CATALYTIC EFFECT OF ALLOXAZINIUM AND ISOALLOXAZINIUM SALTS ON OXIDATION OF SULFIDES WITH HYDROGEN PEROXIDE IN MICELLAR MEDIA

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Received March 9, 2009
Accepted April 21, 2009
Published online June 23, 2009

Dedicated to Dr. Alfred Bader on the occasion of his 85th birthday in recognition of his outstanding contributions to the science of chemistry.

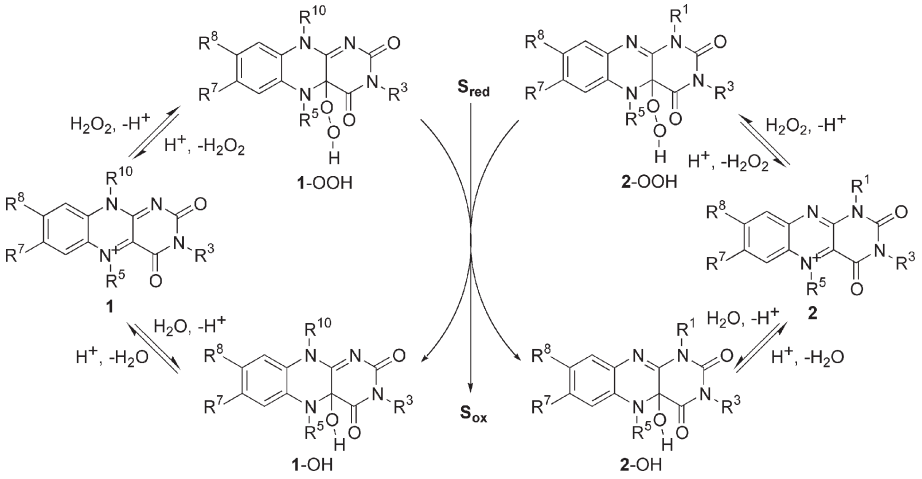
Three novel amphiphilic alloxazinium salts were prepared: 3-dodecyl-5-ethyl-7,8,10-trimethylisoalloxazinium perchlorate (**1c**), 1-dodecyl-5-ethyl-3-methylalloxazinium perchlorate (**2b**), and 3-dodecyl-5-ethyl-1-methylalloxazinium perchlorate (**2c**). Their catalytic activity in thioanisole (**3**) oxidation with hydrogen peroxide was investigated in micelles of sodium dodecylsulfate (SDS), hexadecyltrimethylammonium nitrate ($CTANO_3$) and Brij 35. Reaction rates were strongly dependent on the catalyst structure, on the type of micelles, and on pH value. Alloxazinium salts **2** were more effective catalysts than isoalloxazinium salts **1**. Due to the contribution of micellar catalysis, the v_{cat}/v_0 ratio of the catalyzed and non-catalyzed reaction rates was almost 80 with salt **2b** solubilized in $CTANO_3$ micelles. Nevertheless, the highest acceleration was observed with non-amphiphilic 5-ethyl-1,3-dimethylalloxazinium perchlorate (**2a**) in $CTANO_3$ micelles (v_{cat}/v_0 = 134). In this case, salt **2a** presumably acts as a phase-transfer catalyst bringing hydrogen peroxide from the aqueous phase into the micelle interior. Synthetic applicability of the investigated catalytic systems was verified on semi-preparative scale.

Keywords: Sulfoxidation; Micelles; Micellar catalysis; Organocatalysis; Green chemistry; Flavins; Flavinium salts; Alloxazines; Isoalloxazines; *N*-Alkylalloxans; Oxidations; Surfactants; Phase transfer catalysis.

doi:10.1135/cccc2009030

Flavinium salts have been reported in many cases as efficient catalysts for oxidation of various substrates, using hydrogen peroxide as a terminal oxidant[1–8]. Flavinium salts are usually considered as flavoenzyme mimics which can transform, e.g. sulfides to sulfoxides, tertiary amines to *N*-oxides, and ketones to esters (Baeyer–Villiger oxidation). In the cited works, the term "flavinium salts" has been used for both isoalloxazinium salts **1** substituted in position 10 (similarly as natural riboflavin) and isomeric alloxazinium salts **2**. Flavinium salts as oxidation catalysts have several advantages: (i) they work under mild conditions – the reactions usually proceed smoothly at room temperature in methanol[1–7] or in micellar systems[8] in the presence of less than 2 mole % of the catalyst (relative to the substrate) with turnover number (TON) up to 200 (ref.[5a]); (ii) they exhibit high chemoselectivity in the oxidation of sulfides producing exclusively sulfoxides without overoxidation to sulfones; (iii) the oxidations can be performed even in aqueous solutions[8]; this fact ranks flavinium salts among the environment-friendly organocatalysts. In several instances, chiral flavinium salts affording sulfoxides[6] or esters[7] with moderate enantioselectivity have also been described.

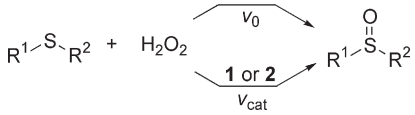
Mechanism of the oxidations with hydrogen peroxide catalyzed by flavinium salts is depicted in Scheme 1. Addition of hydrogen peroxide to flavinium salts **1** or **2** affords flavin-4a-hydroperoxides (**1**-OOH or **2**-OOH,



SCHEME 1
Catalytic action of isoalloxazinium **1** and alloxazinium **2** salts in oxidations of substrates **S** with hydrogen peroxide

respectively) which are the agents oxidizing the substrate[1,9]. 5-Ethylisoalloxazine-4a-hydroperoxide (**1**-OOH) is an analogue of natural riboflavin-4a-hydroperoxide[9] ($R^3 = R^5 = H$, $R^7 = R^8 = CH_3$, R^{10} = ribityl) acting as a versatile oxidizing cofactor in flavin monooxygenases[10]. Isomeric alloxazine-4a-hydroperoxide (**2**-OOH) has no naturally occurring equivalent.

Among the above-mentioned oxidations, sulfoxidation usually serves as a model reaction for testing the flavoenzyme mimics efficiency[1]. It is necessary to emphasize that in sulfoxidations performed in the presence of flavinium salts, a non-catalyzed oxidation proceeds to some extent as well[1,2,5,6] (Scheme 2). The non-catalyzed reaction represents a considerable problem, especially in oxidations catalyzed by chiral flavinium salts. Most likely, it is responsible for the reported[6] moderate stereoselectivity in oxidations of sulfides to sulfoxides. The contribution of the non-catalyzed oxidation to the overall process varies depending on the structure of flavinium salt and on reaction conditions[5], however, no rationale has been given yet. Therefore, the finding which factors may favour catalyzed sulfoxidation over the non-catalyzed reaction seems to be a necessary prerequisite for the development of stereoselective organocatalysts based on flavinium salts.



SCHEME 2
Overall scheme of sulfoxidation with hydrogen peroxide in the presence of flavinium salts; v_{cat} and v_0 are rates of the catalyzed and non-catalyzed reaction, respectively

Especially in the sulfoxidations performed in the presence of isoalloxazinium salts **1** in homogeneous solutions, the contribution of the non-catalyzed reaction is relatively high[5a,8]. Nevertheless, the non-catalyzed reaction can be successfully suppressed. Recently, we have reported[8] on the positive effect of micelles on the v_{cat}/v_0 ratio of the catalyzed and non-catalyzed reaction rates in the case of thioanisole (**3**) oxidation catalyzed by amphiphilic isoalloxazinium salt 10-dodecyl-5-ethyl-3,7,8-trimethylisoalloxazinium perchlorate (**1b**) (Table I). The increased v_{cat}/v_0 ratio in micelles compared to homogeneous solutions results from the effect of micellar catalysis and from the suppression of the non-catalyzed process due to the separation of the lipophilic substrate from the aqueous phase containing hydrogen peroxide. This effect strongly depends on pH and on the nano-

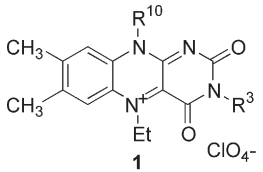
TABLE I
Relative rates v_{cat}/v_0 of thioanisole (**3**) oxidation with hydrogen peroxide catalyzed by flavinium salts **1** (ref.[8])

Reaction medium	Catalyst	v_{cat}/v_0	pH[a]
Methanol–water (50:50 v/v)	**1a**	6.6	2.4
Anionic micelles (SDS[b])	**1b**	24.7	4.4
Cationic micelles ($CTANO_3$[c])	**1b**	38.9	2.4
Non-ionic micelles (Brij 35[d])	**1b**	16.6	3.4

[a] Optimum pH value. [b] Sodium dodecylsulfate. [c] Hexadecyltrimethylammonium nitrate. [d] Poly(ethylene glycol) dodecyl ether; $n \sim 23$.

