Selective Electrosyntheses on Chemically Modified Electrode. II. Anodic Chlorination of Anisole with Cyclodextrin on Electrode Surfaces and in Solution

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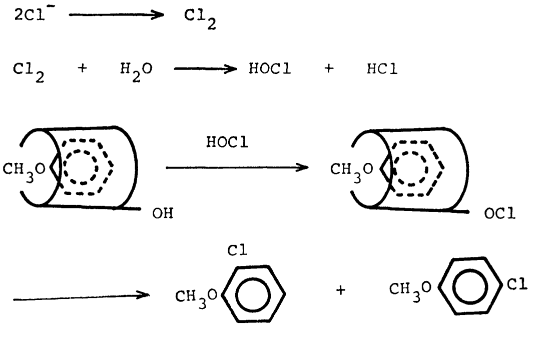
The anodic chlorination of anisole on an α-cyclodextrin (α-CD) chemically modified electrode *via* ether linkage (α-CD-CME) and a naked graphite electrode with α-CD or β-CD in solution was studied. In the presence of CD, the *p*- to *o*-chloroanisole ratio, formed in the reaction, was higher than that in the absence of CD since *o*-positions of anisole included in CD are blocked by the inner wall of CD. Especially, α-CD had a profound effect on the *p*-isomer formation. Increasing the concentration of NaCl added as a supporting electrolyte in the presence of α-CD resulted in a decrease in the ratio because of the inhibition effect of chloride ion on the inclusion of anisole in α-CD, whereas such effect was small in the presence of β-CD. The ratio on α-CD-CME was slightly higher than that on the naked electrode. This indicates that α-CD was introduced on the graphite surface but the surface coverage of α-CD was low, which was in accord with the ESCA results of α-CD-CME.

Many studies of chemically modified electrodes (CMEs) have been developed in order to enhance or to change the characteristics of electrodes, but there have been only a few papers[1-4] on selective electrosyntheses with CMEs. Miller and his co-workers carried out asymmetric reductions[1,2] and asymmetric oxidations[2,3] with CMEs prepared by attaching optically active compounds on the electrode surfaces. However, the optical yields in their works were not high. In order to realize high selectivity in electrolysis with CME, it is necessary that the attached species strongly interact with the substrates as well as resist oxidation or reduction. Cyclodextrins (CDs) meet such requirements. These molecules are cyclic 1,4-linked D-glucopyranose oligomers containing several glucose units and can include various compounds in their cavities in aqueous solution.[5] Especially, α-CD (containing of 6 glucose units) and β-CD (containing of 7 glucose units) have cavities whose sizes are suitable for including benzene and naphthalene rings, respectively. Therefore, these compounds have been studied in various fields because of their catalytic abilities as enzyme models.[6,7] Taking advantage of the environment of α-CD's cavity, Breslow *et al.* carried out the selective chlorination in the presence of α-CD[8] and *O*-alkylated polymer of α-CD.[9]

Such selective chlorination would proceed in the anodic chlorination in the presence of CD (Scheme 1). Chloride ion is first oxidized at the anode to chlorine gas, and second, the nascent state of chlorine is reacted with H_2O to form hypochlorous acid (HOCl).[10] The HOCl formed attacks the anisole included in CD preferentially at the *p*-position because the *o*-positions of anisole are blocked by the inner wall of CD;[11] whereas free anisole is subject to substitution at the *o*-positions as well as at the *p*-position. Our preliminary results of the anodic chlorination of anisole with α-CD-CME (*via* ester linkage) showed that the chlorination occurred preferentially at the *p*-position.[4]



Scheme 1. Mechanism of the anodic chlorination of anisole in the presence of CD.

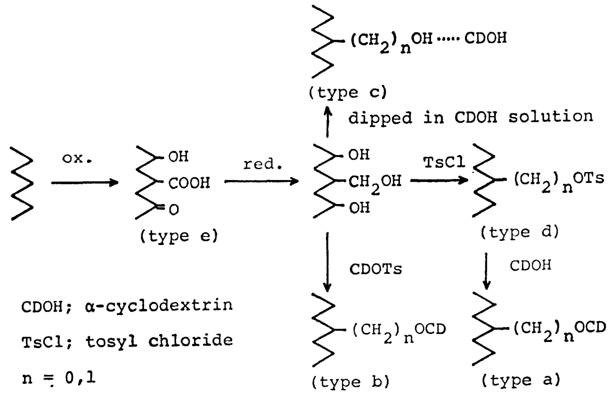
We report here the selective anodic chlorination of anisole on an α-CD-CME (*via* ether linkage) and a naked graphite electrode with α-CD or β-CD in solution in detail. In comparison with Breslow's method of homogeneous or heterogeneous reactions,[8,9] the anodic chlorination in this work has following merits. (1) No reagents such as HOCl difficult to handle are required because the reagent is formed quite easily by electrolysis of chloride salts added as a supporting electrolyte. (2) In a homogeneous reaction, a high concentration of CD is required to attain high selectivity. However, in the anodic chlorination with α-CD-CME, a certain selectivity is expected even in the absence of CD in solution, because the reaction proceeds at electrode surface on which α-CD is introduced by covalent bonding. (3) In Breslow's method with *O*-alkylated polymer of α-CD, an aqueous solution of HOCl should be passed through a column packed with the polymer which was loaded with anisole beforehand. However, in the present work, the above troublesome stepwise operation is omitted, because the reagent (HOCl) is produced electrochemically.

