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Amphiphilic Flavin and 5-Deazaflavin in Anionic Micelle as a Recycle Oxidation Catalyst

by

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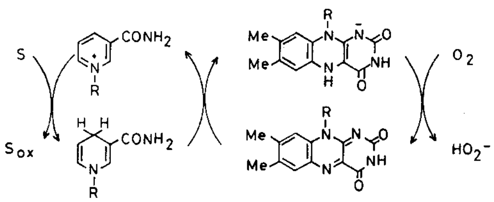
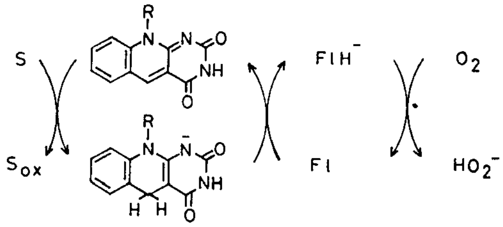
The SDS micelle which binds both amphiphilic flavin (3-methyl-10-dodecylisoalloxazine) and 5-deazaflavin (3-methyl-10-dodecyl-5-deazaisoalloxazine) acts as a recycle catalyst for aerobic oxidation of benzylamine and mimicks an electron bridge from NAD^+ to flavin.

NAD^+ and flavin (Fl) are representative redox coenzymes and present in many biological systems. NAD^+ apparently acts as a "two-electron-carrying shuttle" and has strong oxidizing power but is not subject to reoxidation by molecular oxygen, whereas Fl acts as a "one-electron-carrying shuttle" and is rapidly reoxidized by molecular oxygen. The electron bridge from NAD^+ to Fl is constructed so that two coenzymes may compensate each role as oxidation catalyst and overall, substrate (S) is oxidized by molecular oxygen via the mediation of an electron bridge from NAD^+ to Fl (Scheme I).



Scheme I

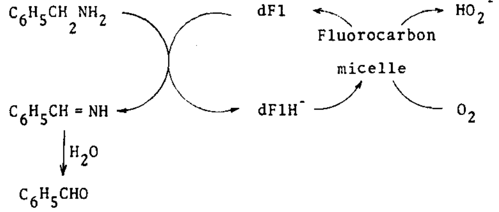
We recently reported that an efficient model electron bridge can be constructed by using 5-deazaisoalloxazine (dFl) and flavin mononucleotide (FMN), the yield in the aerobic oxidation of benzylamine to benzaldehyde being 3500% (Scheme II).[1)]



Scheme II

It has been established that the redox behavior of dFl is analogous to that of NAD^+ rather than to that of Fl.[2)] Thus, the model electron bridge is of a great significance because of the possible connection with the biologically ubiquitous electron bridge from NAD^+ to Fl.

It occurred to us that the recycle number of this electron bridge may be improved by performing the



Scheme III

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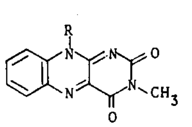
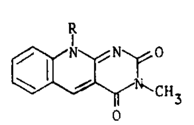
oxidation in a limited micelle phase. It is also interesting to test whether a fluorocarbon micelle, which is capable of dissolving molecular oxygen, facilitates the reoxidation of reduced 5-dFl (Scheme III). With these objects in view, we carried out the oxidation of benzylamine in various aqueous micelles.

Experimental

We have used following isoalloxazines, 5-deazaisoalloxazines, and surfactants.



10-EtFl : R=C_2H_5
10-DodFl : R=$C_{12}H_{25}$



10-EtdFl : R=C_2H_5
10-DoddFl : R=$C_{12}H_{25}$

SDS : $C_{12}H_{25}OSO_3^-Na^+$
CTAB : $C_{16}H_{33}N^+(CH_3)_3Br^-$
F-NBS : $C_9F_{19}O$-$C_6H_4SO_3^-Na^+$

The typical reaction method is as follows. In a three-necked flask were placed Fl (6.32×10^{-6} mole), dFl (6.32×10^{-6} mole), and surfactant. These were dissolved in 15 ml of O_2-saturated water, and then 0.5 ml of benzylamine was added. The reaction mixture was heated at 50°C for 24 h, while molecular oxygen was bubbled into the solution. An aliquot (3 ml) was withdrawn and treated with 2, 4-dinitrophenylhydrazine.[3] The yield of benzaldehyde was determined by the amount of recovered 2, 4-dinitrophenylhydrazone.

