center by steric interaction with the bulkier groups on the stereogenic centers must be looked at with great care.

Supplementary Material Available: Tables of positional and thermal parameters and bond lengths and angles for (*Z*)-**1** (5 pages). Ordering information is given on any current masthead page.

"Remote Control" of Flavin Reactivities by an Intramolecular Crown Ring Serving as a Metal-Binding Site

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Coenzymes are prosthetic groups in enzymes and catalyze the enzyme-mediated reactions in the active sites. Although some of them are capable of catalyzing the reactions even in the absence of apoenzymes, the activities are mostly controlled through the interactions with apoenzymes.[1-5] In particular, allosteric effects by which some catalytic activities of enzymes may be regulated are quite intriguing from a bioorganic viewpoint: that is, binding of an effector to a remote, allosteric site induces activity changes in the active sites.[6] In order to mimic such allosteric functions in synthetic systems, we previously synthesized a crown ether flavin mimic (**1**).[7] The crown ether cavity in **1** is recognized as a binding site not only for spherical metal cations but ammonium cations and others through hydrogen bonding, and the resulting complexation changed the spectral and catalytic behaviors. Roseoflavin (**2**), isolated from a culture medium of Streptomyces strain No. 768,[8] has a dimethylamino group at the 8-position instead of a methyl group in conventional flavin coenzymes and shows an antiflavin reactivity.[9,10] This occurs because the isoalloxazine ring loses its oxidizing ability owing to intramolecular charge transfer from the 8-(dimethylamino) group to the pteridine moiety.[11,12] This finding suggests a new strategy to design flavins (**3**) with the allosteric functionality: that is, the oxidizing ability of **3** should be greatly reduced, as seen in **2**, when the 8-sulfonamide group is dissociated. Furthermore, this dissociation equilibrium can be "remote-controlled" by the metal binding to the crown ether portion.[7,13] Obviously, the molecular design in this paper is stimulated by two preceding concepts, "remote functionalization" in steroid photochemistry[14] and "lariat ethers" in crown ether chemistry.[15-17]

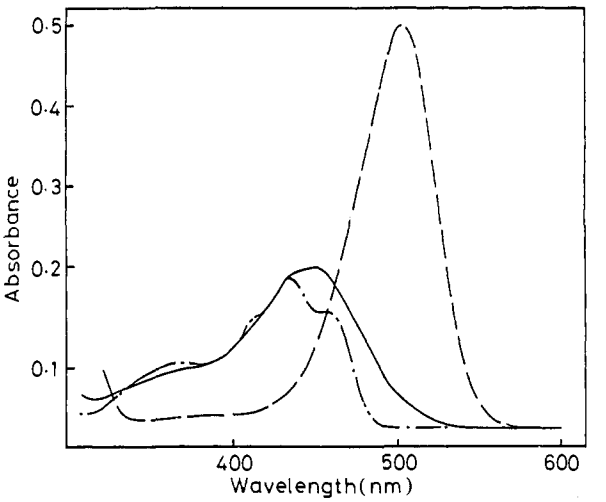
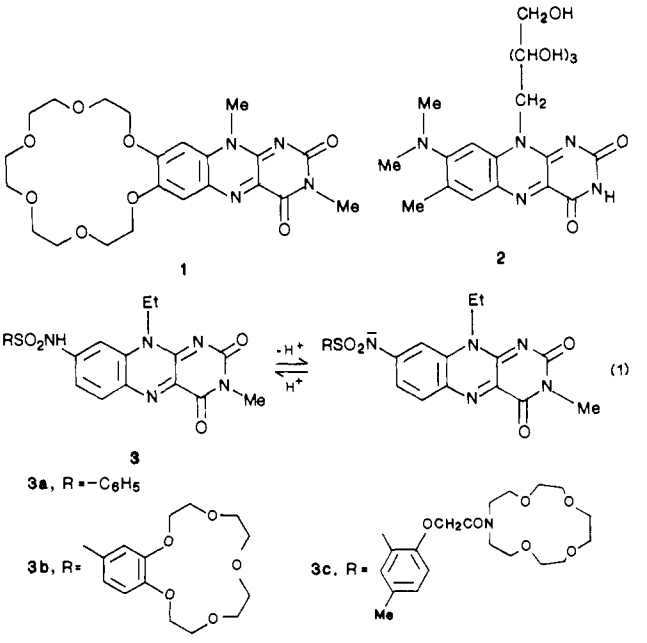


