conveniently summarized in the diagram depicted in Figure 1. Herein the logarithm of the cmc, crc, and cvc for the different surfactants are plotted versus the sum of the hydrophobic fragmental constants (Σf_i)[18] of the 1-alkyl substituents. Different linear relationships for the three types of aggregates separate concentration ranges for the various aggregate morphologies.

In summary, the present approach demonstrates that the aggregate morphology within a series of 1-methyl-4-(C_{12}-alkyl)-pyridinium iodides of almost equal alkyl chain hydrophobicity is primarily determined by the shape of the surfactant molecule. Shape selectivity also governs the aggregation behavior of 1-alkyl-4-*n*-dodecylpyridinium iodides in which the volume of the core is modified through back bending of a sufficiently long 1-alkyl substituent into the hydrophobic interior of the aggregate. It is our contention that systematic studies of alkyl chain packing will become a major activity in surface chemistry. Further studies along these lines are currently underway in our laboratory.

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(17) No details are as yet known about the exact chain packing in the vesicles formed from **9**. However, interdigitation of the alkyl chains to optimize van der Waals interactions may well be assumed similar to the chain packing in asymmetric phosphatidyl choline bilayer membranes, see: Mattai, J.; Sripada, P. K.; Shipley, G. G. *Biochemistry* **1987**, *26*, 3287. Highly asymmetric di-*n*-alkyl phosphates also form vesicles, see: Wagenaar, A.; Rupert, L. A. M.; Engberts, J. B. F. N.; Hoekstra, D. *J. Org. Chem.*, in press.

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Flavin-Catalyzed Oxidation of Amines and Sulfur Compounds with Hydrogen Peroxide

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Mammalian liver contains liver microsomal FAD-containing monooxygenase (EC 1.14.13.8, FADMO), which oxygenates various amines.[1] The enzymatic oxygenation seems to involve the following catalytic cycle.[2,3a] Oxygenation of enzyme-bound reduced flavin (Enz(FlH_2)) with molecular oxygen gives 4a-hydroperoxyflavin (Enz(4a-FlHOOH)), which undergoes monooxygenation of substrates to give 4a-hydroxyflavin (Enz(4a-FlHOH)). Dehydration of Enz(4a-FlHOH) gives oxidized flavin (Enz(Fl_{ox})) (rate-determining step),[3] which is reduced to Enz-(FlH_2). The mechanism of FADMO has been extensively studied by using 4a-hydroperoxyisoalloxazines (4a-FlOOH), and much understanding has been gained;[4,5] however, the catalytic recycling step is still ambiguous.

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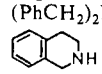
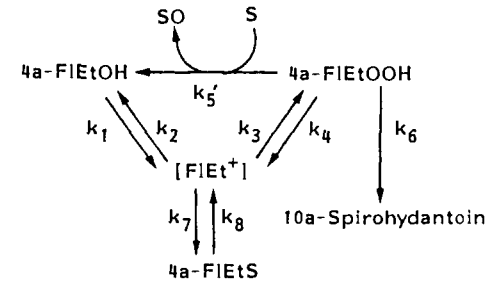
Table I. Flavin-Catalyzed Oxidation of Amines and Sulfur Compounds[a]

substrate	product[b]	isolated yield, %	turnover number
Bu_2NH	$BuN^+(O^-)$=CHPr	61	12
$(PhCH_2)_2NH$	$PhCH_2N^+(O^-)$=CHPh	40	8
		70	14
$(PhCH_2)_2NOH$	$PhCH_2N^+(O^-)$=CHPh	83[c,e]	8
Bu_2S	$Bu_2S\rightarrow O$	99[c,f]	99
Ph_2S	$Ph_2S\rightarrow O$	96[c]	10
$(PhCH_2)_2S$	$(PhCH_2)_2S\rightarrow O$	97[c,d,e]	19
$(PhCH_2)_2S\rightarrow O$	$(PhCH_2)SO_2$	98[c,d]	10
$(PhCH_2)_2S$	$(PhCH_2)SO_2$	96[d]	19

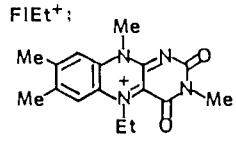
[a] A mixture of substrate (1 mmol), $FlEt^+ClO_4^-$ (0.1 mmol), and H_2O_2 (2 mmol) in methanol was allowed to react at room temperature under argon. [b] Satisfactory IR, NMR, mass spectral data, and analyses have been obtained. [c] H_2O_2 (1 mmol). [d] CH_2Cl_2. [e] $FlEt^+ClO_4^-$ (5 mol %). [f] $FlEt^+ClO_4^-$ (1 mol %).

Scheme I



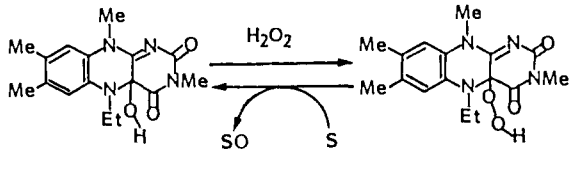
S: Substrate
SO: Oxidized Substrate

$FlEt^+$:



We have found that 4a-hydroxy-5-alkylflavins are readily transformed into 4a-hydroperoxyflavins upon treatment with hydrogen peroxide. This result leads to the finding of the novel catalytic oxidation which may correspond to FADMO.

The treatment of 4a-FlEtOH with 30% aqueous hydrogen peroxide (10 equiv) in methanol at room temperature under argon gave 4a-FlEtOOH in 82% isolated yield.[6] Considering this facile formation of 4a-FlEtOOH, 4a-FlEtOH-catalyzed oxidation of substrates with hydrogen peroxide should occur. Indeed, typically, the reaction of dibutylamine (**1**) with aqueous H_2O_2 in methanol



4a-FlEtOH 4a-FlEtOOH

in the presence of 10 mol % of 4a-FlEtOH gave *N*-butylidenebutylamine *N*-oxide (**2**) in 48% isolated yield (turnover number 10). The catalyst is not limited to 4a-FlEtOH, and flavins such as 4a-FlEtOOH,[7] $FlEt^+ClO_4^-$,[8] 5-ethyl-1,5-dihydro-3-methyllumiflavin (FlEtH),[8] FMNHEt,[9] and FMNHMe[9] can be used as an active catalyst, although the flavins which have no substituent at the 5(N)-position such as 3-methyllumiflavin,[10] riboflavin, and

(6) 4a-FlEtOOH was identified by comparison with the spectral data of the authentic sample.[7]

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FMN are ineffective. It is noteworthy that FADMO undergoes the oxidation, although Enz(4a-FlHOOH) has no substituent at the 5(N)-position. Charge-transfer complexation between Enz-(4a-FlHOOH) and NAD(P)$^+$ retards the elimination of hydrogen peroxide to lead to the oxidation.[2,3a]

We used FlEt$^+$ClO$_4^-$ as a catalyst because of its efficiency and stability. The representative results of the FlEt$^+$ClO$_4^-$-catalyzed oxidation of amines and sulfur compounds are summarized in Table I. Nitrones[11] and sulfoxides, which are versatile synthetic intermediates, can be prepared in a highly efficient manner. Sulfoxides are also oxidized, although the rate of the oxidation is much slower than that of sulfides.

The present catalytic reaction can be rationalized by assuming Scheme I. 4a-FlEtOOH reacts with substrate (S) to give oxidized substrate (SO) and 4a-FlEtOH (the second-order rate constant: k_5').[4a,5,7] 4a-FlEtOH undergoes ionization (k_1, k_2) to give FlEt$^+$ which reacts with hydrogen peroxide to afford 4a-FlEtOOH (k_3, k_4), where k_1, k_2, k_3, and k_4 are pseudo-first-order rate constants.

In order to gain insight into the mechanism, the FlEt$^+$-ClO$_4^-$-catalyzed monooxygenation of methyl phenylsulfide (**3**) with hydrogen peroxide has been investigated in detail by using a solution of H_2O_2 (15 mM), FlEt$^+$ClO$_4^-$ (0.25 mM), and **3** (0.1-2.0 M) in methanol at 30 °C. The observed initial rate (v, $k_5' \times$ [S] $\times$ [4a-FlEtOOH]) of the formation of methyl phenylsulfoxide (**4**) has been determined by GLC analysis of **4**. The maximum rate of the reaction (V_{max}) and the substrate concentration that produced half-maximal rate (K_m) were obtained to be 83 ± 6 mM/h and 4.0 ± 0.3 M, respectively, from Woolf double reciprocal plot. Under the same conditions, 4a-FlEtOOH reacts with **3** to give **4** and 4a-FlEtOH. The second-order rate constant k_5' in MeOH (30 °C) was determined to be 0.18 M^{-1} s^{-1} by monitoring the disappearance of 4a-FlEtOOH at 370 nm. The first-order rate constant of the decomposition of 4a-FlEtOOH (k_6) in MeOH (30 °C) to give 10a-spirohydantoin **5**[12] has been determined to be 1.6×10^{-5} s^{-1} by monitoring the disappearance of the UV absorption of 4a-FlEtOOH at 370 nm. Since k_6 is negligible, V_{max}, K_m, and the concentration of FlEt$^+$ cation ([FlEt$^+$]) can be represented by the following equations: $V_{max} = 0.25\ \text{mM} \times k_1k_3/(k_1 + k_2 + k_3) = 83 \pm 6$ mM/h, $K_m = (k_1k_3 + k_1k_4 + k_2k_4)/(k_1 + k_2 + k_3)/k_5' = 4.0 \pm 0.3$ M, [FlEt$^+$] = $0.25\ \text{mM} \times (k_1k_4 + k_1k_5'[\text{MeSPh}])/(k_1k_3 + (k_1 + k_2)k_4 + (k_1 + k_2 + k_3)k_5'[\text{MeSPh}])$. Concentration of FlEt$^+$ was determined by the UV spectra of the reaction mixture (545 nm).[13] The pseudo-first-order rate constant for the reaction of FlEt$^+$ClO$_4^-$ with aqueous 30% H_2O_2 in MeOH (15 mM solution) to give 4a-FlEtOOH was determined by stopped-flow spectrophotometer to be 5.7 s^{-1}. These results lead to solve the above equations, giving $k_1 = 0.11$ s^{-1}, $k_2 = 0.46$ s^{-1}, $k_3 = 2.5$ s^{-1}, and $k_4 = 3.2$ s^{-1}. Therefore, the rate-determining step is the formation of FlEt$^+$ from 4a-FlEtOH.

