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Suppression of Electroreductive Dimerization of Benzaldehyde by Addition of α-Cyclodextrin

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The effect of α-cyclodextrin (α-CD) on the electroreduction of benzaldehyde was investigated. The reduction in aqueous system produces benzyl alcohol and 1,2-diphenyl-1,2-ethanediol (hydrobenzoin, dimerization product). The addition of α-CD caused the decrease in the yield of hydrobenzoin. This suppression effect was observed both in the controlled potential and controlled current electrolyses. This is accounted for by the retardation of the dimerization rate between the neutral radicals, since inclusion of substrate provides severe steric hindrance around the reaction site. The addition had only a small influence on the stereochemistry of hydrobenzoin formed by the dimerization.

Electrochemical reduction of carbonyl compounds to the corresponding alcohols is an important subject in organic electrochemistry. However, the reduction accompanies the concurrent formation of dimerization products.[1] In order to suppress the dimerization the following conditions are usually employed;[2] (i) low concentration of starting material, (ii) high current density, (iii) low pH, *etc.* We intend to suppress the dimerization from a quite different standpoint, *i.e.*, steric control at "molecular-level" by addition of cyclodextrin (CD).[3] This compound, constructed from cyclic glucose oligomers, has an ability to include a variety of organic substrates in their hydrophobic interior. Taking advantage of this unique property, we have carried out the selective electrosyntheses; the regioselective chlorination of benzene derivatives[4] and the selective reduction of *o*-nitrophenol in the presence of the *p*-isomer.[5] Recently, Smith and Utley demonstrated that CD acts as a proton source in nonaqueous media.[6] Although complexation is observed in polar aprotic media such as dimethyl sulfoxide and *N*,*N*-dimethylformamide, the binding ability of CD is much smaller than that in aqueous media.[3] Therefore, aqueous system should be used in order to draw the ability effectively.

We report herein the suppression of electroreductive dimerization of benzaldehyde by addition of α-CD in aqueous solution. The electrochemical reduction of benzaldehyde have been extensively investigated,[1,2] but the reduction mechanism is not clearly identified.[7] The generally accepted mechanism in neutral aqueous media is as follows:[2]

$$\mathrm{ArCHO} + \mathrm{e} \rightleftharpoons \mathrm{ArCHO}^{-\cdot} \tag{1}$$

$$\mathrm{ArCHO}^{-\cdot} + \mathrm{H}^{+} \longrightarrow \mathrm{ArCHOH}\cdot \tag{2}$$

$$2\mathrm{ArCHOH}\cdot \longrightarrow \mathrm{ArCH(OH)CH(OH)Ar} \tag{3}$$

(1,2-diphenyl-1,2-etnanediol, hydrobenzoin)

$$\mathrm{ArCHOH}\cdot + \mathrm{e} \longrightarrow \mathrm{ArCHOH}^{-} \tag{4}$$

$$\mathrm{ArCHOH}^{-} + \mathrm{H}^{+} \longrightarrow \mathrm{ArCH_2OH}\ \text{(benzyl alcohol)}. \tag{5}$$

In the above mechanism benzyl alcohol is produced *via* ECEC process. However, it can also be formed *via* regeneration mechanism[8] (or disproportionation mechanism) followed by protonation.

$$\mathrm{ArCHO}^{-\cdot} + \mathrm{ArCHOH}\cdot \rightleftharpoons \mathrm{ArCHO} + \mathrm{ArCHOH}^{-} \tag{6}$$

With α-CD, complexation of benzaldehyde is anticipated to reduce the dimerization rate since covering by α-CD produces severe steric hindrance around the reaction site, resulting in suppression of formation of 1,2-diphenyl-1,2-ethanediol (hydrobenzoin). If the dimerization between included molecules is permissible, the addition of α-CD may also affect the stereochemistry of hydrobenzoin[9] since inclusion makes the phenyl group more bulky, so that upon dimerization the approaching of each phenyl group would be sterically hindered.

