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Oxidation of sulfides with hydrogen peroxide catalyzed by synthetic flavin adducts with dendritic bis(acylamino)pyridines

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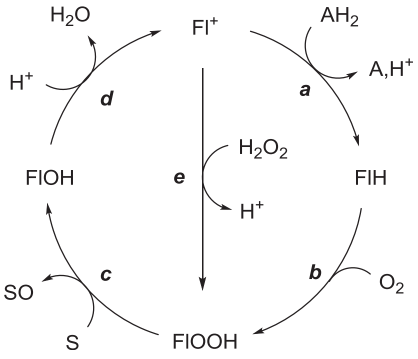
ABSTRACT

The catalytic activities of the cationic synthetic flavin adduct **1** with various dendritic and non-dendritic 2,6-bis(acylamino)pyridines **2** were examined for the oxidation of organic sulfides with H_2O_2. The adduct of 5-ethyllumiflavinium perchlorate **1a** with **2b**–**d** bearing poly(benzyl ether) dendron units acts as an efficient organocatalyst for the oxidative transformation of sulfides to the corresponding sulfoxides under mild conditions.

1. Introduction

The simulation of flavoenzymes[1] with synthetic flavin catalysts[2] is important with respect to the exploitation of environmentally benign processes for oxidative transformation with organocatalysts.[3–5] Model reactions of flavin-containing oxygenases include the reduction of an oxidized form of cationic synthetic flavins (Fl^+) with a reductant (AH_2) (Scheme 1, step *a*), the incorporation of O_2 to give hydroperoxyflavin (FlOOH) (step *b*), oxygen atom transfer from FlOOH to the substrate (S) to form the oxygenated product (SO) (step *c*), and dehydration to complete the catalytic cycle (step *d*). When H_2O_2 is used as an oxidant instead of O_2, the FlOOH active species are formed directly from Fl^+ via an anaerobic shunt process (step *e*).[2] The principle of this organocatalytic process provides green methods for the oxidation of various heteroatom compounds including amines,[6] sulfides,[6] and ketones[7] that proceed with H_2O_2[6a–j,7a,b] or O_2[6k–n,7c] under mild conditions.

To obtain higher efficiency and specificity in this process, much effort has been devoted to create novel flavin catalysts bearing enzyme-like reaction cavities[8] circumferentially arranged at the foregoing FlOOH active center. Chemo and stereoselectivities are reportedly enhanced by employing synthetic flavin catalysts that are modified covalently[9] or non-covalently[10] with dendron units and cyclodextrins,[11] where hydrophilic and hydrophobic interactions in artificial cavities serve as a key factor for the expression of selectivity. Our systematic studies on the development of new organocatalysts bearing novel functions have revealed adducts of 5-ethyllumiflavinium perchlorate (**1a**) with 2,6-bis(acylamino) pyridines bearing poly(benzyl ether)dendron unit **2b**–**d** that



Scheme 1. Catalytic cycle for model reaction of flavin-containing monooxygenase with synthetic flavins.

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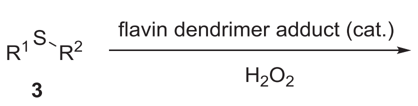
exhibit high catalytic activity for the oxidation of sulfides with H_2O_2 (Eq. 1 and Chart 1). The Michaelis–Menten kinetics indicate that the flavin-dendrimer **1a**·**2c** adduct is reorganized to the corresponding association complex **5**, which acts as a catalytically active species in the foregoing redox processes in Scheme 1. This is a new type of efficient supramolecular catalysis for the oxidative transformation of sulfides with H_2O_2, which has been performed reportedly with a variety of metallo-[12] and organocatalysts.[2,6a,c–n,13]



(1)

2. Results and discussion

2.1. Characterization of flavin adducts with 2,6-bis(acylamino)pyridines

Synthetic cationic flavin **1** (**a**, 5-ethyllumiflavinium perchlorate: R^1=Me, R^2=Me, R^3=H; **b**, 5-ethyl-3-methyllumiflavinium perchlorate: R^1=Me, R^2=Me, R^3=Me), 2,6-bis(acetylamino)pyridine (**2a**, AAP), and its dendritic analogues **2b** (first generation: 2,6-bis(3-{4-[3,5-bis(phenylmethoxy)phenylmethoxy]phenyl}propanoylamino)pyridine, abbreviated as G1PAP), **2c** (second generation: G2PAP), and **2d** (third generation: G3PAP) were synthesized according to procedures given in the literature (Chart 1).[6l,10a,14] When an equimolar amount of 2,4-bis(acylamino)pyridine **2** was added to a solution of **1a**

