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Electrochemical Conversion of Alcohols into Aldehydes Mediated by Lipophilic β-Cyclodextrin Bearing a Ferrocene Moiety

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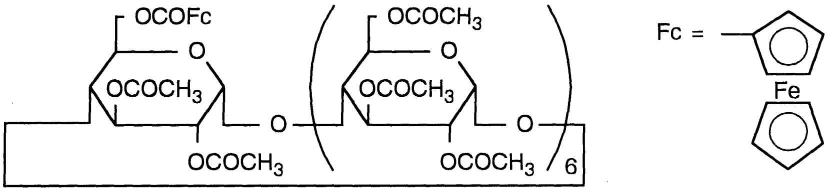
A lipophilic β-cyclodextrin bearing a ferrocene moiety in which remaining hydroxyl groups were acetylated showed a quasireversible redox property in acetonitrile. In the presence of benzyl alcohol or 1-naphthalene methanol, a catalytic current was observed. The results of macroelectrolyses indicated that the electroactive host could oxidize these alcohols into the corresponding aldehydes efficiently and selectively.

Cyclodextrin (CDs) are naturally occurring oligosaccharides composed of glucopyranose units capable of accommodating a variety of organic compounds into their cavity in aqueous solutions.1) Ferrocene and its derivatives are one of the most favorable guest compounds for CDs2) because of their suitable size and shape to be accommodated snugly into the cavity in not only aqueous but also organic solutions.3) The resulting CD-ferrocene complex has been revealed to be a strong oxidant and an efficient electron-transfer mediator for oxidizing NADH in spite of its low concentration in a solution.4) In order to attain high local concentration of the strong oxidant around the CD cavity, we have prepared ferrocene appended-β-CD (**1**) in which the remaining hydroxyl groups were completely acetylated5) to make it soluble in organic solutions. In this communication, we will report the successful results of electrocatalytic oxidation of benzyl alcohol (**4**) and 1-naphthalene methanol (**5**) into benzaldehyde (**6**) and 1-naphthaldehyde (**7**), respectively, in acetonitrile (MeCN) by **1**.



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Cyclic voltammogram (CV) of **1** in MeCN was depicted in Fig. 1-A (curve a), which showed that **1** was oxidized at E_{pa} = 0.72 V (vs. Ag / AgCl). This CV also indicates that the redox process was quasireversible as in the cases of ferrocene and its derivatives. The addition of **4** and 2,6-lutidine as a base to the solution caused a drastic change in the CV pattern (Fig. 1-A, curve b); the oxidation current (i_a) increased and the reduction current (i_c) decreased nearly to zero. This strongly indicates that **1** oxidized **4** catalytically in the presence of 2,6-lutidine.7) Methyl ferrocenecarboxylate (**2**) also showed a quasireversible CV pattern with E_{pa} = 0.69 V (vs. Ag / AgCl), which is slightly negative as compared to E_{pa} of **1**, and negligible increase in i_a was observed in the presence of **4** and 2,6-lutidine. The addition of peracetylated β-CD (**3**) induced a small change in the CV pattern of **2**. These results clearly demonstrate that **2** can hardly oxidize **4** even in the presence of **3** (see Fig. 1-B, 1-C).

It is known that **4** was electrochemically converted into **6** at high potential over 1.5 V.[7,8] From the above preferable results, macroelectrolyses of **4** and its benzologue **5** were performed with a divided cell separated by a

