Anodic Oxidation of Methoxyphenols I.  
Anodic Demethoxylation of Vanillin

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1 Introduction

Recently, the anodic demethoxylation of substituted methoxyphenols has been of great interest as a model reaction of biosynthesis, particularly as metabolites of the neurotransmitters, dopamine and norepinephrine1). Anodic oxidation of methoxyphenols has been studied in aqueous solutions2-5), and, for example, the following reactions are proposed:

\[
\begin{align*}
R\text{-OCH}_2\text{-CH}_2\text{-NH}_2 & \rightarrow 2e^- + H^+ \\
R\text{-OCH}_2\text{-OCH}_2 & \rightarrow H_2O + R\text{-OCH} + CH\text{OH} + H^+ (1)
\end{align*}
\]

where R = CH3, CH2CH3, CH2(OH)CH2NH2, and CH(OH)CH2NH(CH3). However, no information has yet been obtained on the rate of the demethoxylation with water because of extremely fast reaction.

On the other hand, Vermillion and Pearl5) reported that dehydrodivanillin was produced by

\[
\begin{align*}
\text{CHO} & \rightarrow \text{CHO} \\
\text{OCH} & \rightarrow \text{H} \text{-OCH} \rightarrow \text{CHO} + \text{CHO} + \text{HO} + \text{OCH}_2 \text{Cho} (2)
\end{align*}
\]

in an acetonitrile solution containing tetraethylammonium hydroxide. Thus, it would be worthwhile for a better understanding of the rate of demethoxylation to examine the oxidation of methoxyphenols in a nonaqueous solution. Here, we report that vanillin is oxidized by the same reactions as those represented by eq. 1 for R = CHO even in an acetonitrile solution if at least 25 mM of water (0.06%) is contained.

2 Experimental

Vanillin and 3,4-dihydroxybenzaldehyde (analytical GR grade) were used as received. Sodium perchlorate was recrystallized twice from ethanol. Acetonitrile was purified by distillation from P2O5 and from K2CO3, and then three times by slow fractional distillation.

Cyclic voltammograms were measured at a Pt disk electrode (2.0 × 10-3 cm2) using a set of Yanaco P8 polarographs. Current reversal Chronopotentiometry was carried out using a programmable power supply (Nikko Keisoku NPP-1). The working electrode was polished with an oilstone before each measurement. An Ag/0.01 M AgClO4 couple in an acetonitrile was used as a reference electrode and all potentials appearing in this paper are referred to this electrode.

Controlled-potential electrolysis was carried out using a Nikko Keisoku NPGS 301 potentiostat. A two-compartment cell with a fine glass frit was used. The working and the counter electrodes were Pt plates. During the electrolysis, cyclic voltammograms of the solution were measured to check the change of the composition of the solution. After electrolysis, the product was extracted five times with ether. The IR and UV spectra were measured using a Hitachi 125-G and a Hitachi 200-10 spectrophotometer, respectively. Methanol was analyzed by gas chromatograph (Yanaco G-1800) using a column of PEG 6000. The water concentration of the test solutions was determined by the Karl-Fischer titration. All electrochemical experiments were carried out at 25°C and the anolyte was deaerated by bubbling with purified nitrogen.
3 Results and Discussion

Figure 1 shows the change of the cyclic voltammogram during electrolysis in an acetonitrile solution containing 0.1% water. The voltammogram of vanillin exhibited an anodic wave (Ia) having a peak potential (Ep) of 1.2 V. By controlled-potential electrolysis at

$$\begin{align*}
\text{CHO} + 2e^- + 2H^+ \rightarrow \text{CHO}_2
\end{align*}$$

1.3 V, the height of wave Ia decreased and a reduction wave (IIc) at Ep = 0.15 V increased. For both the oxidation of vanillin and the re-reduction at -0.1 V, two electrons/molecule of vanillin were consumed. The IR, UV, and NMR spectra of the product obtained by the re-reduction were identical with those of an authentic sample of 3,4-dihydroxybenzaldehyde (DHBA). In the IR spectrum of the oxidation product of vanillin, the absorption at 1030 cm\(^{-1}\) (\(\nu\) C-OCH\(_3\)) which was observed for vanillin disappeared and C-O stretching absorption at 1730 cm\(^{-1}\) appeared, and both the IR spectrum and the cyclic voltammogram were identical with those of the oxidation product of DHBA obtained by electrolysis at 1.3 V (see Fig. 1d) in an acetonitrile solution. o-Quinoidal structure was also detected by the qualitative test using rhodanine\(^2\). Furthermore, during oxidation of vanillin, methanol was produced quantitatively and no other product such as a dimer was obtained. Thus the following reactions are concluded.

In order to confirm that the above reactions also occur in the time scale of cyclic voltammetry, the voltammograms were measured as a function of either the switching potential (the potential at which the potential sweep is reversed), Ep, or the water concentration of the solution. When Ep became positive, the peak current of wave IIc increased; this is explained in terms of an increase in the duration for demethoxylation (Fig. 2a). The ratio of the peak current of IIc to that of Ia, \(i_{IIc}/i_{Ia}\), increased with an increase in the concentration of water; this indicates that the rate of demethoxylation increased with increasing water concentration (Fig. 2b). For so-called an EC mechanism, the peak potential for oxidation appears at more negative potentials with increasing the rate of the chemical reaction. In the present experiment, as is expected, the peak potential of Ia shifted toward negative potential with increasing water concentration. Thus, the oxidation pathway of vanillin (<10 mM) is given by eq. 3 when at least ca. 25 mM (0.06%) of water is contained, and this fact shows
that the demethoxylation of the intermediate (alkoxyxycarbonium ion) with water is fast.

In current-reversal chronopotentiometry, the ratio of the reverse transition time (τ_r) for the reduction of the demethoxylation product to DHBA to the forward electrolysis time (τ_f) for the oxidation of vanillin, τ_r/τ_f, became smaller than the theoretical value^11 for sufficiently fast demethoxylation as the concentration of water decreased. For example, in the case of −i_0/i_t = 0.414, where i_0 and i_t are forward and reverse currents, respectively, τ_r/τ_f became 0.75~0.93 instead of unity at i_t = 1.5~4.0 s for an acetonitrile solution (containing 0.1% water) of 1 mM vanillin. If the difference between one and observed value of τ_r/τ_f, 1−(τ_r/τ_f), is assumed to be due to a delay in the demethoxylation of the intermediate, the pseudo first-order rate constant of demethoxylation can be estimated to be approximately 2 s⁻¹. Thus, the rate of demethoxylation with water, which has not yet been measured, may be detectable in acetonitrile solutions containing small amounts of water.

Similar results to those reported in the present paper for vanillin were also obtained for the anodic oxidation of o-, p-methoxyphenol, and eugenol in acetonitrile solutions, and the results of further precise experiments and theoretical calculations for obtaining the rate constant of the demethoxylation will be communicated later.

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References: