

Formation of a Transient Radical Ion Pair in the Reactions of 1,5-Dihydroflavin with Hydride Acceptors

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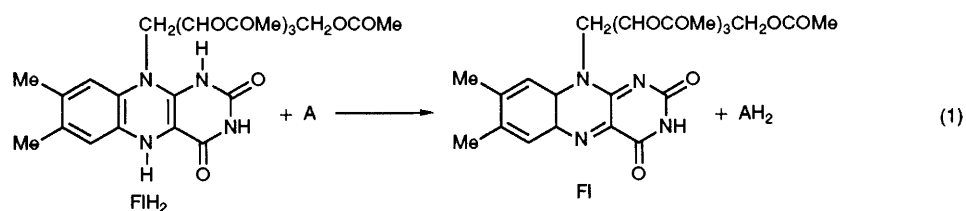
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The formation of a transient radical ion pair has been detected directly in the reactions of 1,5-dihydroriboflavin-2',3',4',5'-tetraacetate (FIH₂) with hydride acceptors (tetracyano-*p*-quinodimethane, tetracyanoethylene and *p*-benzoquinone derivatives) in deaerated acetonitrile, providing unequivocal evidence for an electron transfer pathway in the overall two-electron redox reactions of FIH₂ with hydride acceptors.

Considerable efforts have so far been devoted to understand the mechanisms of the two-electron redox reactions of flavoenzymes and analogues.¹⁻³ It is now generally believed that the two-electron reduction of hydride acceptors (A) by 1,5-dihydroflavins (FIH₂) proceeds *via* electron transfer from FIH₂ to A, followed by proton and hydrogen transfer to yield the final products (FI and AH₂).⁴⁻⁶ To the best of our knowledge, however, the radical ion pair (FIH₂^{•+} A^{•-}) which would be formed by the initial electron transfer from FIH₂ to A has never been detected directly. We report herein the first direct detection of the transient radical ion pair formed in the reactions of 1,5-dihydroriboflavin-2',3',4',5'-tetraacetate (FIH₂) with hydride acceptors such as tetracyano-*p*-quinodimethane (TCNQ), tetracyanoethylene (TCNE) and 2,3-dicyano-5,6-dichloro-*p*-benzoquinone (DDQ). This finding combined with the kinetic study provides unequivocal

evidence for transfer of electron-proton-hydrogen in the overall hydride transfer from FIH₂ to the hydride acceptors.

FIH₂ was prepared by the reduction of riboflavin-2',3',4',5'-tetraacetate (FI) by sodium dithionite according to the literature.⁷ The FIH₂ can reduce various hydride acceptors (A), TCNQ, TCNE, or DDQ, and other *p*-benzoquinone derivatives in deaerated MeCN at 298 K to yield FI and AH₂ [eqn. (1)]. The products were identified by ¹H NMR spectra. Upon mixing deaerated MeCN solutions of FIH₂ and TCNQ, the rapid build up of absorbance due to TCNQ^{•-} (λ_{max} = 842 nm)⁸ as well as that due to FIH₂^{•+} (λ_{max} = 504 nm)⁹ is observed by using a stopped-flow spectrophotometer. Both the TCNQ^{•-} and FIH₂^{•+} decay with the same rate as that of the formation of FI (λ_{max} = 442 nm),⁹ as shown in Fig. 1. It is noteworthy that the decay and formation rates obey exactly first-order kinetics irrespective of different initial concentra-



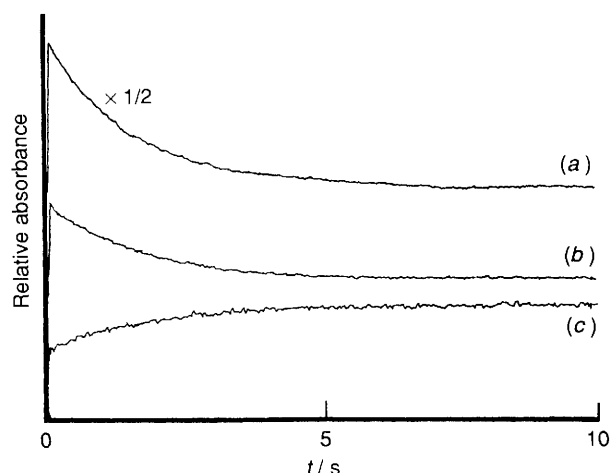
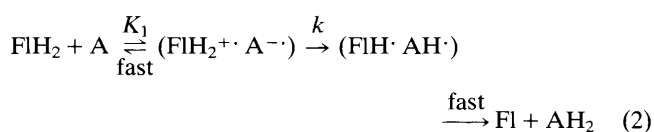