The kinetics of the catalytic oxidation of amines is complex, because an equilibrium between FlEt$^+$ and the adduct of substrates, 4a-FlEtS (Scheme I, k_7, k_8), has to be considered. It is known that secondary amines add to FlEt$^+$ to give the 4a-amino adducts.[4a] The pseudo-first-order rate constant of the formation of 4a-FlEt-NBu$_2$ from FlEt$^+$ and **1** has been determined to be $>10^3$ s^{-1}. The reaction of 4a-FlEtOH with **1** in MeOH gave 4a-FlEt-NBu$_2$ quantitatively. The pseudo-first-order rate constants of the formation of 4a-FlEt-NBu$_2$ (355 nm, ϵ 7100) from 4a-FlEtOH and **1** in MeOH were determined to be constant (1.5×10^{-4} s^{-1}) upon changing the concentration of **1** (0.007-0.10 M) by monitoring the UV absorption of 4a-FlEtOH (355 nm, ϵ 8600). Apparently, 4a-FlEtOH undergoes ionization to give FlEt$^+$, which reacts with **1** to afford 4a-FlEt-NBu$_2$. Under the same conditions, FlEt$^+$ also reacts with H_2O_2 to give 4a-FlEtOOH because of higher nucleophilicity of OOH$^-$ in comparison with secondary amines.[14] The v value of the oxidation of **1** (0.2 M, 0.20 mM/h) is smaller than that of **3** (0.2 M, 3.9 mM/h); however, the k_5' value of the oxidation of **1** (0.36 M^{-1} s^{-1}) is larger than that of **3** (0.18 M^{-1} s^{-1}). The k_1 value of **1** (ca. 10^{-4} s^{-1}) is smaller than that of **3** (0.11 s^{-1}), and the k_3 value of **1** is larger than that of **3**.[15] The v value of the oxidation of **3** (0.3M) in the presence of **1** (0.04 M) by using 4a-FlEtOH as the catalyst (0.015 M) was determined to be 1.4 mM/h, which is smaller than the v value (2.5 mM/h) obtained under the same conditions by using 4a-FlEt-NBu$_2$ as the catalyst, indicating that the k_1 value is smaller than the k_8 value. Therefore, the rate-determining step of the oxidation of secondary amines seems to be the formation of FlEt$^+$ ion (k_1).

The present catalytic oxidation is highly useful, because potential flavin hydroperoxide, which has ca. 10^4 times oxidizing potential in comparison with hydrogen peroxide,[4a] can be generated catalytically.[16]

Acknowledgment. We thank Dr. M. Sawada (The Institute of Scientific and Industrial Research, Osaka University) for use of a stopped-flow spectrophotometer and for helpful discussions.

Supplementary Material Available: A listing of observed initial rates of formation of **4** (Table S1) (1 page). Ordering information is given on any current masthead page.

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(13) [FlEt$^+$]:[4a-FlEtOH]:[4a-FlEtOOH] was determined to be 15:73:12 ([MeSPh] = 0.2 M).

(14) N_+ value of OOH$^-$ (8) is larger than those of R_2NH (5-6) and OH$^-$ (4.8), see: Ritchie, C. D. in *Solute-Solvent Interactions*; Coetzee, J. F., Ritchie, C. D., Eds.; Marcel Dekker: New York, 1976; Vol. 2, pp 229-270.

(15) k_3 value of **1** (under basic conditions) is larger than that of **3** (under acid conditions) because of higher concentration of OOH$^-$ in the presence of amine substrate.

(16) Application of our process, see: Shinkai, S.; Yamaguchi, T.; Manabe, O.; Toda, F. *J. Chem. Soc., Chem. Commun.* **1988**, 1399-1401.

Formation of a Cyclopropyl Eicosanoid via an Allene Oxide in the Coral *Plexaura homomalla*: Implications for the Biosynthesis of 5,6-*trans*-Prostaglandin A_2

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The Caribbean soft coral *Plexaura homomalla* produces large quantities of prostaglandin (PG) A_2 (**1**) as the methyl ester acetate (ca. 2-3% of its dry weight) by a pathway which is distinct from the mammalian cyclooxygenase/endoperoxide route.[1] This alternative pathway may involve an 8-lipoxygenase and formation of an allene oxide intermediate, although there is as yet no firm evidence linking either to biosynthesis of the prostaglandins.[2] Allene oxide **2** was recently isolated from incubation of 8(*R*)-hydroperoxyeicosatetraenoic acid (**3**) with an acetone powder preparation of *P. homomalla*.[3] It is the facility with which allene oxides can form cyclopentenones[4] which makes this pathway seem attractive for the biosynthesis of PGA_2.

[†] Department of Chemistry.

[‡] Department of Pharmacology.

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