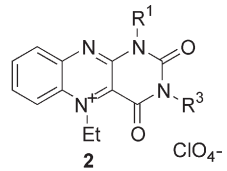
aggregate type: it is especially pronounced in cationic micelles ($CTANO_3$) where the v_{cat}/v_0 ratio is almost 40.

Bäckvall[5a] reported that in contrast to isoalloxazinium salt **1a**, alloxazinium salt **2a** strongly favours catalyzed oxidation of various sulfides over the non-catalyzed reaction in homogeneous solutions. The observed v_{cat}/v_0 values were comparable with those obtained in reactions catalyzed by the most efficient amphiphilic isoalloxazinium salt **1b** in cationic micelles. This fact inspired us to investigate sulfoxidation catalyzed by amphiphilic alloxazinium salts **2** in micelles to combine both the effect of the catalyst structure and the contribution of micellar catalysis. It is known[11] that the reactivity of amphiphilic compounds in micelles depends markedly on the relative position of the polar head group, hydrophobic alkyl chain, and the reactive function. Therefore, we decided to prepare two isomeric amphiphilic alloxazinium salts **2b** and **2c**. To extend the structure–activity study of amphiphilic flavinium salts, a new isoalloxazinium salt **1c** was involved in this study as well.



1

	R^3	R^{10}
a	CH_3	CH_3
b	CH_3	$C_{12}H_{25}$
c	$C_{12}H_{25}$	CH_3



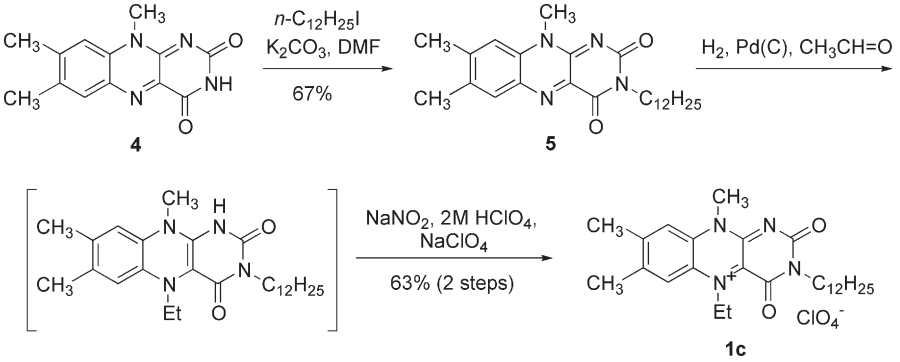
2

	R^1	R^3
a	CH_3	CH_3
b	$C_{12}H_{25}$	CH_3
c	CH_3	$C_{12}H_{25}$

RESULTS AND DISCUSSIONS

Preparation of Flavinium Catalysts

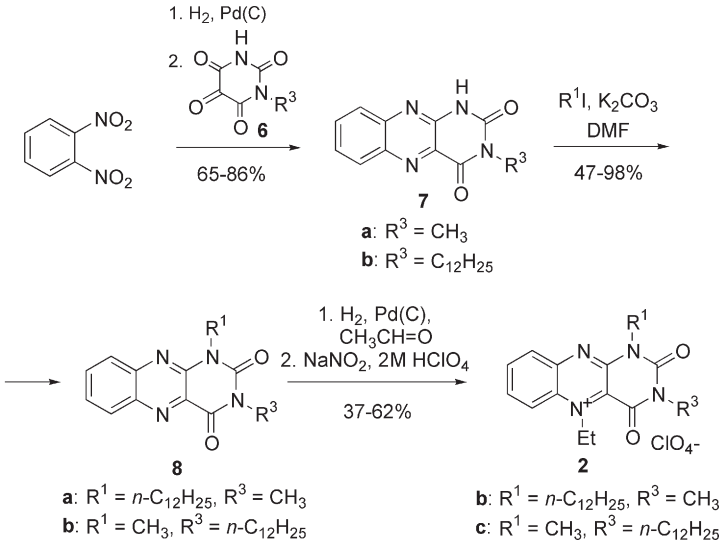
Preparation of isoalloxazinium catalysts **1a** and **1b** was described in our previous paper[8]. Amphiphilic 3-dodecylisoalloxazinium salt **1c** was prepared starting from lumiflavin **4** (synthesis of **4** was published elsewhere[12]), which was alkylated with dodecyl iodide in the presence of potassium carbonate. 3-Dodecyl-7,8,10-trimethylisoalloxazine (**5**) thus obtained was converted to the final salt **1c** by the reaction with acetaldehyde under reductive conditions followed by oxidation of the resulting 5-ethyl-1,5-dihydro derivative with sodium nitrite in perchloric acid (Scheme 3).



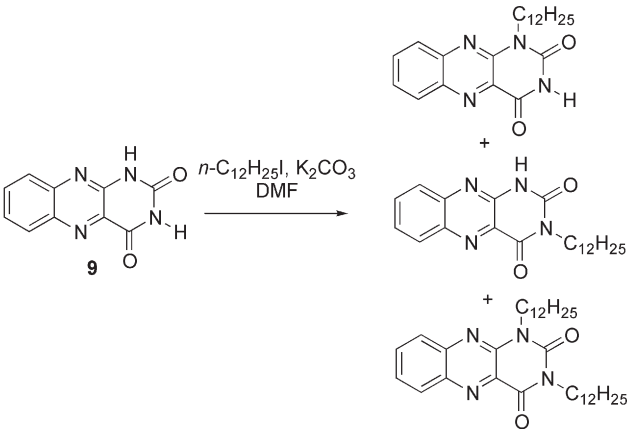
SCHEME 3
Preparation of isoalloxazinium salt **1c**

Alloxazine **2a** was prepared according to the procedure described by Murahashi[5e]. Synthesis of lipophilic alloxazinium salts **2b** and **2c** is depicted in Scheme 4. Benzene-1,2-diamine prepared by hydrogenation of 1,2-dinitrobenzene was condensed with *N*-alkylalloxans **6**. The condensation proceeds with excellent regioselectivity yielding 3-alkylalloxazines **7** as the sole products. Their alkylation with appropriate alkyl iodides afforded 1,3-dialkylated alloxazines **8** which were converted to 5-ethylalloxazinium salts **2b** and **2c** using the above-described method (i.e. reaction with acetaldehyde under reductive conditions followed by oxidation). *N*-Methyl- (**6a**) and *N*-dodecylalloxan (**6b**) were obtained by the oxidation of corresponding *N*-alkylbarbituric acids with chromium(VI) oxide using a modified procedure described for the preparation of unsubstituted alloxan[13]. The described synthesis of alloxazines **8** gave better results than a procedure

involving consecutive alkylation of unsubstituted alloxazine **9** which leads to a mixture of alkylated alloxazines (Scheme 5).



SCHEME 4
Preparation of amphiphilic alloxazinium salts **2b** and **2c**



SCHEME 5
Alkylation of alloxazine **9**

Sulfoxidations Catalyzed by Amphiphilic Flavinium Salts

Catalytic activity of the newly prepared amphiphilic flavinium salts **1c**, **2b** and **2c** in oxidation of sulfides with hydrogen peroxide was investigated under the conditions used in our previous study[8] performed with salt **1b**. Thioanisole (**3**) was oxidized with 1.5 equivalents of hydrogen peroxide in anionic (SDS), cationic ($CTANO_3$) and non-ionic (Brij 35) micelles in the presence of 1.5 mole % of flavinium salt (relative to the substrate) at 25 °C (for details, see Experimental). Oxidations in homogeneous solutions (water/methanol 50:50, v/v) catalyzed by hydrophilic flavinium salts **1a** and **2a** were performed as a reference.