Fig. 1 The decay of the absorbance at (a) $\lambda = 840$ nm (TCNQ $^{\cdot-}$) and (b) 504 nm (FIH $_2^+$), and the rise of the absorbance at (c) $\lambda = 442$ nm (FI) in the reaction of FIH $_2$ (1.67×10^{-5} mol dm $^{-3}$) with TCNQ (1.67×10^{-5} mol dm $^{-3}$) in deaerated MeCN at 298 K

tions of FIH $_2$ and TCNQ (1.7×10^{-5} – 3.3×10^{-5} mol dm $^{-3}$). Such formation of a radical ion pair and the first-order decay which coincides exactly with the formation of FI are also observed in the reactions of FIH $_2$ with TCNE and DDQ. The first-order decay rate constants are in order 6.8×10^2 s $^{-1}$ (FIH $_2^+ \cdot$ DDQ $^{\cdot-}$) $> 5.5 \times 10^{-1}$ s $^{-1}$ (FIH $_2^+ \cdot$ TCNQ $^{\cdot-}$) $> 5.4 \times 10^{-2}$ s $^{-1}$ (FIH $_2^+ \cdot$ TCNE $^{\cdot-}$), in agreement with the order of proton affinity of the radical anions.^{2,3,10} Thus, the initial fast electron transfer from FIH $_2$ to A to produce the transient radical ion pair (FIH $_2^+ \cdot$ A $^{\cdot-}$) may be followed by the rate-determining proton transfer from FIH $_2^+ \cdot$ to A $^{\cdot-}$ in the radical ion pair and the subsequent fast hydrogen (or electron and proton) transfer to yield the final product [eqn. (2)].



It is well known that the proton affinity of the radical anions (A $^{\cdot-}$) increases as electron transfer reduction of A becomes energetically disfavoured.^{2,3,10} Thus, one can expect the change of the rate-determining step from the proton transfer in the radical ion pair to the initial electron transfer when the hydride acceptors (DDQ, TCNQ, and TCNE), which are rather strong electron acceptors, are replaced by much weaker one-electron reductants that have more negative one-electron reduction potentials (E_{red}^0) than DDQ ($E_{\text{red}}^0 = 0.51$ V vs. SCE), TCNE (0.22 V), or TCNQ (0.19 V).^{9,10} In fact, the rate of the reactions of FI with various quinones which have negative E_{red}^0 values obey ordinary second-order kinetics, showing a first-order dependence on the concentration of each reactant, when the formation of radical ion pair has not been detected. Moreover, the logarithm of the observed second-order rate constant ($\log k_{\text{obs}}$) increases with an increase in the E_{red}^0 values as shown in Fig. 2. The slope of the correlation becomes closer to 16.9 (= $F/2.3RT$), which is indicative of the rate-determining electron transfer (*c.f.* the broken line in Fig. 2), with a decrease in the E_{red}^0 value.¹¹ The observed curvature, *i.e.* the deviation from the broken linear line clearly demonstrates the gradual change of the rate-determining step from the initial electron transfer to the proton transfer in the radical ion pair with an increase in the E_{red}^0 value. Extension of

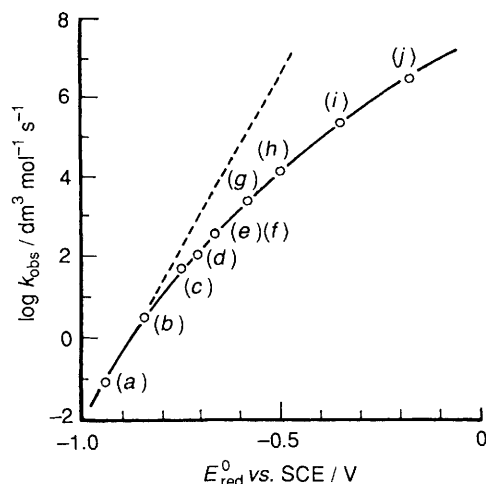


Fig. 2 Plot of $\log k_{\text{obs}}$ for the reactions of FIH $_2$ with (a) anthraquinone, (b) tetramethyl-*p*-benzoquinone, (c) trimethyl-*p*-benzoquinone, (d) coenzyme Q $_0$, (e) 2,5-dimethyl-*p*-benzoquinone, (f) 2,6-dimethyl-*p*-benzoquinone, (g) methyl-*p*-benzoquinone, (h) *p*-benzoquinone, (i) chloro-*p*-benzoquinone, (j) 2,6-dichloro-*p*-benzoquinone in deaerated MeCN at 298 K vs. the one-electron reduction potentials (E_{red}^0) of quinones. The broken line shows the linear correlation between k_{obs} and E_{red}^0 for the rate-limiting electron transfer with the slope of 16.9 V $^{-1}$ ($F/2.3RT$) vs. SCE (saturated calomel electrode).

such a correlation agrees well with the observed rapid build up of the radical ion pair and subsequent first-order decay by proton transfer in the case of strong electron acceptors (DDQ, TCNQ, and TCNE).

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