Experimental

All controlled potential and controlled current electrolyses were carried out with a Yanaco VE-8 electrolyzer at room temperature. The cell was a divided H-type with a mercury pool cathode (area 6 cm^2) and a graphite or Pt gauze anode. The catholyte consisted of 25 ml phosphate buffers (pHs 4.6, 7.0, and 9.1) containing 25 mmol dm^{-3} benzaldehyde. In the controlled potential electrolysis, the potentials were referenced to a saturated calomel electrode (SCE) and the cathode potential was set at −1.3 V (at pH 4.6) and at −1.4 V *vs.* SCE (at pHs 7.0 and 9.1).

After the electrolysis, the catholyte was extracted with ether and the extract was analyzed by gas chromatography. Gas chromatographic analysis was carried out using a Shimadzu GC-4CM machine equipped with hydrogen flame ionization detector. The column used in the analyses of benzyl alcohol and unreacted benzaldehyde was 200 mm × 3 mm ϕ SUS packed with 10% Carbowax 20 M on Chromosorb W, and the column temperature was kept at 170 °C. Nitrogen was used as the carrier gas. Hydrobenzoin and its stereochemistry (*dl*/*meso* ratio) were determined by the reported method.[9]

Cyclic voltammetric experiments were carried out using a conventional instruments with a hanging mercury drop electrode (HMDE) in a phosphate buffer and the potentials were measured with respect to an SCE.

The dissociation constant for α-CD–benzaldehyde complex were determined by spectroscopic methods.[10] The analysis showed that the dissociation constant for the complex is $(4.3\pm0.9)\times10^{-3}$ mol dm^{-3}.

Results and Discussion

For mechanistic study, polarography is more appropriate and more accurate,[5,7] but cyclic voltammetry was carried out to see the effect of α-CD on the reduction of benzaldehyde in the present study due to

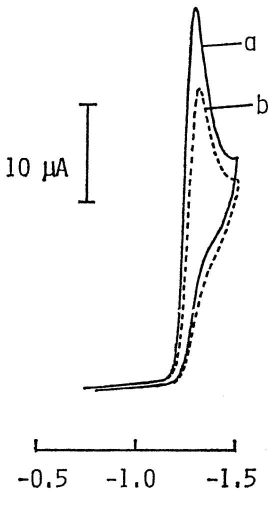

Fig. 1. Cyclic voltammograms of 2.0 mmol dm^{-3} benzaldehyde in the absence (a) and presence (b) of 10 mmol dm^{-3} α-CD at pH 7.0.
Electrode: HMDE, scan rate: 80 mV s^{-1}.

its convenience. Figure 1 shows the cyclic voltammograms of 2 mmol dm^{-3} benzaldehyde in the absence (curve (a)) and presence (curve (b)) of 10 mmol dm^{-3} α-CD in aqueous phosphate buffer (pH 7.0). Curve (a) shows an irreversible reduction peak at −1.30 V *vs.* SCE. As shown in curve (b), upon addition of α-CD to the electrolyte solution, the peak current becomes lower and the peak potential shifts slightly (*ca.* 20 mV) in the cathodic direction. The decrease in peak current is accounted for by the decrease in the effective diffusion coefficient due to the complex formation of benzaldehyde with large α-CD molecule.[5] As described below, the addition of α-CD results in suppression of electroreductive dimerization of benzaldehyde and consequently in the increase in the number of electrons, *n*, consumed for the reduction of one molecule of benzaldehyde. The decrease of the diffusion coefficient is therefore more than that would be expected without change in *n*. The shift in peak potential is probably caused by the "micro-solvent effect"[3] of α-CD; the similar effect has been also observed in the electroreduction of *p*-nitrophenol in the presence of α-CD.[5] In the present conditions concentrations of benzaldehyde and α-CD are 2 and 10 mmol dm^{-3}, respectively), *ca.* 70% of benzaldehyde exists as the complexed form.