In all cases, the efficiency of the catalysts was evaluated as the v_{cat}/v_0 ratio of the catalyzed and non-catalyzed reaction rates. The rate v_{cat} of the catalyzed reaction was calculated from the observed reaction rate v_{obs} and the rate v_0 of the non-catalyzed reaction (from Scheme 2, $v_{cat} = v_{obs} - v_0$). To determine the contribution of blank (v_0), we measured the rate of thioanisole (**3**) oxidation with hydrogen peroxide in the absence of flavinium salt in the corresponding reaction media in independent experiments. The initial rates of the respective reactions (up to 20% conversion of the substrate) were used as the reaction rates v_{obs} and v_0. The obtained data allow a comparison of the reaction rate of the catalyzed reaction (following at low conversions the first-order kinetics) and the non-catalyzed reaction (following the second order kinetics). Despite the fact that this approach is not strictly correct it has been widely used to evaluate the catalytic activity of flavinium salts in many previous studies[4,5a,5b,8]. The obtained kinetic data (v_{cat}/v_0) at various pH values in micellar media as well as in homogeneous solutions are summarized in Fig. 1.

The results obtained with amphiphilic alloxazinium salts **2b** and **2c** correspond qualitatively with those obtained with isoalloxazinium derivative **1b** (ref.[8]). The observed similarity ensues from the fact that the mechanism of sulfoxidation catalyzed by both types of flavinium salts is the same (Scheme 1). The highest acceleration of the oxidation catalyzed by salts **1** and **2** was observed in cationic micelles. The efficiency of both types of flavinium salts is pH-dependent. All the relative rate v_{cat}/v_0 versus pH profiles exhibit a distinct maximum with the only exception of the reactions in SDS catalyzed by alloxazinium derivatives **2** (ref.[14]). The explanation of the "bell-shaped" profile observed in all cases lies in an opposite effect of proton on two steps of the oxidation catalytic cycle (Scheme 1). While the decomposition of 4a-hydroxyflavins **1**-OH or **2**-OH to flavinium salts **1** or **2** requires protonation of the hydroxy group in pseudobases **1**-OH or **2**-OH,

and, consequently, it is facilitated at lower pH values, the formation of flavin-4a-hydroperoxides **1**-OOH or **2**-OOH from salts **1** or **2** proceeds with a loss of proton thus being disfavoured under the same conditions[15]. The optimum pH value depends also on the aggregate type. In anionic micelles, the maximum relative rates v_{cat}/v_0 occur at higher pH values while in cationic micelles they are shifted to lower pH values.

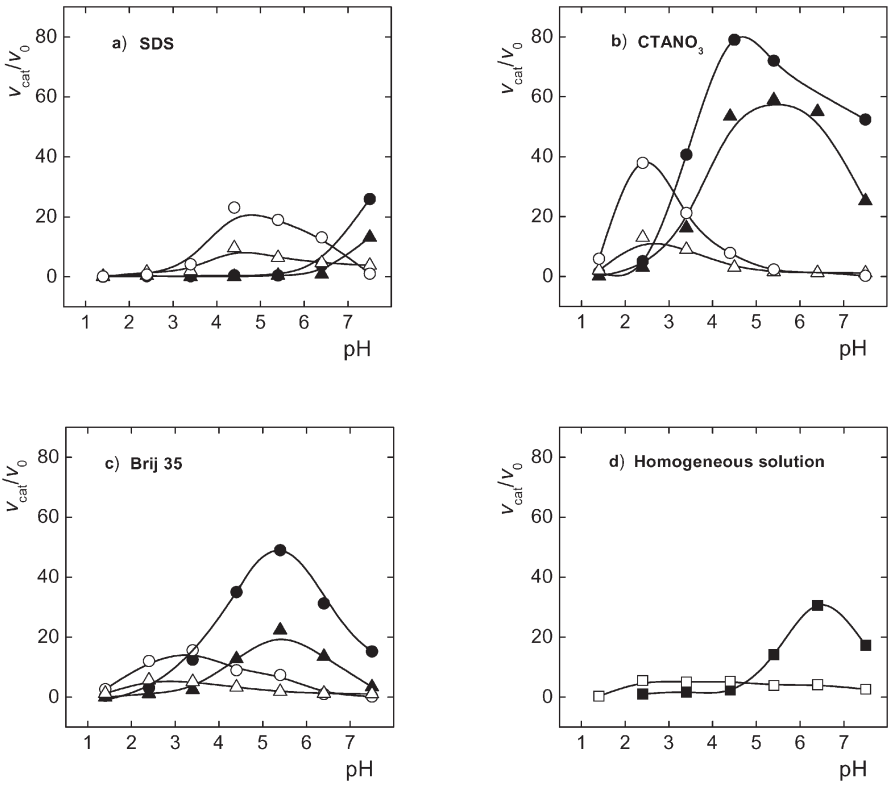
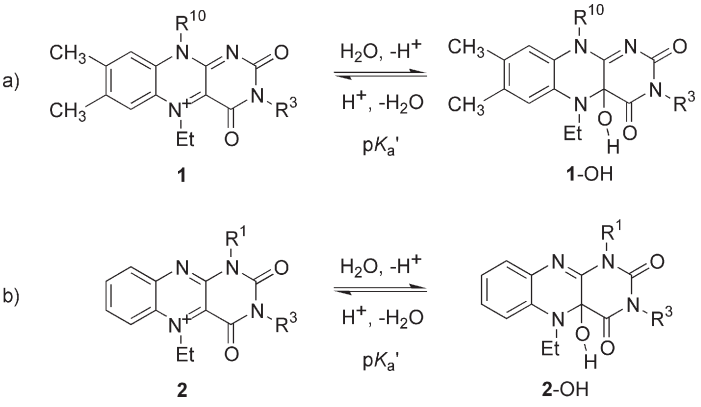


FIG. 1

pH dependence of the v_{cat}/v_0 ratio of initial rates of catalyzed and non-catalyzed oxidation of **3** with hydrogen peroxide in micelles of SDS (a), $CTANO_3$ (b), Brij 35 (c) and in homogeneous solutions (methanol/water 50:50, v/v) (d). Isoalloxazinium salts **1a** (□), **1b** (○), **1c** (△) and alloxazinium salts **2a** (■), **2b** (●), **2c** (▲) were used as catalysts. Conditions: c(**3**) = 1.5×10^{-2} mol l^{-1}, $c(H_2O_2) = 2.25 \times 10^{-2}$ mol l^{-1}, c(**1** or **2**) = 2.3×10^{-4} mol l^{-1}, c(buffer) = 1.0×10^{-1} mol l^{-1}, c(surfactant) = 1.0×10^{-1} mol l^{-1}; t = 25 °C. The lines help the eyes to follow the data points

Nevertheless, there are important quantitative differences in the activity of isoalloxazinium **1** and alloxazinium **2** derivatives. As expected, alloxazinium salts **2** are more efficient catalysts than isoalloxazinium salts **1** regardless of the type of the reaction system[14]. While the relative rate v_{cat}/v_0 of the thioanisole (**3**) oxidation in the presence of 1.5 mole % isoalloxazinium salt **1b** was approximately 40 under optimum conditions[8], the same reaction catalyzed by the same molar amount of alloxazinium salt **2b** was accelerated by the factor of 80 in comparison with the non-catalyzed oxidation.

In comparison with isoalloxazinium salts **1**, the optimum pH values for alloxazinium catalysts **2** are greater by ca. 3 units. We suppose that this shift is a consequence of the aromaticity of pyrazinium grouping in alloxazinium salts **2**. In contrast to oxidations catalyzed by flavinium salts **1**, in analogous catalytic cycle involving flavinium salts **2** the transformation of pseudobases **2**-OH to flavinium salts **2** (Scheme 1) should be accompanied by the gain of delocalization energy which might be a driving force for this step[5a]. This assumption is supported by the obtained apparent pK_a' values describing the equilibrium between flavinium salt and the corresponding pseudobase (Scheme 6). Apparent pK_a' constants are derived as follows: formally, the formation of 4a-hydroxyflavin (pseudobase) represents the addition of water to flavinium salt with the simultaneous release of proton. Higher apparent pK_a' values of alloxazinium salts **2** in comparison with those obtained for isoalloxazinium salts **1** (by 3–6 units, depending on the medium – Table II) thus indicate easier elimination of water from pseudobase **2**-OH.