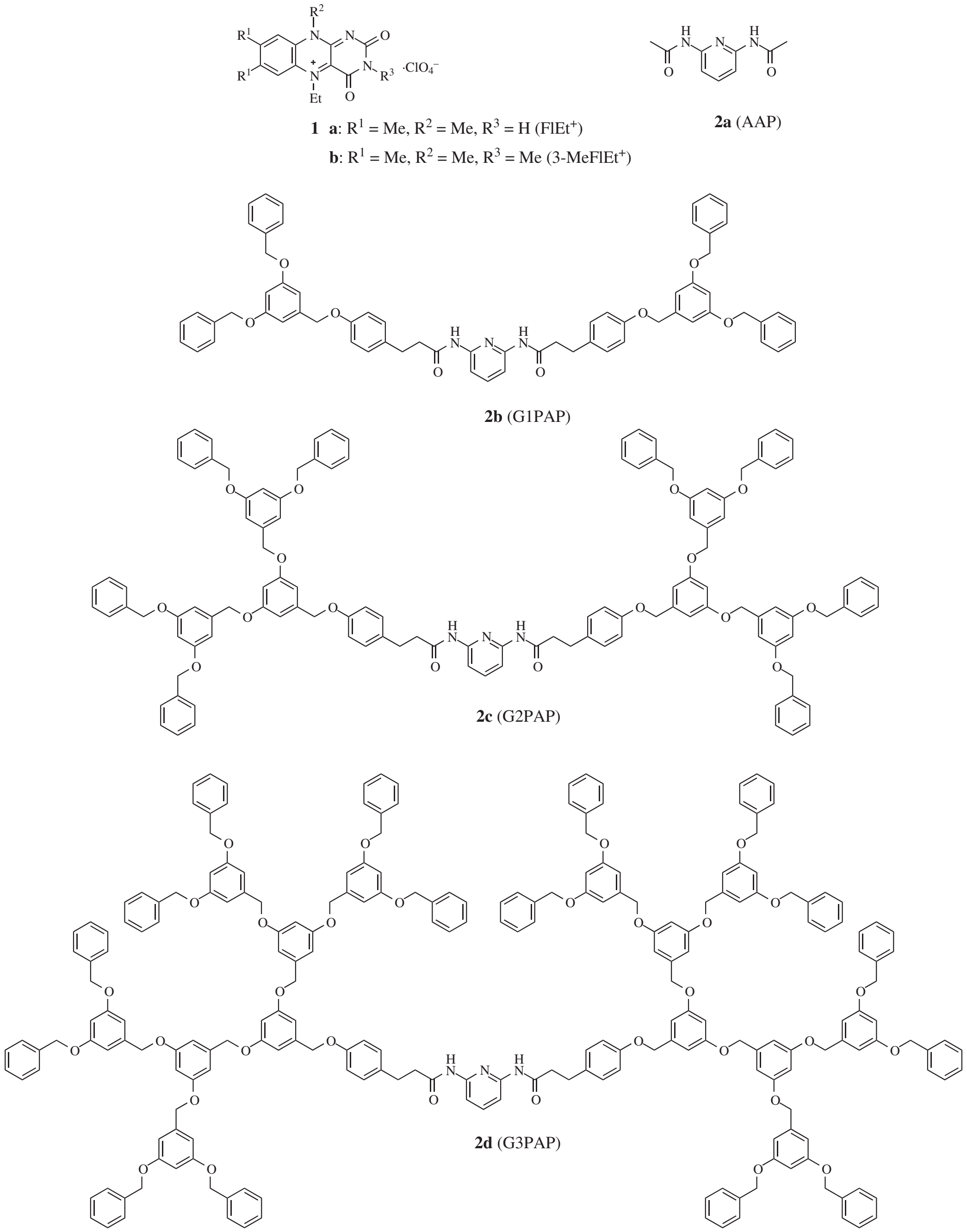


Chart 1. Structures of cationic flavins **1** and 2,6-bis(acylamino)pyridines **2**.