Figure 2 depicts the relationship between the ratio of hydrobenzoin to benzyl alcohol, [HB]/[BA], and the conversion of benzaldehyde in the controlled potential electrolysis at −1.3 V *vs.* SCE. The [HB]/[BA] ratio is high at low conversions but decreases with increasing conversion (*i.e.*, decreasing the concentration of unreacted benzaldehyde). This indicates that the hydrobenzoin formation is predominated over the benzyl alcohol formation at beginning of the electrolysis. The tendency is quite consistent with that reported by Aoki and Sekine[7] in which they explained this phenomenon by the concentration effect.

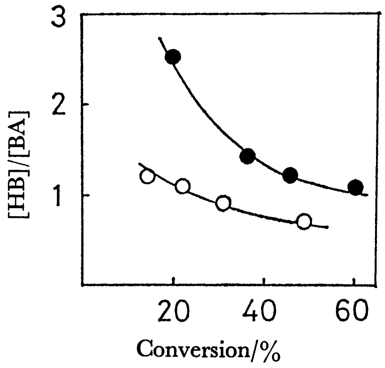

Fig. 2. Relationship between [HB]/[BA] ratio and conversion observed in the controlled potential electrolysis at −1.3 V *vs.* SCE (pH 4.6).
●: Without CD, ○: with α-CD (40 mmol dm^{-3}), initial concentration of benzaldehyde: 25 mmol dm^{-3}.

Table 1. The [HB]/[BA] ratio observed in the controlled potential electrolysis under different pH conditions[a)]

pH	Without CD	With α-CD (40 mmol dm^{-3})
4.6	1.2±0.2	0.5±0.2
7.0	2.2±0.4	0.7±0.2
9.1	2.8±0.5	1.0±0.3

a) Cathode potential: −1.3 V *vs.* SCE (at pH 4.6), −1.4 V *vs.* SCE (at pHs 7.0 and 9.1). Initial concentration of benzaldehyde: 25 mmol dm^{-3}. Conversion: 40—60%.

The [HB]/[BA] ratios observed in the presence of α-CD are lower than those in the absence of α-CD. This clearly suggests that α-CD suppresses the hydrobenzoin formation, *i.e.*, dimerization reaction. Under the initial conditions (concentrations of benzaldehyde and α-CD are 25 and 40 mmol dm^{-3}, respectively), *ca.* 80% of benzaldehyde in the electrolyte solution is included in α-CD's cavity since the dissociation constant for the complex is (4.3±0.9)×10^{-3} mol dm^{-3}. Even if the reduction products, benzyl alcohol and hydrobenzoin, can be trapped strongly by α-CD, the inclusion ratio of benzaldehyde is maintained above 75% through electrolysis. In spite of the fact that such high complex formation is maintained, the suppression effect of α-CD on the dimerization becomes small as the electrolysis proceeds as shown in Fig. 2. At relatively high conversions, benzyl alcohol formation takes precedence over the hydrobenzoin formation, therefore, α-CD cannot exhibit its ability effectively under such conditions.

Table 1 shows the [HB]/[BA] ratios observed in the controlled potential electrolyses under different pH conditions. In all cases the addition of α-CD resulted in decreases in the ratio, indicating that α-CD suppresses the dimerization. From Table 1 it can be seen that the ratio is dependent on the pH of the electrolyte. However, the trend cannot be attributed mainly to the pH effect since the cathode potentials in the present cases are not sufficiently negative with respect to the half-wave potentials.[7] We selected the relatively mild potentials since sufficiently negative potentials (*i.e.*, high current densities) favored