SCHEME 6
The equilibrium between flavinium salt and pseudobase for isoalloxazinium salts (**1**) (a) and alloxazinium salts (b)

TABLE II
Apparent pK_a' values of flavinium salt–pseudobase equilibrium for selected derivatives

Flavinium salt	p$K_{a'}$			
	H_2O	SDS	$CTANO_3$	Brij 35
1a	2.8	1.8	0.6	2.8
1b	–	3.9	0.1	1.4
2a	7.9	8.9	5.6	6.4
2b	–	9.6	3.5	5.2

Comparing the catalytic efficacy of regioisomers in both isoalloxazine and alloxazine series (**1b** vs **1c** and **2b** vs **2c**), we observed that the isomers **1b** and **2b** with lipophilic alkyl chain attached to the "upper" site of the flavinium skeleton (i.e. in the positions 1 or 10) were more efficient than their isomers with lipophilic alkyl chain in the position 3. We assume that the relative position of the polar head group and the hydrophobic alkyl chain in amphiphilic salts **1b** and **2b** favours their orientation at micellar surface with the position 4a directed at aqueous phase; this orientation facilitates the attack by hydrogen peroxide.

*Sulfoxidations Catalyzed by Non-lipophilic Flavinium Salts **1a** and **2a** in Micellar Media*

In the next part of this study we have tested the catalytic activity of the non-amphiphilic salts **1a** and **2a** in the oxidation of thioanisole (**3**) in micellar media to establish the role of lipophilic alkyl chain in **1b**, **1c** and **2b**, **2c**. As we had expected, the introduction of lipophilic alkyl chain into position 10 of the isoalloxazinium skeleton (salt **1b**) increased its catalytic activity in comparison with salt **1a** (Figs 1a–1c and 2a); however, this increase was only moderate. Surprisingly, the introduction of lipophilic alkyl chain into position 3 of the isoalloxazinium skeleton (salt **1c**) even decreased the catalytic activity as compared with non-amphiphilic homologue **1a**. This unexpected effect of the hydrophobic alkyl chain on catalytic activity of flavins in micellar systems is especially pronounced in the case of alloxazinium salts **2**. Despite the fact that the catalytic activity of amphiphilic salt **2b** in $CTANO_3$ (Fig. 1b) was really high, even higher

than the activity of the most efficient flavin reported so far[4–8], it was overcome by that of the non-amphiphilic homologue **2a**. We observed relative rate v_{cat}/v_0 = 134 at optimum[14] pH (Fig. 2b).

These interesting results lead us to consider the functioning of flavinium salts on the micellar phase – bulk aqueous phase interface. Lipophilic salts are tightly bound in micelles by hydrophobic interactions. Consequently, reactions of flavinium subunit with agents coming from the aqueous phase (proton, hydrogen peroxide) proceed at the interface only. On the other hand, non-amphiphilic salts can be easily extracted into the aqueous phase and may act similarly as phase-transfer catalysts[16]. For sulfoxidations in micelles catalyzed by non-amphiphilic flavinium salts, we propose the following mechanism (Fig. 3): first, relatively hydrophilic flavinium salt **Fl**$^+$ is extracted into the aqueous phase and reacts with hydrogen peroxide forming flavin-4a-hydroperoxide **Fl**-OOH. This neutral species is less hydrophilic and, therefore, it can be easily extracted back into the micellar pseudophase where it reacts with the lipophilic substrate. Pseudobase **Fl**-OH resulting from the oxidation eliminates water with the formation of flavinium salt **Fl**$^+$.

The above-mentioned hypothesis is supported by the values of binding constants[17] K_S determined for flavininium salts **2** and their corresponding pseudobases **2**-OH to micelles of $CTANO_3$ (Table III). The binding constant K_S of salt **2a** is approximately 10 times lower than that of pseudobase

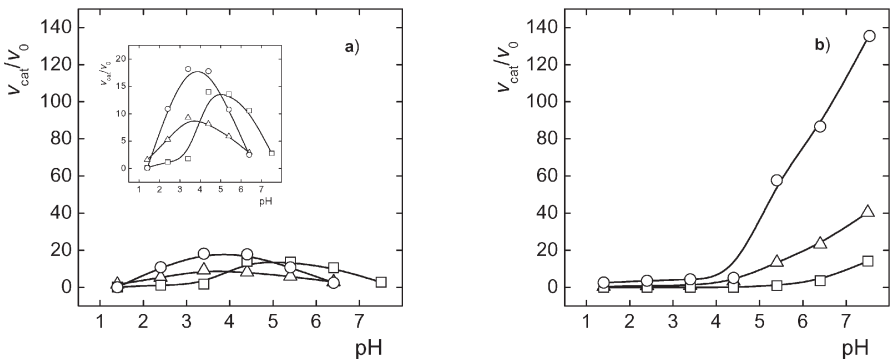


FIG. 2

pH dependence of the v_{cat}/v_0 ratio of initial rates of catalyzed and non-catalyzed oxidation of **3** with hydrogen peroxide in micelles of SDS (□), $CTANO_3$ (○) and Brij 35 (△). Flavinium salts **1a** (a) and **2a** (b) were used as catalysts. Conditions: c(**3**) = 1.5 × 10^{-2} mol l^{-1}, $c(H_2O_2)$ = 2.25 × 10^{-2} mol l^{-1}, c(**1a** or **2a**) = 2.3 × 10^{-4} mol l^{-1}, c(buffer) = 1.0 × 10^{-1} mol l^{-1}, c(surfactant) = 1.0 × 10^{-1} mol l^{-1}; t = 25 °C. The lines help the eyes to follow the data points

2a-OH. It is reasonable to assume that the binding constant value of the hydroperoxide **2a**-OOH should be similar to that of pseudobase **2a**-OH. The binding constants values of lipophilic salt **2b** and its pseudobase **2b**-OH indicate that both these species are relatively tigthly bound to micelle.

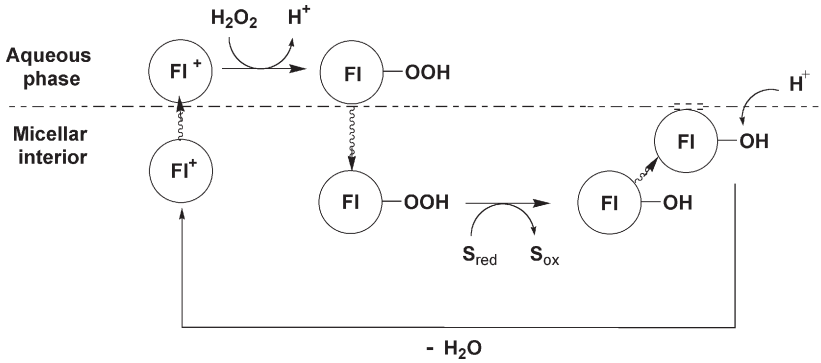


FIG. 3
Proposed mechanism of sulfoxidation catalyzed by non-amphiphilic flavins in micellar systems

TABLE III
Binding constant K_S of alloxazinium salts **2** and pseudobase **2**-OH to micelles of $CTANO_3$

Compound	K_S, mol^{-1} l
2a	13
2a-OH	156
2b	196
2b-OH	750

Semipreparative Sulfoxidations Catalyzed by Flavinium Salts

To demonstrate the applicability of our catalytic systems based on micellar solutions of flavinium salts, we performed sulfoxidation of thioanisole (**3**) on semipreparative scale (100 mg of the substrate) using the most efficient catalysts both from isoalloxazine and alloxazine series (salts **1b** and **2a**, respectively). Oxidations were carried out in cationic and in anionic micelles at optimal pH and at 25 °C using small excess of hydrogen peroxide. Reaction time was generally 30 min; if the catalyzed reaction was not complete, the time was extended until complete conversion was achieved (TLC). Optimized isolation procedure (see Experimental) afforded pure product free of surfactant.

The results summarized in Table IV clearly show that all catalytic systems employing salt **2a** gave full conversion within about 30 min (Table IV, entries 3, 4 and 8). Moreover, the reaction catalyzed with **2a** can be successfully performed even with substantially decreased amount of the catalyst (Table IV, entries 4 and 5). In this case, turnover number (TON) reached an imposing value of 840. Similarly as in kinetic experiments, isoalloxazinium salt **1b** was less efficient than alloxazinium catalyst **2a**. To achieve complete conversion, sulfoxidations catalyzed with **1b** require longer time both in SDS and in $CTANO_3$ micelles (Table IV, entries 2 and 7). Blanks (entries 1 and 6) afforded only minor amounts of sulfoxide after 30 min.