Figure 1. Absorption spectra of **3c** (1.03×10^{-5} M) in acetonitrile at 30 °C: (---) neutral **3c** ([CF_3COOH] = 2.32×10^{-5} M); (- - -) anionic **3c** ([1,8-diazabicyclo[5.4.0]-7-undecene] = 1.70×10^{-5} M), (—) **3c**·Ca^{2+} complex ([$Ca(ClO_4)_2$] = 7.65×10^{-3} M).



3a-c were synthesized by the reaction of 3-methyl-8-chloro-10-ethylisoalloxazine with the corresponding sulfonamides in sulfolane in the presence of potassium carbonate.[8] The products were identified by IR, NMR, and elemental analysis. In acidic aqueous solution **3a-c** gave a yellow color characteristic of "regular" flavins (λ_{max} 433 nm for **3a**, 435 nm for **3b**, and 436

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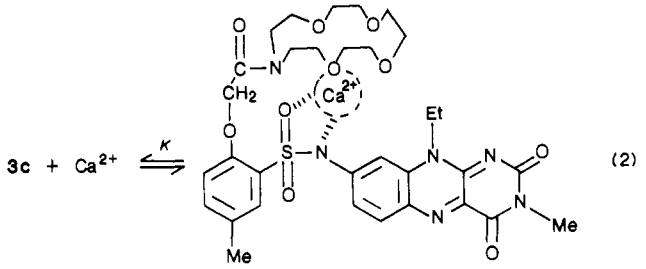
Table I. Quantum Yields (Φ_{ox}) for Photooxidation of Benzyl Alcohol by **3** and 3-Methyl-10-ethylisoalloxazine[a]

solvent	$[Ca(ClO_4)_2]$/ mM	Φ_{ox}/% **3c**	**3a**	3-methyl-10-ethylisoalloxazine
water (pH 3.5)	0	0.60	0.64[b]	3.34
water (pH 7.5)	0	0.04	ca. 1×10^{-3} [b]	2.47
MeCN	0	0.05	0.04	0.08
MeCN	0.199	0.08	0.07	
MeCN	1.01	0.13	0.07	
MeCN	2.55	0.20	0.08	

[a] Three-Milliliter aliquots of the substrate solutions in a 1-cm quartz cell were deaerated and were irradiated under nitrogen at room temperature with a 300-W high-pressure Hg lamp. The extraneous lines of the lamp other than 366 nm were filtered out:[21] [**3**] = 2.00×10^{-4} M, [benzyl alcohol] = 5.00×10^{-2} M. [b] Neutral **3a** was sparingly soluble in water, so that the photooxidation was carriedout in 40 vol % aqueous acetonitrile.

nm for **3c**), while in alkaline aqueous solution they gave a red color similar to roseoflavin (λ_{max} 476 nm for **3a**, 478 nm for **3b**, and 485 nm for **3c**). The pK_a values for the dissociation of the 8-sulfonamide groups (eq 1) were determined spectrophotometrically at 30 °C: pK_a = 4.85 for **3a**, 4.93 for **3b**, and 5.54 for **3c**. The results show that the higher the pK_a, the more the λ_{max} shifts to longer wave-lengths.[19]

In an aqueous system the absorption spectra of **3a-c** were unaffected by the addition of alkali and alkaline earth metal cations. In acetonitrile the absorption spectra of **3a** and **3c** were scarcely affected by the addition of these metal cations (as perchlorate salts) but **3c** gave a new absorption band at 452 nm on the addition of $Ca(ClO_4)_2$ which increased with increasing Ca^{2+} concentration (Figure 1). This is probably due to the "lariat effect" by which the dissociation of the 8-sulfonamide group is facilitated to serve as a cap for the Ca^{2+} ion bound to the crown cavity. The association constant (K) was estimated to be 4.27×10^4 M^{-1} from a plot of OD_{452} vs. $[Ca(ClO_4)_2]$.