Results and Discussion

We have reported that 10-DodFl and 10-DoddFl form micelle-like aggregates in aqueous solution.[4-6] The aggregate formation is spectrophotometrically detected on the basis of a phenomenon that the absorption band at the visible region gives a well-resolved fine structure. The redox reactivities of 10-DodFl and 10-DoddFl are surprisingly suppressed in the aggregate state. On the other hand, when they are dissolved in the micelle phase, the fine structure has disappeared owing to deaggregation of the amphiphiles and the redox reactivities are markedly enhanced. These findings suggest that the micelle may provide a favorable reaction environment for the recycle oxidation of benzylamine.

The results of the recycle oxidation are summarized in Table 1. It has been noticed that aerobic oxidation of benzylamine by dFl exceeds 100%.[7] The peculiar phenomenon is due to reoxidation of reduced dFl by molecular oxygen, although the rate is extremely slow in comparison to that of reduced Fl.[2] Under the present reaction conditions, oxidation by 10-EtdFl in aqueous solution gave 180% of benzaldehyde. Addition of 10-EtFl, which is expected to accelerate the reoxidation process of reduced 10-EtdFl, enhanced the yield up to 280%.

Examination of Run No. 3-6 in Table 1 reveals that (i) the recycle number of 10-DoddFl bound to the SDS micelle is significantly enhanced, (ii) addition of riboflavin or 10-EtFl has almost no effect, and (iii) the combination of 10-DoddFl and 10-DodFl, both of which are greatly partitioned to the micelle phase, is most efficient as a recycle catalytic system. Probably, riboflavin and 10-EtFl, which are classified as hydrophilic flavins, are hardly partitioned to the micelle phase and cannot mediate the reoxidation process of micelle-bound reduced 10-DoddFl.

The effect of the fluorocarbon micelle is recorded in Run No. 7-9. Contrary to our expectation, the recycle number was hardly improved by the addition of F-NBS. Since the fine structure of 10-DoddFl disappears in the aqueous solution of 6.0 mM F-NBS, the phase separation which is frequently seen between hydrocarbon detergents and fluorocarbon detergents[8] is hardly conceivable between F-NBS and 10-DoddFl. We noticed, however, that the aqueous solution (15 ml) of 10-DoddFl (6.32×10^{-6} mole) and F-NBS (6.0 mM) is clear, whereas the solution becomes slightly turbid on the addition of benzylamine (0.5 ml). Probably, the poor reaction environment is elucidated as such that the partition coefficient of benzylamine to the fluorocarbon micelle is very small. It is not yet clear, therefore, that the fluorocarbon micelle has a favorable effect on the reoxidation of reduced dFl.

In conclusion, the present study establishes that amphiphilic Fl and dFl bound to the anionic micelle mediate the recycle oxidation of benzylamine, the highest yield being 1780%. This is an interesting model for the electron bridge from NAD^+ to Fl constructed in the micellar environment.

Table 1. Yield of benzaldehyde calculated on the basis of 5-deazaisoalloxazine.

Run	dFl	Fl	Surfactant (mM)	Yield %
1	10-EtdFl	None	None	180
2	10-EtdFl	10-EtFl	None	280
3	10-DoddFl	None	SDS(40)	680
4	10-DoddFl	riboflavin	SDS(40)	600
5	10-DoddFl	10-EtFl	SDS(40)	650
6	10-DoddFl	10-DodFl	SDS(40)	1780
7	10-DoddFl	None	F-NBS(6.0)	160
8	10-DoddFl	riboflavin	F-NBS(6.0)	190
9	10-DoddFl	10-DodFl	F-NBS(6.0)	280
10	10-DoddFl	riboflavin	CTAB(40)	310

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