TABLE IV
Preparative sulfoxidation of **3** with hydrogen peroxide catalyzed with flavinium salts[a]

Entry	Medium	pH	Catalyst	Catalyst loading mole%	Reaction time[b] min	Yield[c] %
1	SDS	4.4	none	–	30	9
2	SDS	4.4	**1b**	1.5	90	97
3	SDS	7.5	**2a**	1.5	30	97
4	SDS	7.5	**2a**	0.3	30	96
5	SDS	7.5	**2a**	0.1	40	96[d]
6	$CTANO_3$	2.4	none	–	30	4
7	$CTANO_3$	2.4	**1b**	1.5	120	94
8	$CTANO_3$	7.5	**2a**	1.5	30	97

[a] 100 mg of **3** was oxidized with 1.5 equivalents of hydrogen peroxide in the presence of the catalyst (0.1–1.5 mole %) in 4 ml of buffered solution of surfactant (c(SDS) = 0.1 mol l^{-1}, c($CTANO_3$) = 0.02 mol l^{-1}). [b] Reaction time was 30 min or until the conversion was complete with the exception of blank experiments. [c] Isolated yield. [d] TON = 840; calculated from isolated yield.

CONCLUSION

The results of our current study clearly demonstrate that alloxazinium salts **2** are more efficient catalysts of the sulfides oxidation with hydrogen peroxide than isoalloxazinium salts **1**. In comparison with homogeneous catalytic systems operating with common "hydrophilic" flavinium salts[1–7], micellar systems made of cationic surfactants and containing amphiphilic alloxazinium salt **2b** with the hydrophobic alkyl chain in position 1 are

more efficient. The obtained value of the relative rate v_{cat}/v_0 (about 80) gives evidence of a significant contribution of micellar catalysis. However, to our great surprise, replacing amphiphilic alloxazinium salt **2b** in cationic micelles by non-amphiphilic salt **2a** lead to further increase in the catalytic activity. We have concluded that the species involved in the catalytic cycle (i.e. salt **2a** and hydroperoxide **2a**-OOH) have their hydrophilic and lipophilic properties well balanced and therefore salt **2a** may act like a phase-transfer catalyst bringing hydrogen peroxide from the aqueous phase into the micelle interior. We assume that the concept of phase-transfer catalysis with covalently bound peroxide in sulfoxidations catalyzed by flavinium salts can be applied even to real two-phase systems. Investigation of this possibility will be the subject of our next study.

EXPERIMENTAL

General

Temperature data are uncorrected. NMR spectra were recorded on a Varian Mercury Plus 300 (299.97 MHz for ^{1}H and 75.44 MHz for ^{13}C) and a Bruker Avance DRX 500 spectrometer (500.13 MHz for ^{1}H and 125.77 MHz for ^{13}C). Chemical shifts are given in ppm relative to tetramethylsilane (δ 0.0) used as an internal standard, coupling constants (*J*) are given in Hz. TLC analyses were carried out on a DC Alufolien Kieselgel 60 F_{254} (Merck). Preparative column chromatography separations were performed on a silica gel Kieselgel 60 0.040–0.063 mm (Merck). Elemental analyses (C, H, N) were performed on a Perkin–Elmer 240 analyser; determination of Cl was made on an X-ray fluorescence spectrometer ARL 9400 XP$^+$. UV-Vis spectra were recorded on a Varian Cary 50 spectrophotometer. HPLC analyses were performed on an Ecom HPLC System (column: Separon SGX C18, 150 × 4.6 mm; 0.5 ml min^{-1}) using UV spectrophotometric detection.

Chemicals

Starting materials and reagents used for the preparation of the catalysts were obtained from Aldrich, Lancaster and Fluka, and were used without purification. Solvents and substrates used for kinetic experiments (analytical grade) were purchased from Fluka and Penta. The concentration of hydrogen peroxide was determined by manganometric titration. Preparation and characterization of isoalloxazinium catalysts **1a** and **1b** was described in our previous paper[8]. Alloxazinium salt **2a** was prepared according to the procedure described by Murahashi[5e]. Synthesis of lumiflavin **4** (used for synthesis of **1c**) is published elsewhere[12]. *N*-Substituted barbituric acids (used for the synthesis of *N*-alkylalloxans **6**) were prepared from *N*-substituted ureas[18] by the reaction with malonic acid (in the case of methyl homologue) or with diethyl malonate (in the case of dodecyl derivative). *N*-Methylurea for the synthesis of *N*-methylbarbituric acid was obtained from Sigma–Aldrich. *N*-Dodecylurea was prepared from the corresponding *N*-dodecylamine and sodium cyanate according to the described procedure[19].

3-Dodecyl-5-ethyl-10-methylisoalloxazinium perchlorate (**1c**). Acetaldehyde (0.7 ml, 12.5 mmol) and palladium on carbon (10%, 21 mg) were added to a suspension of **5** (50 mg, 0.118 mmol) in acetic acid (14 ml) and water (1.4 ml). The resulting mixture was stirred for 3 days in an autoclave under H_2 (0.6 MPa) at room temperature. Then the catalyst was filtered off, acetic acid was evaporated under reduced pressure, and the remaining green solid was dried in vacuo. The residue was suspended in 2 M perchloric acid (1.5 ml), and sodium perchlorate (0.321 g, 2.29 mmol) and sodium nitrite (0.119 g, 1.72 mmol) were added. Methanol (7.5 ml) was added to this system in order to obtain a homogeneous solution. The mixture was then stirred at 10 °C for 2 h. Methanol was evaporated under reduced pressure, the precipitated solid was filtered off, washed with 2 M perchloric acid and dried in vacuo. Yield 41 mg (63%). Violet crystalline solid, m.p. 104–107 °C. ^{1}H NMR (500 MHz, CD_3CN): 0.91 t, 3 H, J = 6.6 (alkyl-CH_3); 1.31 m, 16 H ($(CH_2)_8$); 1.66 m, 2 H ($NCH_2CH_2CH_2$); 1.80 t, 3 H, J = 6.5 ($N^+CH_2CH_3$); 2.20 m, 2 H (NCH_2CH_2); 2.59 s, 3 H (7-CH_3Ar); 2.65 s, 3 H (8-CH_3Ar); 4.01 t, 2 H, J = 7.3 (NCH_2); 4.17 s, 3 H (NCH_3); 4.99 bs, 1 H (N^+CH**H**); 6.06 bs, 1 H (N^+CH**H**); 7.90 s, 1 H (9-H_{Ar}); 8.23 s, 1 H (6-H_{Ar}). ^{13}C NMR (125 MHz, CD_3CN): 14.4 (alkyl-CH_3); 15.5 ($N^+CH_2CH_3$); 20.3 (7-CH_3Ar); 21.4 (8-CH_3Ar); 23.3 (alkyl-CH_2); 27.3 (alkyl-CH_2); 27.4 (alkyl-CH_2); 27.7 (alkyl-CH_2); 29.9 (alkyl-CH_2); 30.21 (alkyl-CH_2); 30.26 (alkyl-CH_2); 30.32 (alkyl-CH_2); 30.4 (alkyl-CH_2); 32.1 (NCH_3); 32.4 (alkyl-CH_2); 42.3 (NCH_2); 53.2 (N^+CH_2); 118.8 (CH_{Ar}); 121.7 (CH_{Ar}); 127.6 (C_{Ar}); 131.3 (C_{Ar}); 136.7 (C_{Ar}); 143.0 (CH_3-C_{Ar}); 150.2 (C_{Ar}); 153.4 (CH_3-C_{Ar}); 153.9 (CO); 156.9 (CO). For $C_{27}H_{41}ClN_4O_6 \cdot 3H_2O$ (525.05) calculated: 53.41% C, 7.80% H, 5.84% Cl, 9.23% N; found: 53.36% C, 7.39% H, 5.96% Cl, 9.14% N.

5-Ethyl-1,3-dimethylalloxazinium perchlorate (**2a**). Salt **2a** was prepared according to the published procedure[5e]. Yield 84%. Orange solid, m.p. 246–249 °C. ^{1}H NMR (500 MHz, CD_3CN): 1.84 t, 3 H ($N^+CH_2CH_3$); 3.54 s, 3 H (3-NCH_3); 3.85 s, 3 H (1-NCH_3); 5.00 bs, 1 H (N^+CH**H**); 6.10 bs, 1 H (N^+CH**H**); 8.27–8.38 m, 3 H (7,8,9-H_{Ar}); 8.55 d, 1 H, J = 8.9 (6-H_{Ar}). ^{13}C NMR (125 MHz, CD_3CN): 15.6 ($N^+CH_2CH_3$); 30.7 (3-NCH_3); 31.6 (1-NCH_3); 52.9 (N^+CH_2); 120.7 (CH_{Ar}); 122.7 (C_{Ar}); 131.1 (CH_{Ar}); 137.1 (CH_{Ar}); 137.8 (CH_{Ar}); 148.0 (C_{Ar}); 148.8 (C_{Ar}); 149.8 (CO); 156.4 (CO). For $C_{14}H_{15}ClN_4O_6 \cdot H_2O$ (388.77) calculated: 43.25% C, 4.41% H, 9.12% Cl, 14.41% N; found: 43.52% C, 4.19% H, 9.27% Cl, 14.34% N.

