Electron transfer properties of active aldehydes derived from thiamin coenzyme analogues

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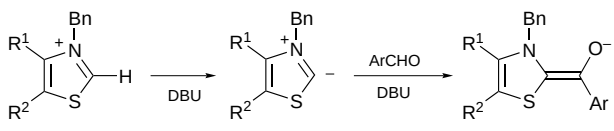
The rate constants and reorganization energies of electron transfer reactions between active aldehydes, derived from thiamin coenzyme analogues, and the corresponding one-electron oxidized radical species have been determined to demonstrate the efficient electron transfer properties of the active aldehydes.

The conjugate base of 2-(α-hydroxyethyl)thiamin, a so called 'active aldehyde', derived from thiamin diphosphate coenzyme and pyruvate in the presence of a base is known to act as an efficient electron transfer catalyst which can mediate electron transport from pyruvate to various physiological electron acceptors. These include the lipoamide in pyruvate dehydrogenase multienzyme complex,[1] flavin adenine dinucleotide (FAD) in pyruvate oxidase[2] and the Fe_4S_4 cluster in pyruvate-ferredoxin oxidoreductase.[3] However, very little is known about the redox behaviour of active aldehydes because of their instability and tendency to undergo acyloin condensation with a second pyruvate molecule in the absence of oxidizing agents.[4] We report herein that active aldehyde **2**$^-$ derived from thiazolium salts **1a**–**c** and *o*-tolualdehyde in the presence of a strong base (Scheme 1) can be stabilized by the steric bulk of an *o*-methyl group and that the radical species produced by the one-electron oxidation of stabilized active aldehydes can be readily detected by EPR spectroscopy. The important electron transfer properties of the active aldehydes, such as reorganization energies of electron transfer reactions between the active aldehydes and the corresponding one-electron oxidized radical species, are determined by analysing linewidth variations in the EPR spectra.

The active aldehyde **2a**$^-$ (λ_{max} = 380 nm)[5] was prepared by the addition of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) to an MeCN solution of **1a** and *o*-tolualdehyde, keeping the ratio of the components constant (**1a** : *o*-tolualdehyde : DBU = 1 : 50 : 2). Then, the solution was partially electrolysed at −0.70 V *vs*. SCE, which is between the redox potentials for the **2a**$^-$/**2a**$^{\cdot}$ (−0.96 V *vs*. SCE in MeCN) and **2a**$^{\cdot}$/**2a**$^+$ couples (−0.52 V *vs*. SCE in MeCN),[6] to give the corresponding radical species **2a**$^{\cdot}$. EPR spectra for **2a**$^{\cdot}$ were obtained at different concentrations of **2a**$^-$, as shown in Fig. 1. The spectra of the radical species were persistent for several hours after the electrolysing potential had been switched off. The hyperfine splitting constants shown in Table 1 and the maximum slope linewidths (ΔH_{msl}) were determined from a computer simulation of the EPR spectra (Fig. 1). The ΔH_{msl} value thus determined increases linearly with an increase in the concentration of **2a**$^-$, as shown in Fig. 2. Such linewidth variations of the EPR spectra can be used to investigate the rate processes involving the radical species.[7] The rate constants (k_{et}) of the electron transfer reactions between **2a**$^-$ and **2a**$^{\cdot}$ [eqn. (1)] were



1a R^1 = Me, R^2 = H
b R^1 = R^2 = Me
c R^1 = R^2 = H

Ar = *o*-MeC_6H_4

2$^-$

Scheme 1

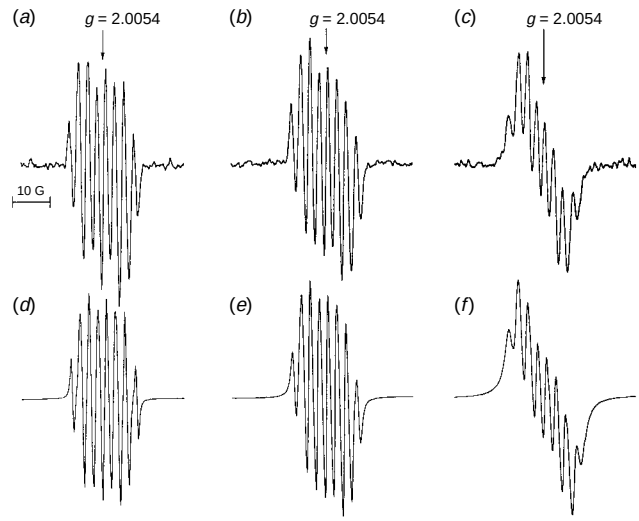
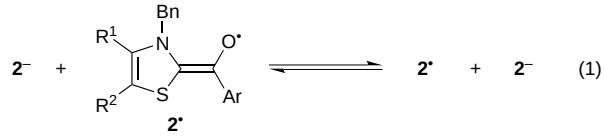