(2)

In order to examine the potential correlation between the spectral change and the oxidizing ability, we carried out the anaerobic photooxidation of benzyl alcohol.[20] The results (Table I) indicate that (i) in an aqueous system the quantum yields (Φ_{ox}) for neutral **3a** and **3c** (at pH 3.5) were greater by 16-640-fold than those for the corresponding anionic species (at pH 7.5), whereas the Φ_{ox} for 3-methyl-10-ethylisoalloxazine was scarcely affected by mediam pH; (ii) the Φ_{ox} values in acetonitrile are smaller by more than 1 order of magnitude than those in an aqueous system; and (iii) most importantly, the Φ_{ox} for **3c** increases with increasing Ca^{2+} concentration but that for **3a** increases only slightly. Fact i suggests that the photooxidizing ability of the anionic **3** is significantly quenched by the intramolecular charge transfer from the dissociated 8-sulfonamide group. On the other hand, fact iii is well correlated with the spectral data: that is, Ca^{2+} ion bound to the crown cavity of **3c** induces the spectral change and enhances the photooxidizing ability.[22] Conceivably, Ca^{2+} ion can suppress the intramolecular charge transfer through the interaction with the 8-sulfonamide anion serving as a cap for this metal cation.

In conclusion, this paper demonstrated that in **3c** the crown ether moiety serving as an allosteric site can induce the activity change in the flavin moiety serving as a catalytic site. The close imitation of natural control mechanisms suggests that in a sense **3c** is a well-constructed miniature of "allosteric" enzymes.

Acknowledgment. We are indebted to Dr. M. Ohnishi for the quantum-yield determinations. We thank Professor M. Takagi for helpful discussions. This research was supported by a grant from the Ministry of Education of Japan.

(19) We also found that the absorption and fluorescence spectra are sensitively affected by the solvent effect. For example, a plot of the fluorescence quantum yield (Φ_f) for neutral **3c** vs. $E_T(30)$ showed a linear relationship (r = 0.98) as expressed by $\Phi_f = 1.07E_T(30) - 0.017$.

(20) A standard actinometer (potassium trioxalatoferrate(III)) was used for the quantum-yield determinations on the photochemical reaction of **3** (2.00×10^{-4} M) and benzyl alcohol (5.00×10^{-2} M). The further details of the experimental method were described previously.[21]

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Cluster Framework Rearrangements. An Unusual Transformation of a Butterfly Cluster into a Rhombus. The Crystal and Molecular Structures of $Os_4(CO)_{12}(\mu_3\text{-}S)(\mu\text{-}HC_2R)$, R = Ph and CO_2Me

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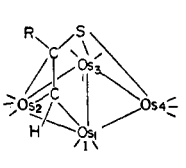
The ability of transition-metal cluster compounds to undergo structural transformations of their metal frameworks has been shown to play an intimate and important role in their chemistry.[1,2] Most frequently these transformations are induced by ligand additions or eliminations, but they can also be induced by ligand transformations. Some recent reports have been described unusual examples of dynamically rapid degenerate rearrangements.[3]

In our recent studies we have observed the formation of the unusual butterfly cluster complexes $Os_4(CO)_{12}[\mu_4\text{-}\eta^3\text{-}SC(R){=}CH]$ (**1a,b** R = Ph, CO_2Me) by the insertion of terminal alkynes into



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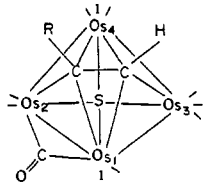

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a metal-sulfur bond in the cluster compound $Os_4(CO)_{12}(\mu_3\text{-}S)$.[4] When refluxed in octane solvent, these compounds are decarbo-

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