1-Dodecyl-5-ethyl-3-methylalloxazinium perchlorate (**2b**). Salt **2b** was prepared from alloxazine **8a** (50 mg, 0.126 mmol) according to the procedure described for **1c**. Yield 34 mg (51%). Brown solid, m.p. 114–118 °C. ^{1}H NMR (500 MHz, CD_3CN): 0.86 t, 3 H, J = 6.5 (alkyl-CH_3); 1.26 m, 16 H ($(CH_2)_8$); 1.44 m, 2 H ($NCH_2CH_2CH_2$); 1.73 m, 2 H (NCH_2CH_2); 1.84 t, 2 H, J = 7.0 ($N^+CH_2CH_3$); 3.50 s, 3 H (NCH_3); 4.46 t, 2 H, J = 7.5 (NCH_2); 5.13 bs, 1 H (N^+CH**H**); 6.21 bs, 1 H (N^+CH**H**); 8.23–8.31 m, 3 H (7,8,9-H_{Ar}); 8.55 d, 1 H, J = 8.9 (6-H_{Ar}). ^{13}C NMR (125 MHz, CD_3CN): 14.4 (alkyl-CH_3); 15.6 ($N^+CH_2CH_3$); 23.4 (alkyl-CH_2); 27.2 (alkyl-CH_2); 27.7 (alkyl-CH_2); 29.9 (alkyl-CH_2); 30.1 (alkyl-CH_2); 30.2 (alkyl-CH_2); 30.28 (alkyl-CH_2); 30.33 (alkyl-CH_2); 30.4 (alkyl-CH_2); 30.7 (alkyl-CH_2); 32.6 (N-CH_3); 45.1 (NCH_2); 52.9 (N^+CH_2); 120.7 (CH_{Ar}); 122.7 (C_{Ar}); 131.1 (CH_{Ar}); 137.1 (CH_{Ar}); 137.7 (CH_{Ar}); 148.0 (C_{Ar}); 148.4 (C_{Ar}); 149.5 (CO); 156.4 (CO). For $C_{25}H_{37}ClN_4O_6 \cdot H_2O$ (543.07) calculated: 55.29% C, 7.24% H, 6.53% Cl, 10.32% N; found: 54.90% C, 7.26% H, 6.40% Cl, 10.30% N.

3-Dodecyl-5-ethyl-1-methylalloxazinium perchlorate (**2c**). Salt **2c** was prepared from alloxazine **8b** (70 mg, 0.176 mmol) according to the procedure described for **1c**. Yield 50 mg (76%). Brown solid, m.p. 143–147 °C. ^{1}H NMR (500 MHz, CD_3CN): 0.86 t, 3 H, J = 6.6 (alkyl-CH_3); 1.25 m, 16 H ($(CH_2)_8$); 1.39 m, 2 H ($NCH_2CH_2CH_2$); 1.67 m, 2 H (NCH_2CH_2); 1.76 t, 3 H, J = 7.0 ($N^+CH_2CH_3$); 3.78 s, 3 H (NCH_3); 4.07 m, 2 H (NCH_2); 5.13 bs, 1 H (N^+CH**H**); 6.21 bs, 1 H (N^+CH**H**); 8.22–8.32 m, 3 H (7,8,9-H_{Ar}); 8.54 d, 1 H, J = 8.9 (6-H_{Ar}).

^{13}C NMR (125 MHz, CD_3CN): 14.4 (alkyl-CH_3); 15.6 ($N^+CH_2\mathbf{C}H_3$); 23.4 (alkyl-CH_2); 27.5 (alkyl-CH_2); 27.7 (alkyl-CH_2); 29.9 (alkyl-CH_2); 30.0 (alkyl-CH_2); 30.2 (alkyl-CH_2); 30.27 (alkyl-CH_2); 30.34 (alkyl-CH_2); 30.4 (alkyl-CH_2); 31.5 (N-CH_3); 32.6 (alkyl-CH_2); 44.7 (NCH_2); 52.9 (N^+CH_2); 120.6 (CH_{Ar}); 122.7 (C_{Ar}); 130.8 (CH_{Ar}); 136.7 (CH_{Ar}); 137.6 (CH_{Ar}); 147.5 (C_{Ar}); 148.5 (C_{Ar}); 149.4 (CO); 156.0 (CO). For $C_{25}H_{37}ClN_4O_6 \cdot H_2O$ (543.07) calculated: 55.29% C, 7.24% H, 6.53% Cl, 10.32% N; found: 55.17% C, 7.38% H, 6.34% Cl, 10.19% N.

3-Dodecyl-7,8,10-trimethylisoalloxazine (**5**). A mixture of lumiflavin **4** (0.800 g, 1.88 mmol), potassium carbonate (2.160 g, 15.63 mmol), and dodecyl iodide (2.770 g, 9.35 mmol) in dry DMF (180 ml) was stirred at room temperature for 45 h. The salts were filtered off and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (chloroform/methanol 100:5) and by crystallization from ethanol/ water (2:1). Yield 1.050 g (79%). Yellow solid, m.p. 195–196 °C. ^{1}H NMR (500 MHz, $CDCl_3$): 0.87 t, 3 H, J = 6.9 (alkyl-CH_3); 1.24 m, 16 H (($CH_2)_8$); 1.34 m, 2 H ($NCH_2CH_2C\mathbf{H}_2$); 1.71 m, 2 H ($NCH_2C\mathbf{H}_2$); 2.44 s, 3 H (7-CH_3Ar); 2.54 s, 3 H (8-CH_3Ar); 4.09 m, 2 H (NCH_2); 4.10 s, 3 H (NCH_3); 7.40 s, 1 H (9-H_{Ar}); 8.04 s, 1 H (6-H_{Ar}). ^{13}C NMR (125 MHz, $CDCl_3$): 14.3 (alkyl-CH_3); 19.7 (7-CH_3Ar); 21.7 (8-CH_3Ar); 22.9 (alkyl-CH_2); 27.2 (alkyl-CH_2); 28.0 (alkyl-CH_2); 29.0 (NCH_3); 29.48 (alkyl-CH_2); 29.55 (alkyl-CH_2); 29.60 (alkyl-CH_2); 29.75 (alkyl-CH_2); 29.83 (alkyl-CH_2); 29.86 (alkyl-CH_2); 32.1 (alkyl-CH_2); 42.3 (NCH_2); 115.5 (CH_{Ar}); 131.9 (C_{Ar}); 132.8 (CH_{Ar}); 134.8 (C_{Ar}); 136.0 (C_{Ar}); 136.9 (8-CH_3-$\mathbf{C}_{Ar}$); 148.0 (7-CH_3-$\mathbf{C}_{Ar}$); 149.2 (C_{Ar}); 155.8 (CO); 159.9 (CO). For $C_{25}H_{36}N_4O_2$ (424.59) calculated: 70.72% C, 8.55% H, 13.20% N; found: 70.28% C, 8.92% H, 13.27% N.

N-Methylalloxan hydrate (**6a**). Chromium oxide (26.3 g, 264 mmol) was dissolved in a mixture of acetic acid (100 ml) and water (12 ml). Reaction mixture was cooled with ice and *N*-methylbarbituric acid (24.4 g, 172 mmol) was added in small portions keeping the temperature below 50 °C. After the addition was complete, the reaction mixture was stirred at 45–50 °C for 30 min. The reaction mixture was allowed to stay at 4 °C for 1 week and then it was tempered to room temperature. The solid was filtered off, washed with cold acetic acid (3 × 20 ml) and diethyl ether (25 ml) and dried in vacuo. Yield 22.3 g (74%). White crystals, m.p. 134–138 °C (ref.[20] 150–151 °C). ^{1}H NMR (300 MHz, DMSO-d_6): 3.04 s, 3 H (CH_3); 7.62 m, 2 H ($C(OH)_2$); 11.43 m, 1 H (NH). ^{13}C NMR (75 MHz, DMSO-d_6 + 4% D_2O): 28.2 (CH_3); 86.0 ($C(OH)_2$); 166.4 (CO); 168.7 (CO); 169.6 (CO). For $C_5H_6N_2O_5$ (174.11) calculated: 34.49% C, 3.47% H, 16.09% N; found: 34.27% C, 3.50% H, 15.86% N.

