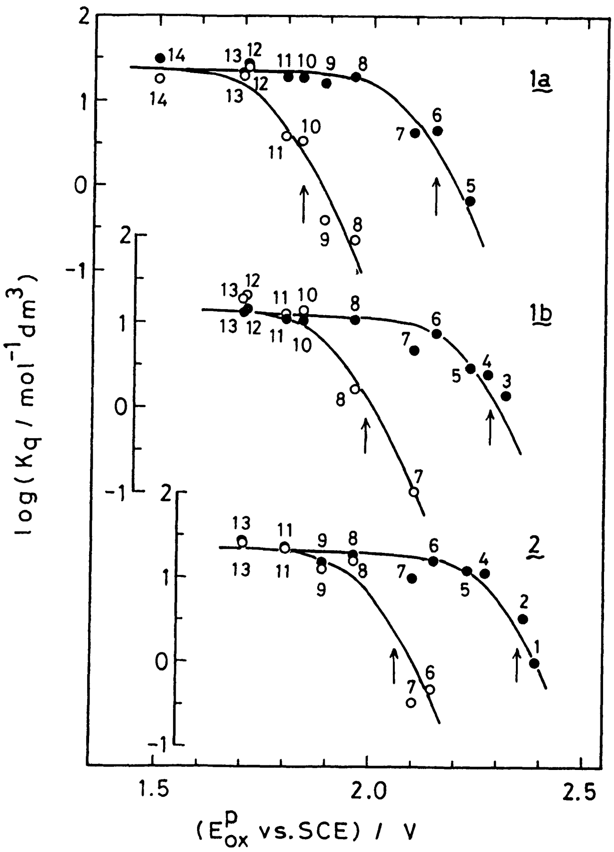

Fig. 1. Plots of the logarithm of the quenching constant K_q *vs.* the oxidation peak potential E^p_{ox} of quenchers for the fluorescence quenching of flavin analogues (**1a**, **1b**, and **2**) by methyl and methoxy substituted benzenes in the absence of Mg^{2+} ion (○) and the presence of 0.10 mol dm^{-3} Mg^{2+} ion (●) in MeCN. Numbers refer to the quenchers: 1) MeC_6H_5, 2) *p*-ClC_6H_4Me, 3) *p*-BrC_6H_4Me, 4) *m*-$(Me)_2C_6H_4$, 5) *o*-$(Me)_2C_6H_4$, 6) *p*-$(Me)_2C_6H_4$, 7) 1,3,5-$(Me)_3C_6H_3$, 8) $MeOC_6H_5$, 9) 1,2,3,4-$(Me)_4C_6H_2$, 10) $(Me)_5C_6H$, 11) *m*-Me-C_6H_4MeO, 12) *p*-MeC_6H_4MeO, 13) *m*-$(MeO)_2C_6H_4$, 14) *p*-$(MeO)_2C_6H_4$. The solid lines are drawn by the simulation based on Eqs. 3-5. The arrows indicate the E^p_{ox} values at which the Gibbs energy change ΔG of the electron transfer (Eq. 5) is zero.

E^{0}_{red} can be evaluated by applying the Rehm-Weller Gibbs energy relationship (Eq. 3)10) to the correlation between log K_q and E^{p}_{ox} in Fig. 1 as follows. In

$$\Delta G^{\ddagger} = (\Delta G/2) + [(\Delta G/2)^{2} + (\Delta G^{\ddagger}_{0})^{2}]^{1/2} \tag{3}$$

Eq. 3, $\Delta G^{\ddagger}_{0}$ represents the activation Gibbs energy when the Gibbs energy change ΔG of the actual electron transfer process, $[\mathrm{Fl}^{*}\ \mathrm{D}] \rightarrow [\mathrm{Fl}^{\cdot-}\ \mathrm{D}^{\cdot+}]$, is zero; the value is generally taken as 0.10 V,10) and $\Delta G^{\ddagger}$ is related to K_q by Eq. 4,10,11)

$$K_q = \tau[Z^{-1}\exp(\Delta G^{\ddagger}/RT) + k_{\mathrm{diff}}{}^{-1}]^{-1} \tag{4}$$

where τ is the lifetime of Fl^{*}, Z is the collision frequency which is generally taken as 1×10^{11} $\mathrm{mol}^{-1}\,\mathrm{dm}^{3}\,\mathrm{s}^{-1}$, and k_{diff} is the diffusion rate constant 2×10^{10} $\mathrm{mol}^{-1}\,\mathrm{dm}^{3}\,\mathrm{s}^{-1}$.10,11) From Eqs. 3 and 4, the dependence of log K_q on ΔG for each flavin analogue in Fig. 1 can be evaluated by using the τ values which are determined from the diffusion-limited value of K_q in Fig. 1 by Eq. 4. On the other hand, ΔG is related to the oxidation peak potential E^{p}_{ox} of D as shown by Eq. 5,

$$\Delta G = E^{p}_{\mathrm{ox}} - E^{0}_{\mathrm{red}} - \Delta E_{0,0} + w_{p} + C \tag{5}$$