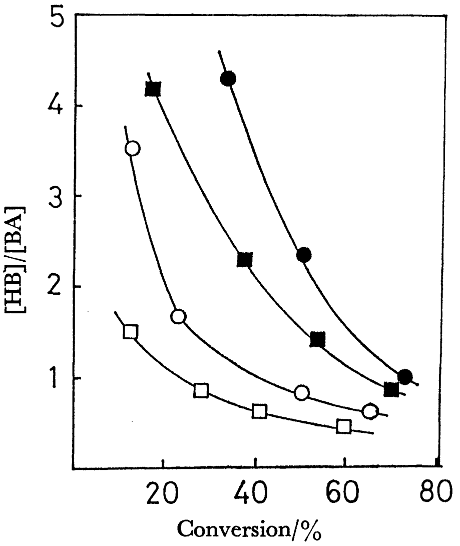

Fig. 3. Relationship between [HB]/[BA] ratio and conversion observed in the controlled current electrolysis at pH 4.6.
●: 0.33 A dm^{-2}, without CD, ○: 0.33 A dm^{-2} with α-CD (40 mmol dm^{-3}), ■: 0.50 A dm^{-2}, without CD, □: 0.50 A dm^{-2}, with α-CD (40 mmol dm^{-3}), initial concentration of benzaldehyde: 25 mmol dm^{-3}.

benzyl alcohol formation;2) such conditions are not suitable for demonstrating the effect of α-CD.

The current density has a large influence on the product ratio.2) Then, we carried out the controlled current electrolysis of benzaldehyde in the presence of α-CD. Figure 3 depicts the relationship between the [HB]/[BA] ratio and conversion of benzaldehyde in the controlled current electrolyses at 0.33 and 0.50 A dm^{-2}. Benzyl alcohol formation is favored at high current density in agreement with previous results.2) In this case, the addition of α-CD also led to decrease in the [HB]/[BA] ratio.

As described above, α-CD can suppress the dimerization reaction both in the controlled potential and in the controlled current electrolyses. It seems possible that the dimerization rate in Eq. 3 is suppressed by the steric hindrance caused by the bulky α-CD molecule since benzaldehyde is included in the interior of α-CD. The anion radical and neutral radical of benzaldehyde must be included in α-CD judging from the results by Smith and Utley;6) however, the determination of dissociation constants of the inclusion complexes is impossible since these radicals undergo following-up chemical reactions which are complicated. The suppression effect of α-CD may also explained by some influences of α-CD on other elementary reactions. However, the exact mechanism for the electroreduction of benzaldehyde is still unclear,7) therefore, further discussion is beyound this paper. The current efficiencies of the electrolyses were higher than 70% and the addition of α-CD did not affect the current efficiency.

Table 2. Diastereomeric ratio (*dl*/*meso* ratio) of hydrobenzoin formed by the controlled potential electrolysis[a)]

pH	Without CD	With α-CD (40 mmol dm^{-3})
7.0	0.96	1.11
9.1	0.85	0.97

a) Cathode potential: -1.4 V *vs*. SCE. Initial concentration of benzaldehyde: 25 mmol dm^{--3}.

Finally we investigated the effect of α-CD on the stereochemistry of hydrobenzoin formed by the dimerization reaction. The *dl*/*meso* ratios9) of hydrobenzoin are listed in Table 2. The effect of α-CD is quite small, though the addition of α-CD results in a slight increase in the *dl*/*meso* ratio. This result indicates that dimerization between molecules included in α-CD hardly takes place due to the steric hindrance. The dimerization would occur between free molecules; in the presence of α-CD *ca*. 20% of benzaldehyde exists in the free form at any instance. Therefore, the addition of α-CD cannot largely affect the stereochemistry of hydrobenzoin. The above argument also suggest that α-CD suppresses the dimerization rate (Eq. 3).

In conclusion, the addition of α-CD to the electrolyte solution results in suppression of electroreductive dimerization of benzaldehyde (hydrobenzoin formation). This is probably attained by reducing the dimerization rate between the intermediate radicals, since inclusion of substrate in α-CD provides a severe steric hindrance around reaction sites. The addition has a small influence on the stereochemistry of hydrobenzoin formed in the present electrolysis. This also supports the suppression effect of α-CD on the dimerization rate.

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