N-Dodecylalloxan hydrate (**6b**). Chromium oxide (1.1 g, 10.88 mmol) was dissolved in a mixture of acetic acid (20 ml) and water (2 ml). The reaction mixture was cooled with ice and *N*-dodecylbarbituric acid (2.93 g, 9.87 mmol) was added in small portions keeping the temperature below 50 °C. After the addition of all the substrate, the reaction mixture was stirred at 45–50 °C for 30 min. Reaction mixture was diluted with water (125 ml) and extracted with ethyl acetate (3 × 150 ml). Organic layer was washed with water and dried over magnesium sulfate. After the evaporation of the solvent in vacuo, the crude product was purified by column chromatography (ethyl acetate/hexane 1:1). Yield 0.94 g (29%). White pasty compound. ^{1}H NMR (300 MHz, DMSO-d_6): 0.83 t, 3 H, J = 7.0 (alkyl-CH_3); 1.22 m, 18 H (($CH_2)_9$); 1.45 m, 2 H ($NCH_2C\mathbf{H}_2$); 3.62 t, 2 H, J = 7.6 (NCH_2); 7.61 m, 2 H ($C(OH)_2$); 11.40 m, 1 H (NH). For $C_{16}H_{26}N_2O_4 \cdot H_2O$ (328.41) calculated: 58.52% C, 8.59% H, 8.53% N; found: 58.27% C, 8.54% H, 8.66% N.

3-Methylalloxazine (**7a**). A solution of 1,2-dinitrobenzene (2.000 g, 11.90 mmol) in acetic acid (100 ml) was hydrogenated in the presence of palladium on carbon (10%, 0.150 g) at 0.1 MPa at room temperature. Total reaction time was 3 h. The reaction mixture was filtered

through Celite, and a hot solution (70 °C) of boric acid (0.819 g, 13.24 mmol) and *N*-methylalloxan monohydrate (2.071 g, 11.89 mmol) in acetic acid (75 ml) was added immediately. The mixture was stirred at room temperature for 20 h. The precipitate formed was filtered off, washed with acetic acid and diethyl ether, and dried in vacuo. Yield 1.750 g (65%). Cream crystalline solid, m.p. 285 °C. ^{1}H NMR (300 MHz, DMSO-d_6): 3.29 s, 3 H (CH_3); 7.77 m, 1 H (7-H_{Ar}); 7.92 m, 2 H (6,8-H_{Ar}); 8.18 d, 1 H, J = 8.2 (6-H_{Ar}); 12.23 s, 1 H (NH). ^{13}C NMR (125 MHz, DMSO-d_6): 29.1 (NCH_3); 127.9 (CH_{Ar}); 129.1 (CH_{Ar}); 129.7 (C_{Ar}); 130.7 (CH_{Ar}); 133.7 (CH_{Ar}); 139.9 (C_{Ar}); 143.5 (C_{Ar}); 145.2 (C_{Ar}); 150.3 (CO); 160.0 (CO). For $C_{11}H_8N_4O_2$ (228.21) calculated: 57.89% C, 3.53% H, 24.55% N; found: 58.12% C, 3.41% H, 24.55% N.

3-Dodecylalloxazine (**7b**). A solution of 1,2-dinitrobenzene (0.248 g, 1.48 mmol) in acetic acid (20 ml) was hydrogenated in the presence of palladium on carbon (10%, 20 mg) at 0.1 MPa at room temperature. Total reaction time was 3 h. The reaction mixture was filtered through Celite, and a hot solution (70 °C) of boric acid (0.102 g, 1.65 mmol) and *N*-dodecylalloxan (0.485 g, 1.48 mmol) in acetic acid (14 ml) was added immediately. The mixture was stirred at room temperature for 20 h. The precipitate formed was filtered off, washed with acetic acid and diethyl ether and dried in vacuo. Yield 0.487 g (86%). Yellow solid, m.p. 279–282 °C. ^{1}H NMR (300 MHz, DMSO-d_6): 0.83 t, 3 H, J = 6.8 (alkyl-CH_3); 1.21 m, 18 H ((CH_2)$_9$); 1.61 m, 2 H ($NCH_2C\mathbf{H}_2$); 3.90 m, 2 H (NCH_2); 7.77 m, 1 H (7-H_{Ar}); 7.93 m, 2 H (6,8-H_{Ar}); 8.19 d, 1 H, J = 8.2 (6-H_{Ar}); 12.20 s, 1 H (NH). ^{13}C NMR (125 MHz, DMSO-d_6): 14.1 (alkyl-CH_3); 22.6 (alkyl-CH_2); 26.8 (alkyl-CH_2); 27.4 (alkyl-CH_2); 29.21 (alkyl-CH_2); 29.26 (alkyl-CH_2); 29.32 (alkyl-CH_2); 29.5 (alkyl-CH_2); 29.60 (alkyl-CH_2); 29.63 (alkyl-CH_2); 31.7 (alkyl-CH_2); 42.4 (NCH_2); 127.9 (CH_{Ar}); 129.2 (CH_{Ar}); 129.6 (C_{Ar}); 130.7 (CH_{Ar}); 133.8 (CH_{Ar}); 139.8 (C_{Ar}); 143.6 (C_{Ar}); 145.4 (C_{Ar}); 150.4 (CO); 160.0 (CO). For $C_{22}H_{30}N_4O_2$ (382.51) calculated: 69.08% C, 7.91% H, 14.65% N; found: 69.38% C, 7.74% H, 14.48% N.

1-Dodecyl-3-methylalloxazine (**8a**). A mixture of alloxazine **7a** (0.800 g, 3.51 mmol), potassium carbonate (2.422 g, 17.53 mmol), and dodecyl iodide (2.077 g, 7.01 mmol) in dry DMF (40 ml) was stirred in inert atmosphere (N_2) at room temperature for 22 h. The salts were filtered off and washed with chloroform. Solvents from the filtrate were removed under reduced pressure. Dichloromethane (70 ml) and water (20 ml) were added to the residue and after separation of the organic layer, the aqueous phase was washed with dichloromethane (7 × 20 ml). Organic phase was dried over anhydrous magnesium sulfate. After the evaporation of the solvent in vacuo, the crude product was purified by column chromatography (chloroform/methanol 100:3). Yield 1.373 g (99%). Yellow solid, m.p. 152 °C. ^{1}H NMR (500 MHz, $CDCl_3$): 0.87 t, 3 H, J = 6.5 (alkyl-CH_3); 1.26 m, 16 H ((CH_2)$_8$); 1.44 m, 2 H ($NCH_2CH_2C\mathbf{H}_2$); 1.82 m, 2 H ($NCH_2C\mathbf{H}_2$); 3.60 s, 3 H (NCH_3); 4.44 t, 2 H, J = 7.6 (NCH_2); 7.75 t, 1 H, J = 8.0 (7-H_{Ar}); 7.89 t, 1 H, J = 8.1 (8-H_{Ar}); 8.02 d, 1 H, J = 8.4 (6-H_{Ar}); 8.34 d, 1 H, J = 8.4 (9-H_{Ar}). ^{13}C NMR (125 MHz, $CDCl_3$): 14.1 (alkyl-CH_3); 22.6 (alkyl-CH_2); 26.8 (alkyl-CH_2); 27.4 (alkyl-CH_2); 29.1 (NCH_3); 29.21 (alkyl-CH_2); 29.30 (alkyl-CH_2); 29.33 (alkyl-CH_2); 29.47 (alkyl-CH_2); 29.57 (alkyl-CH_2); 29.61 (alkyl-CH_2); 31.9 (alkyl-CH_2); 42.8 (NCH_2); 127.9 (CH_{Ar}); 129.0 (CH_{Ar}); 129.6 (C_{Ar}); 130.8 (CH_{Ar}); 133.7 (CH_{Ar}); 139.9 (C_{Ar}); 143.4 (C_{Ar}); 145.0 (C_{Ar}); 150.3 (CO); 159.9 (CO). For $C_{23}H_{32}N_4O_2$ (396.54) calculated: 69.67% C, 8.13% H, 14.13% N; found: 69.94% C, 7.90% H, 13.84% N.

