Redox Behavior of Active Aldehydes Derived from Thiamin Coenzyme Analogs

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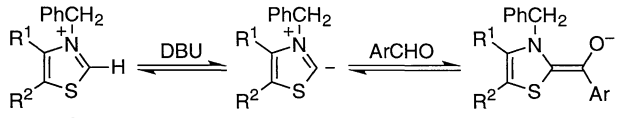
Redox behavior of active aldehydes of thiamin coenzyme models has been investigated using 3-benzylthiazolium salts and *o*-tolualdehyde in the presence of a base. The use of a sterically hindered aldehyde has precluded benzoin condensation of the active aldehydes, leading to the formation of relatively stable active aldehydes. The redox potentials of the active aldehydes have been determined by cyclic voltammetry for the first time, and they are sufficiently negative to reduce C_{60} to the corresponding dianion (C_{60}^{2-}).

Catalysis of coenzyme thiamin diphosphate (ThDP) has been attracted considerable interest in enzymatic electron-transfer reactions from pyruvate to various physiological electron acceptors.[1] The ThDP model systems using various thiazolium salts have been studied extensively, demonstrating that electron accepting substrates, such as nitrobenzene, ferricyanide, and flavin derivatives, can be reduced by pyruvate or simple aldehydes in the presence of thiazolium salts and a base.[2–5] In these redox processes, the enolate anion of 2-(α-hydroxyalkyl)ThDP, so-called "active aldehyde", is known to be formed as an active intermediate.[6] However, very little is known about the redox behavior of the active aldehyde intermediate, since this species readily undergoes acyloin-type condensation with second pyruvate or aldehyde molecule in the absence of electron acceptors.[7] Such instability of the active aldehyde has precluded the direct determination of its detailed redox behavior,[8] which is of importance for elucidation of the biological redox mechanism. We report herein the generation of relatively stable active aldehydes (**2a-c**) derived from thiazolium salts (**1a-c**) and *o*-tolualdehyde in the presence of a strong base (DBU: 1,8-diazabicyclo[5.4.0]undec-7-ene), which enables us to determine the redox potentials of the active aldehydes **2a-c** for the first time.



1 **2**

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

Ar = *o*-MeC_6H_4

Cyclic voltammograms were measured for **2a-c** prepared *in situ* by adding DBU (1.0×10^{-2} mol dm^{-3}) to a deaerated acetonitrile (MeCN) solution of **1a-c** (5.0×10^{-3} mol dm^{-3}), *o*-tolualdehyde (0.25 mol dm^{-3}), and 0.10 mol dm^{-3} tetrabutylammonium perchlorate (TBAP) at 298 K. Generation of **2a-c** (λ_{max} = 380 nm) was confirmed by UV spectroscopy.[4d,5,9] In all cases, two reversible one-electron redox peaks were observed.[10] No reversible peaks can be observed when benzaldehyde and acetaldehyde are used instead of *o*-tolualdehyde under otherwise the same experimental conditions, demonstrating that the benzoin condensation is prevented owing to the steric

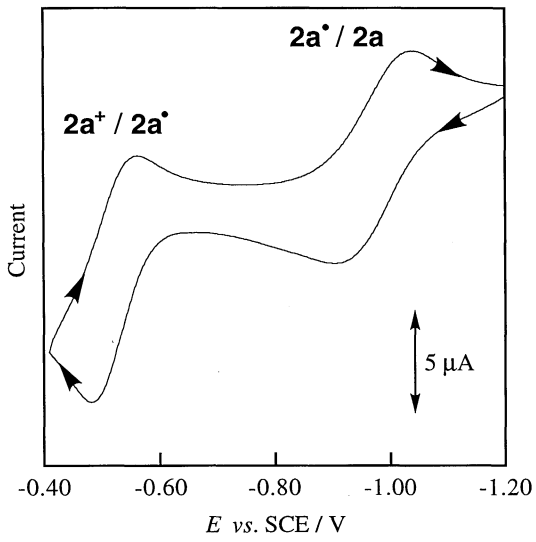


Figure 1. Cyclic voltammogram of an active aldehyde derived from **1a** (5.0×10^{-3} mol dm^{-3}), *o*-tolualdehyde (0.25 mol dm^{-3}), and DBU (1.0×10^{-2} mol dm^{-3}) in deaerated MeCN containing 0.10 mol dm^{-3} TBAP at 298 K; sweep rate 0.10 V s^{-1}.

Table 1. The oxidation potentials (*vs.* SCE) of **2a-c** in MeCN determined by cyclic voltammetry

Active aldehyde	$E^0_{ox(1)}$ / V	$E^0_{ox(2)}$ / V
2a	–0.96	–0.52
2b	–0.97	–0.56
2c	–0.95	–0.50

bulkiness of *o*-methyl group and thus relatively stable "active aldehydes" are formed. A typical cyclic voltammogram is shown in Figure 1, from which the redox potentials are determined as listed in Table 1. The redox potentials in Table 1 are consistent with the proposal by Jordan and co-workers such that the redox potential of the active aldehyde, which can reduce flavin derivatives, must be more negative than –0.67 V *vs.* SCE.[4d] First and second oxidation of **2a-c** occurs at around –0.95 ~ –0.97 V and –0.50 ~ –0.56 V *vs.* SCE, respectively. No prominent change in the value of the potentials could be observed depending on the substituents on the thiazolium rings.

The reducing ability of **2a-c** has been examined using C_{60} as an oxidant. This oxidant is chosen, since the first and second reduction potentials of C_{60} are –0.42 V and –0.84 V *vs.* SCE.[11] Thus, two-electron reduction of C_{60} can be expected, judging from the more negative oxidation potential of **2a** than the second reduction potential of C_{60}. In fact, when DBU (0.18 mol dm^{-3}) is added to a solution containing **1a** (2.2×10^{-3} mol dm^{-3}), *o*-

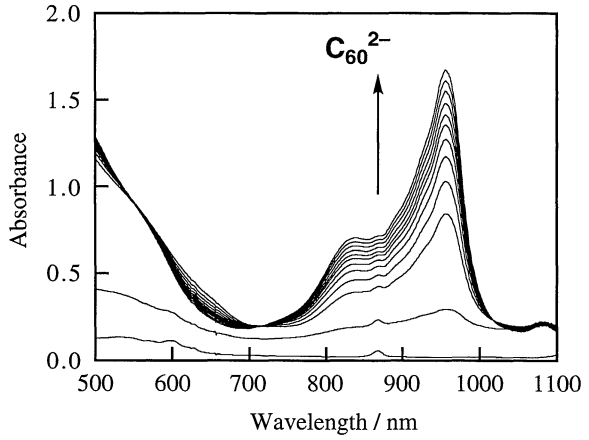


Figure 2. Spectral change observed upon addition of DBU (0.18 mol dm^{-3}) to a deaerated PhCN solution of **1a** (2.2 x 10^{-3} mol dm^{-3}), *o*-tolualdehyde (0.12 mol dm^{-3}), and C_{60} (1.0 x 10^{-4} mol dm^{-3}) at 298 K; interval = 2 s.

tolualdehyde (0.12 mol dm^{-3}), and C_{60} (1.0 x 10^{-4} mol dm^{-3}) in benzonitrile (PhCN) at 298 K, quantitative formation of C_{60}^{2-} (λ_{max} = 955 nm) is observed as shown in Figure 2. In the absence of **1a**, one-electron reduced product ($C_{60}^{\bullet-}$) was mainly formed instead of C_{60}^{2-} by the electron transfer from DBU to C_{60} as reported by Skiebe and co-workers.[12] Thus, the formation of C_{60}^{2-} demonstrates that the active aldehyde **2a** having more negetive oxidation potentials than –0.84 V is formed *in situ* and acts as a strong reducing agent. The increase of the rate of the reduction of C_{60} with an increase in the concentration of DBU or *o*-tolualdehyde as well as the slow increase in absorbance due to C_{60}^{2-} indicates that the formation of **2a** is the rate-determining step.

The above results demonstrate clearly that a thizolium salt serves as an efficient redox catalyst by forming the active aldehyde with *o*-tolualdehyde in the presence of a base, which has a strong reducing ability. The structure of each oxidation state of the active aldehyde is now under investigation.

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