where $\Delta E_{0,0}$ indicates the 0,0-excitation energy of Fl, w_p is the small interaction energy in the $[\mathrm{Fl}^{\cdot-}\ \mathrm{D}^{\cdot+}]$ radical ion pair, and C is a constant which is the difference between E^{0}_{ox} and E^{p}_{ox}.9,11) Thus, the curve obtained for log K_q *vs.* ΔG can well be fitted with each plot of log K_q *vs.* E^{p}_{ox} by sliding the curve of log K_q *vs.* ΔG appropriately in the direction of the abscissa E^{p}_{ox}, as shown by the solid lines in Fig. 1. Then, the arrows in Fig. 1 indicate the E^{p}_{ox} values $(E^{p}_{\mathrm{ox}})_{0}$ at which $\Delta G = 0$. According to Eq. 5, $(E^{p}_{\mathrm{ox}})_{0}$ is related to E^{0}_{red} by Eq. 6. The $(E^{p}_{\mathrm{ox}})_{0}$

$$(E^{p}_{\mathrm{ox}})_{0} = E^{0}_{\mathrm{red}} + \Delta E_{0,0} - w_{p} - C \tag{6}$$

values of **1a**-**c** and **2** in the absence of Mg^{2+} ion are listed in Table 1.

The addition of $\mathrm{Mg(ClO_4)_2}$ to the Fl-D system causes a significant increase of the quenching constant K_q in the range smaller than the diffusion-limited value in the absence of Mg^{2+} ion, as shown by the closed circles in Fig. 1, where the solid lines are drawn by the simulation based on Eqs. 3-5 as described above. The $(E^{p}_{\mathrm{ox}})_{0}$ values of **1a**-**c** and **2** in the presence of 0.10 mol dm^{-3} Mg^{2+} ion, which are indicated by the arrows in the cases of **1a**, **1b**, and **2** (Fig. 1), are shifted in the positive direction (0.27 - 0.31 V) relative to those in the absence of Mg^{2+} ion (Table 1). It should be noted that the

Table 1. The oxidation peak potentials $(E^{p}_{\mathrm{ox}})_{0}$ of the electron donors where ΔG of the electron transfer of **1a**-**c** and **2** is zero in the absence and presence of 0.10 mol dm^{-3} Mg^{2+} ion and the change of the reduction potential $\Delta E^{0}_{\mathrm{red}}$ of **1a**-**c** and **2** by the complex formation with Mg^{2+} ion.

Flavin analogue	$(E^{p}_{\mathrm{ox}})_{0}$ a)	$(E^{p}_{\mathrm{ox}})_{0}$ b)	$\Delta E^{0}_{\mathrm{red}}$ c)
1a	1.85	2.16	0.21
1b	1.99	2.28	0.17
1c	2.06	2.33	0.19
2	2.06	2.35	0.21

a) In the absence of Mg^{2+} ion. b) In the presence of 0.10 mol dm^{-3} Mg^{2+} ion. c) Determined using Eq. 6, see text and Ref. 12.

singlet excited state of Fl has not been quenched by 0.10 mol dm^{-3} Mg^{2+} ion and the presence of 0.10 mol dm^{-3} $NaClO_4$ has caused almost no effect on K_q in contrast with the case of $Mg(ClO_4)_2$. At the Mg^{2+} concentration (0.10 mol dm^{-3}), most flavin and 5-deazaflavin molecules form the 1 : 1 complex with Mg^{2+} ion (Eq. 1), based on the formation constants described above. Thus, according to Eq. 6, the observed shifts of $(E^{p}_{ox})_0$ are ascribed to those of E^{0}_{red}, $\Delta E_{0,0}$, and w_p of **1a**-**c** and **2** by the complex formation with Mg^{2+} ion. The shifts of $\Delta E_{0,0}$ of **1a**-**c** and **2** by the complex formation with Mg^{2+} ion have been determined as 0.10, 0.12, 0.08, and 0.08 V, respectively, from the blue-shifts of the absorption and fluorescence spectra. Thus, by assuming the shift of w_p is zero,12) the positive shifts of E^{0}_{red} of **1a**-**c** and **2** by the complex formation with Mg^{2+} ion are evaluated from those of $(E^{p}_{ox})_0$ and $\Delta E_{0,0}$ by using Eq. 6 as listed in Table 1.

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8) In the presence of 2.8×10^{-2} and 8.3×10^{-2} mol dm^{-3} H_2O, the K values of **2** (1.5×10^{2} and 6.5×10 mol^{-1} dm^{3}, respectively) become smaller than the K value (1.7×10^{2} mol^{-1} dm^{3}) in dry MeCN where the H_2O concentration is much less than 1×10^{-3} mol dm^{-3}.

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12) Strictly speaking, the w_p value of $[Fl^{\cdot -}\ D^{\cdot +}]$ may be more negative by about 0.1 V (Ref. 11) than that of $[Mg^{2+}Fl^{\cdot -}\ D^{\cdot +}]$ and thereby the ΔE_{red} values in Table 1 give the lowest limit.

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