Structure–Property Relationships

Flavin Derivatives with Tailored Redox Properties: Synthesis, Characterization, and Electrochemical Behavior


Abstract: This study establishes structure–property relationships for four synthetic flavin molecules as bioinspired redox mediators in electro- and photocatalysis applications. The studied flavin compounds were disubstituted with polar substituents at the N1 and N3 positions (alloxazine) or at the N3 and N10 positions (isoalloxazines). The electrochemical behavior of one such synthetic flavin analogue was examined in detail in aqueous solutions of varying pH in the range from 1 to 10. Cyclic voltammetry, used in conjunction with hydrodynamic (rotating disk electrode) voltammetry, showed quasi-reversible behavior consistent with freely diffusing molecules and an overall global 2e\textsuperscript{−}/2H\textsuperscript{+} proton-coupled electron transfer scheme. UV/Vis spectroelectrochemical data was also employed to study the pH-dependent electrochemical behavior of this derivative. Substituent effects on the redox behavior were compared and contrasted for all the four compounds, and visualized within a scatter plot framework to afford comparison with prior knowledge on mostly natural flavins in aqueous media. Finally, a preliminary assessment of one of the synthetic flavins was performed of its electrocatalytic activity toward dioxygen reduction as a prelude to further (quantitative) studies of both freely diffusing and tethered molecules on various electrode surfaces.

Introduction

As part of a broader project on bioinspired electro- and photocatalysis assemblies\textsuperscript{[1,2]} we describe below the results of a study on the electrochemical behavior of four synthetic flavins in aqueous media. Flavins are biologically important yellow molecules with a common three-ring isoalloxazine structural motif, of which three natural analogues are well known: riboflavin, flavin mononucleotide (FMN), and flavin adenine dinucleotide (FAD) (Figure 1). All three molecules share the common feature of 7,8-dimethyl substitution of the benzene subnucleus but differ in the side chains at the N10 position. Additionally, lumiflavin, is a riboflavin analogue in which the ribotyl substituent at the N10 position is photochemically cleaved to a methyl group (Figure 1). The isoalloxazine moiety (particularly the bis-imine (shown in red) of the quinone-like core) forms the electroactive part of the molecules while the N10 substituents aid in apoprotein-cofactor binding and specificity.\textsuperscript{[3–5]} The other substituents (at the C7 and C8, N1, N3, and N5 positions, Figure 1), as elaborated further in what follows, have direct effects on stability, solubility, pK\textsubscript{a}, and redox potential.

Figure 1. Synthetic flavins in the present study and their relationship to natural analogues. RF and LF stand for riboflavin and lumiflavin, respectively. Redox-active centers are highlighted in red.

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