Fig. 1 EPR spectra (X-band) of **2a**$^{\cdot}$ observed in the presence of different concentrations of **2a**$^-$: (*a*) 1.5 × 10^{-3}, (*b*) 6.5 × 10^{-3} and (*c*) 3.0 × 10^{-2} M (in MeCN at 298 K, microwave frequency 9.21 GHz; modulation frequency 100 kHz; modulation amplitude 2.5 × 10^{-3} G; microwave power 10 mW; scan rate 19 G min^{-1}), and the corresponding computer simulation spectra using the hyperfine splitting values shown in Table 1 and linewidths of (*d*) 0.50, (*e*) 0.70 and (*f*) 1.55 G



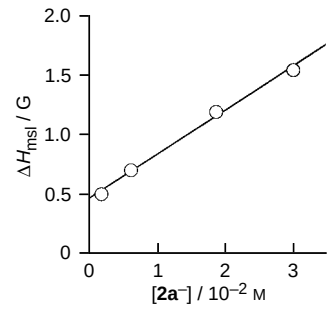


Fig. 2 Plot of [**2a**$^-$] *vs*. ΔH_{msl} for EPR spectra of **2a**$^{\cdot}$ in MeCN at 298 K

determined using eqn. (2), where ΔH_{msl} and ΔH^0_{msl} are the

$$k_{et} = \frac{1.57 \times 10^7 (\Delta H_{msl} - \Delta H^0_{msl}}{(1 - P_i)[\mathbf{2}^-]} \quad (2)$$

maximum slope linewidth of the EPR spectra in the presence and absence of $\mathbf{2}^-$, respectively, and P_i is a statistical factor which can be taken as nearly zero. The k_{et} values for other active aldehydes $\mathbf{2b}^-$ and $\mathbf{2c}^-$ were determined in a similar manner and are listed in Table 1. The reorganization energies (λ) of the electron transfer reactions are obtained from the k_{et} values using eqn. (3) ($Z = 10^{11}$ M^{-1} s^{-1}),[8] and the λ values are also listed in

$$k_{et} = Z \exp(-\lambda/4kT) \quad (3)$$

Table 1. No prominent change in the k_{et} or λ values is observed depending on the presence of methyl substituents on the thiazolium rings. The λ values are as small as those of fast electron transfer exchange systems such as *p*-benzoquinone/semiquinone radical anion (55 kJ mol^{-1} in DMF) and naphthalene/radical anion of naphthalene (50 kJ mol^{-1} in DMF) systems.[9]

The largely negative oxidation potentials of the active aldehydes derived from thiamin coenzyme analogues and the small reorganization energies for the electron transfer reactions indicate that the active aldehydes have strong electron donor abilities and that they are suitable for fast electron transfer systems where they can act as efficient electron transfer catalysts in electron transfer from pyruvate to physiological electron acceptors in enzymatic systems.

Table 1 Hyperfine splitting values for $\mathbf{2}^{\cdot}$ produced by the one-electron oxidation of $\mathbf{2}^-$ and the observed rate constants (k_{et}) and the reorganization energies (λ) of the electron transfer reactions between $\mathbf{2}^-$ and $\mathbf{2}^{\cdot}$ in MeCN at 298 K[a]

	Hyperfine splitting/G				
Active aldehyde	a_{N-} (N)	a_{H-} (N–CH_2)	a_{H-} (C–5)	$k_{et}/10^8$ M^{-1} s^{-1}[b]	λ/kJ mol^{-1}[b]
$\mathbf{2a}^-$	4.71	2.35	2.89	5.6	52
$\mathbf{2b}^-$	4.75	2.07	2.64	6.6	50
$\mathbf{2c}^-$	4.89	2.66	2.66	4.5	54

[a] ±0.5 K. [b] Experimental error = ±5%.

Footnote and References

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Received in Cambridge, UK, 30th June 1997; 7/04559J