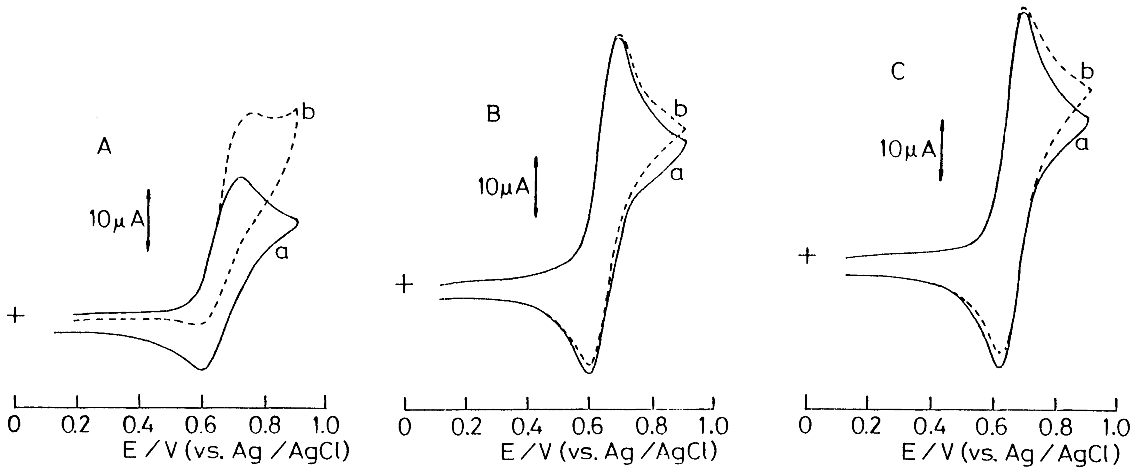


Fig. 1. Cyclic voltammograms of ferrocene derivatives (A, **1**; B, **2**; C, **2** in the presence of **3**), alone (a), or in the presence of **4** and 2,6-lutidine (b) in MeCN solutions. Conditions: Sweep rate, 50 mV s^{-1}; working electrode, glassy carbon (0.283 cm^2); reference electrode, Ag/AgCl; supporting electrolyte, Et_4NClO_4 (0.1 M(=mol dm^{-3})); concentrations of **1**, **2**, **3**, **4**, and 2,6-lutidine were 1.92, 2.10, 10.0, 0.161, and 0.144 mM, respectively.

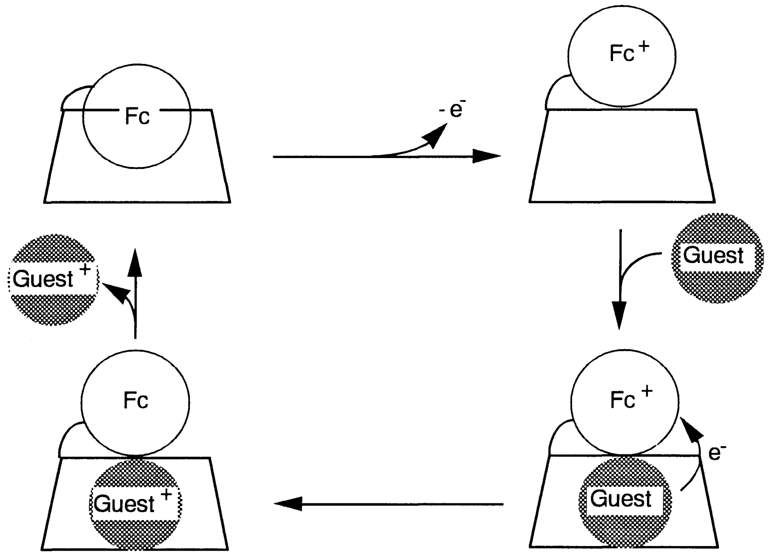
Table 1. Results on the Macroelectrolyses of Benzyl Alcohol (**4**) and 1-Naphthalene Methanol (**5**) into Corresponding Aldehydes at Constant Potential with the Ferrocene Derivatives [a)]

Mediator	Alcohol	Additive	Charge Passed	Electrolysis Time[b)]	Yield in Electricity[c)]	Aldehyde Yield[d)]	Turnover Number[c)]
(conc / mM)	(conc / mM)	(conc / mM)	C	h	%	%	
1 (11.2)	**4** (337)	-	323	12	36.8	36.8	22.2
2 (11.8)	**4** (381)	-	1.81	24	14.2	0.07	0.045
2 (11.8)	**4** (385)	**3** (48.2)	13.6	24	25.0	0.91	0.594
1 (11.1)	**5** (338)	-	327	12	96.0	96.0	58.5
2 (11.8)	**5** (341)	-	32.1	24	62.1	6.05	3.50
2 (11.8)	**5** (350)	**3** (48.2)	38.9	24	82.5	9.50	5.64

a) All experiments were performed at the following conditions: Volume of the solutions, 5 cm^3; working Electrode, carbon felt (3.15 cm^2); setting potential, 0.9 V (vs. Ag/AgCl); supporting electrolyte, Et_4NClO_4 (0.1 M). For each case 2,6-lutidine equimolar to the alcohol was added as a base. b) Time when no current was observed was regarded as the end of the electrolysis. c) Yield in Electricity (%) = $96500 \cdot n \cdot X_p \cdot 100/PC$, Turnover Number = $X_p \cdot n/X_m$, n : the number of mediator participating in a reaction cycle, 2 for those reactions, X_p and X_m : the amount of the product and mediator, respctviely, PC : Chrage Passed. d) Quantitative analyses were performed on gas chromatography equipped with Cp-Cyclodextrin capillary column (ϕ 3 mm x 25 m). During electrolysis products except for the corresponding aldehyde (**6** or **7**) were found as minor components.