3-Dodecyl-1-methylalloxazine (**8b**). A mixture of alloxazine **7b** (0.410 g, 1.07 mmol), potassium carbonate (0.741 g, 5.36 mmol), and methyl iodide (0.761 g, 5.36 mmol) in dry DMF (15 ml) was stirred in inert (N_2) atmosphere at room temperature for 22 h. The salts were filtered off and washed with chloroform. Solvents from the filtrate were removed under re-

duced pressure. Dichloromethane (40 ml) and water (15 ml) were added to the residue and after separation of the organic layer, aqueous phase was washed with dichloromethane (7 × 15 ml). The organic phase was dried over anhydrous magnesium sulfate. After the evaporation of the solvent in vacuo, the crude product was purified by column chromatography (chloroform/methanol 100:3). Yield 0.210 g (49%). Yellow solid, m.p. 99–102 °C. ^{1}H NMR (500 MHz, $CDCl_3$): 0.87 t, 3 H, J = 6.6 (alkyl-CH_3); 1.24 m, 16 H ($(CH_2)_8$); 1.37 m, 2 H ($NCH_2CH_2CH_2$); 1.73 m, 2 H (NCH_2CH_2); 3.82 s, 3 H (NCH_3); 4.17 t, 2 H, J = 7.5 (NCH_2); 7.75 t, 1 H, J = 8.1 (7-H_{Ar}); 7.89 t, 1 H, J = 8.2 (8-H_{Ar}); 8.02 d, 1 H, J = 8.4 (6-H_{Ar}); 8.34 d, 1 H, J = 8.3 (9-H_{Ar}). ^{13}C NMR (125 MHz, $CDCl_3$): 14.1 (alkyl-CH_3); 22.6 (alkyl-CH_2); 26.8 (alkyl-CH_2); 27.4 (alkyl-CH_2); 28.9 (NCH_3); 29.21 (alkyl-CH_2); 29.29 (alkyl-CH_2); 29.34 (alkyl-CH_2); 29.47 (alkyl-CH_2); 29.57 (alkyl-CH_2); 29.61 (alkyl-CH_2); 31.8 (alkyl-CH_2); 42.5 (NCH_2); 127.9 (CH_{Ar}); 129.0 (CH_{Ar}); 129.6 (C_{Ar}); 130.8 (CH_{Ar}); 133.7 (CH_{Ar}); 139.9 (C_{Ar}); 143.4 (C_{Ar}); 145.0 (C_{Ar}); 150.3 (CO); 159.9 (CO). For $C_{23}H_{32}N_4O_2$ (396.54) calculated: 69.67% C, 8.13% H, 14.13% N; found: 69.61% C, 8.01% H, 13.99% N.

Kinetic Measurements

The oxidation of thioanisole (**3**) (both in micellar and in homogeneous solutions) was performed in vials thermostatted to 25.0 ± 0.5 °C. The reaction mixtures were prepared by mixing aliquot portions of stock solutions of reactants and other additives: thioanisole (**3**) (c = 6.00 × 10^{-1} mol l^{-1} in methanol), flavinium salt **1** or **2** (c = 9.0 × 10^{-3} mol l^{-1} in methanol, freshly prepared; it was not added in blank experiments), surfactant (c = 1.00 × 10^{-1} mol l^{-1} in water), internal standard (1,3-dimethoxybenzene, c = 3.0 × 10^{-2} mol l^{-1} in 0.1 M solution of surfactant) and phosphate buffer (c = 5.00 × 10^{-1} mol l^{-1}). The prepared mixtures were thermostatted for 20 min before the experiment was started. The reactions were initiated by the addition of 100 μl of hydrogen peroxide solution (c = 4.50 × 10^{-1} mol l^{-1} in water) to the prepared mixture. The resulting concentrations of reactants and auxiliaries in the reaction mixtures were as follows: c(**3**) = 1.5 × 10^{-2} mol l^{-1}, c(H_2O_2) = 2.25 × 10^{-2} mol l^{-1}, c(flavinium salt) = 2.3 × 10^{-4} mol l^{-1}, c(1,3-dimethoxybenzene) = 7.5 × 10^{-3} mol l^{-1}, c(buffer) = 1.0 × 10^{-1} mol l^{-1}, c(surfactant) = 1.0 × 10^{-1} mol l^{-1}.

The concentration of methyl phenyl sulfoxide was monitored by HPLC using 1,3-dimethoxybenzene as an internal standard. Sample preparation: 100 μl of the reaction mixture was diluted with 100 μl of acetonitrile.

Preparative Sulfoxidations in SDS Micelles. General Procedure

Aqueous solution of SDS (c = 5.00 × 10^{-1} mol l^{-1}; 800 μl) was mixed with deionized water (1 200 μl) and phosphate buffer (c = 5.00 × 10^{-1} mol l^{-1}; 2 000 μl). Thioanisole (95 μl, 0.805 mmol) and flavinium salt (0.0120 or 0.0024 or 0.0008 mmol) were added. The reaction mixture was emulgated by sonication and thermostatted to 25.0 ± 0.5 °C for 20 min. The reaction was initiated by the addition of 124 μl of hydrogen peroxide (30% aqueous solution; 1.2 mmol) to the prepared mixture. After 30 min or after complete conversion was achieved (monitored by TLC using toluene as a mobile phase), sodium perchlorate (4 g) and diethyl ether (10 ml) were added. The resulting suspension was allowed to stand for 15 min and then filtered. The filtrate was separated in a separatory funnel and the aqueous phase was extracted with diethyl ether (10 × 6 ml). The combined ethereal extracts were dried over anhydrous sodium sulfate and evaporated to dryness. The crude product was analyzed by ^{1}H NMR.

Preparative Sulfoxidations in $CTANO_3$ Micelles. General Procedure

Aqueous solution of $CTANO_3$ (c = 5.00 × 10^{-1} mol l^{-1}; 160 μl) was mixed with deionized water (1 840 μl) and phosphate buffer (c = 5.00 × 10^{-1} mol l^{-1}; 2 000 μl). Thioanisole (95 μl, 0.805 mmol) and flavinium salt (0.012 mmol) were added. The reaction mixture was emulgated by sonication and thermostatted to 25.0 ± 0.5 °C for 20 min. The reaction was initiated by the addition of 124 μl of hydrogen peroxide (30% aqueous solution; 1.2 mmol) to the prepared mixture. After 30 min or after complete conversion was achieved (monitored by TLC using toluene as a mobile phase), sodium perchlorate (4 g) and diethyl ether (10 ml) were added. The resulting suspension was allowed to stand for 15 min and then filtered. The filtrate was separated in a separatory funnel and the aqueous phase was extracted with diethyl ether (10 × 6 ml). The combined ethereal extracts were dried over anhydrous sodium sulfate and evaporated to dryness. The crude product was analyzed by ^{1}H NMR.

Study of Flavinium Salt–Pseudobase Equilibrium

The apparent pK_a' values of **1** and **2** were calculated using Origin 6.1 software[21] (Boltzmann function) by non-linear regression analysis of absorbance versus pH data at the maximum absorption wavelengths of **1** and **1**-OH or **2** and **2**-OH. The pK_a's given in Table II are the means of the obtained values. Either phosphate buffer (for pH > 1.6) or HNO_3 (for pH < 1.6) was used to adjust the pH values of the systems. Acidity function (H_0) values[22] were used instead of pH values for HNO_3 solutions.

Binding Constants of Flavinium Salts and Their Pseudobases in Cationic Micelles

The values of the binding constant K_S of **2** and **2**-OH to micelles of $CTANO_3$ were measured spectrophotometrically[17] from the variation of absorbance A_{obs} at 450 nm (in the case of salt **2**) or 296 nm (in the case of pseudobase **2**-OH) with surfactant concentration c_{surf} at pH value by 2 units lower (for K_S of flavinium form) or by 2 units higher (for K_S of pseudobase) than corresponding pK_a' in the appropriate micellar system. The binding constant was calculated using Eq. (*1*) (see note in ref.[17])

$$(A_{obs} - A_w)/[D_n] = A_M K_S - A_{obs} K_S \qquad (1)$$

where A_{obs} is the observed absorbance, A_W and A_M are the corresponding absorbances of **2** in water and in micellar pseudophase and $[D_n]$ is the concentration of micellized surfactant ($[D_n] = c_{surf}$ – cmc; cmc stands for critical micelle concentration). The values of A_W were measured in independent experiments. The binding constant was obtained as a slope of the linear plot $(A_{obs} - A_w)/[D_n]$ versus A_{obs}. Phosphate buffer was used to adjust pH values of the systems.

The authors wish to thank the Czech Science Foundation (Grant No. 203/07/1246) for the financial support.

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