Nafion membrane. Macroelectrolyses of **4** and **5** were also carried out using **2** with and without **3**. The results were shown in Table 1, which demonstrates that **4** and **5** were oxidized into the corresponding aldehydes efficiently by **1**. The control experiments using **2** showed scarce effect of **2** on oxidizing **4** and **5**. In all cases, the oxidation current decreased gradually with increasing electrolysis time. This may be due to the decomposition of the ferrocene unit. However, the yield in electricity for **1** is identical to that of product yield, indicating that **4** or **5** consumed in the reaction was completely converted into **6** or **7** by **1**. Although the product yields for **2** (with and without **3**) are extremely low, the corresponding yields in electricity were found to be relatively high.

It is known that the complexation of CDs with a guest occurs usually in aqueous solution.[1)] However, ferrocene can be accommodated by CDs even in organic media.[3)] Indeed, induced circular dichroism (ICD) of **1** in an MeCN solution was observed with the ICD values of 1080 (340 nm), 1000 (418 nm), and -1650 degree mol^{-1} dm^3 cm^{-1} (480 nm), indicating that the ferrocene moiety of **1** existed in[9)] or near[10)] the CD cavity of **1**. The ICD disappeared and no new band appeared under the electrolysis conditions, indicating that the ferricinium cation could not interact with the CD cavity of **1**. These findings agreed with the previous suggestion[4)] that ferricinium cation was hardly incorporated into a β-CD cavity. Although a complex between β-CD and the ferricinium cation is a minor species in a solution, it acts as a strong oxidant.[4)] The formation of the *intramolecular* complex of **1** may result in the slightly positive E_{pa} value as compared to that of **2**. However, it seems to be difficult to explain fully the large difference in converting the alcohols into the aldehydes between the cases of **1** and **2** with the fact of such small E_{pa} shift. When **1** is oxidized, the positively charged ferricinium cation moiety is excluded from the cavity and it becomes vacant into which other substrates can insert. The resulting *intermolecular* complex between **1** and **4**, though the concentration of the complex is sufficiently low, facilitates the electron transfer from **4** to the ferricinium cation because the mutual location of the two species is fixed and, thus, the distance becomes short. This mechanism may result in the fact that the oxidation of **5** into **7** was more efficient than that of **4** into **6**, since the naphthalene ring is more suitable to β-CD cavity than the benzene ring. In accordance with this mechanism, one electron oxidized species of **4**, then, is excluded from the cavity owing to its charged nature as well as to the re-insertion of the ferrocene moiety recovered by the electron transfer. This proposed reaction mechanism is illustrated in Scheme 1.



Scheme 1.

On the other hand, an ICD measurement for **2** in the presence of **3** revealed that **2** could not interact with **3**. This strongly indicates that ferrocene/ferricinium cation couple acts as an efficient electron mediator which can oxidize the alcohols into the corresponding aldehydes only in the case where ferrocene is attached on the CD framework.

The negligible ability of **2** on the oxidation of **4** even in the presence of **3** may reveal that the short distance for the electron transfer from the accommodated **4** to the ferricinium cation existing near the cavity is necessary for the efficient conversion of **4** into **6**.[11] The oxidant moiety of **1** might be less solvated and the rate of the electron transfer might be fast because the CD molecular wall protects the chraged moiety from the approaches of a solvent molecule and other species.

In summary, we found that **1** was an effective electron-transfer mediator for the electrocatalytic conversion of alcohols, **4** and **5**, into the corresponding aldehydes, **6** and **7**. Our result indicates that **1** is an efficient mediator for oxidation of alcohols under a mild condition. In addition, to our knowledge, **1** would be the first example of a ferrocene-based electron-transfer mediator which oxidizes alcohols efficiently. In this regard, electrocatalytic oxidation of other substrates by **1** and other ferrocene-appended CDs as well as substantiating reaction kinetics are now under way.

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5) Compound **1** was prepared form 6^{A}-O-ferrocenecarbonyl-β-CD[5] and acetic anhydride in pyridine. Purification with SiO_2 column afforded pure **1**. MS (FAB) M/Z 2187 ($[M+H]^+$); ^{1}H-NMR (CD_3CN, TMS), δ 1.94-2.18(m, acetyl, overlapped with CH_3CN), 3.84-4.07 (m, 7 H, C^4H), 4.12-4.47 (m, 28 H, C^5H, C^6H, ferrocene), 4.72-4.86 (m, 9H, C^2H, ferrocene), 5.04-5.26 (m, 7H, C^1H), 5.33-5.46 (m, 7H, C^3H). Anal. Found: C, 50.36; H, 5.67%. Calcd for $C_{93}H_{118}O_{56}Fe\cdot 2H_2O$: C, 50.22; H, 5.53%.

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