Experimental

A graphite plate (Tokai Carbon Co. G 2080) was cut into 30×20×2 mm plates for electrolyses and 17×5×2 mm plates for ESCA measurements. An AEI model ES 200 was used for ESCA measurements with a Mg anode under a vacuum of $10^{-8}-10^{-9}$ Torr. The binding energies were computed and corrected by the method reported.[12] All electrolyses were carried out with a Yanaco VE-8 controlled potential electrolyzer. The supporting electrolyte was NaCl, and the reference electrode was a saturated calomel electrode (SCE) inserted near the anode. The electrolysis cell was a divided

H-type with a graphite anode (30×20×2 mm) and a Pt gauze cathode. The anolyte consisted of anisole and NaCl dissolved in 50 ml of water (non-buffered), and was stirred with a magnetic bar. The cell was set in a thermostat kept at constant temperature. After electrolysis, the anolyte was extracted with ether three times and dried with Na_2SO_4 and then concentrated with an evaporator for gas chromatography (Shimadzu GC-6A). The injection and column temperatures of the gas chromatograph were 210 °C and 150 °C, respectively. The column was 2 m×3 ϕ SUS packed with 10% Carbowax 20 M on Chromosorb W. Quantitative analyses of the chloroanisoles formed were carried out by comparison with a calibration line of authentic samples. The ratios of *para*- to *ortho*-isomer (*p*-/*o*- ratios), the conversion of anisole, and the yields of monochloroanisoles of all products were determined using these gas chromatographic data.

Synthetic Procedure for α-CD-CME. The graphite plates were first dipped in water for 2 h to remove water soluble impurities on the surface and were then treated with a solution of 0.2 M $K_2Cr_2O_7$ in concd H_2SO_4 for 2 h to introduce the surface functional groups containing oxygen.[13] The oxidized electrodes were reduced electrochemically at −1.5 V *vs.* SCE in aqueous 0.5 M Na_2SO_4 solution to increase the hydroxyl groups on the graphite surface.[13] The reduced graphite electrodes were reacted with tosyl chloride (TsCl) in dry pyridine for several weeks and then treated with an aqueous solution of 0.1 M α-CD in 0.1 M KOH for 4 days. After the reaction, the electrodes were washed with water repeatedly to remove the adsorbed α-CD on the graphite surfaces. Another method for the modification of graphite electrodes with α-CD was as follows. Reduced graphite was reacted with α-CD tosylate[14] in 0.1 M KOH solution (pyridine:H_2O=30:70) for a week, followed by thorough washing with water. To compare these α-CD-CMEs with a physically adsorbed α-CD electrode, the reduced graphite electrode was dipped into 0.1 M KOH aqueous solution containing α-CD (0.1 M) for 10 h, and then washed with water (Scheme 2).



Scheme 2. Synthetic procedure for α-CD-CME and α-CD adsorbed electrode.

Results and Discussion

The potential range in the anodic chlorination must be carefully chosen because the substrate, anisole, is oxidized when the anode potential exceeds *ca.* 1.3 V *vs.* SCE in aqueous NaCl solution. At such a high potential, side reactions can also occur and *p*-/*o*- ratio or other values become inaccurate, and furthermore, the graphite electrode itself is oxidized. Consequently, it is desirable to set the anodic potential as low as possible. However, at low anodic potentials, the chlorination cannot occur or proceeds very slowly because chlorine generation starts at 0.9—1.0 V *vs.* SCE in aqueous NaCl solution, so that the anodic potential of 1.20 V *vs.* SCE was used.

In the Absence of CD. Increasing the concentration of anisole resulted in an increase in the *p*-/*o*- ratio and also an increase in the yields of chloroanisoles (Table 1, expts. 1 and 2). The *p*-/*o*- ratio was gradually decreased with increasing conversion of anisole during the electrolysis both on the untreated graphite (expts. 3, 4, and 5) and on the oxidized graphite (expts. 6 and 7). But a higher *p*-/*o*- ratio was observed on the untreated graphite electrode than the oxidized one. The yield of chloroanisoles was independent of the mode of preparation of the electrode, *i.e.* whether graphite electrode was oxidized or not. The influence of the concentration of NaCl added in the anolyte at low conversion of anisole was not great (expts. 2, 3, and 8). A slight tendency of the *p*-/*o*- ratio to increase was observed with a decrease in the concentration of NaCl. The temperature during electrolysis did not affect the *p*-/*o*- ratio in the temperature range 0—30 °C, but did affect the yield of chloroanisoles (expts. 8 and 9). It took *ca.* 10 min to convert 10% of anisole in the anolyte and the current efficiency was *ca.* 50%. The *p*-/*o*- ratios in the present work are a little lower than those in the previous report.[4] This might be attributed to the difference in the surface properties of the graphite plates used. The ratios on the oxidized electrodes in the present work, however, showed only slight deviations. After electrolysis (10% conversion of anisole), the pH

Table 1. Anodic chlorination of anisole in the absence of CD

Expt.	Conv/%[a]	*p*-/*o*-[b]	Mono/%[c]	Concn of NaCl/M	Concn of anisole/10^3M	Anode	Temp/°C
1	10.6	5.9	90	1.0	2.0	untreated	20
2	4.2	2.3	82	1.0	1.0	untreated	20
3	4.3	2.4	83	0.5	1.0	untreated	20
4	19	2.3	79	0.5	1.0	untreated	20
5	48	1.8	78	0.5	1.0	untreated	20
6	7.9	2.1	81	0.5	1.0	oxidized	20
7	24	1.6	80	0.5	1.0	oxidized	20
8	5.1	2.6	82	0.1	1.0	untreated	20
9	7.0	2.7	70	0.1	1.0	untreated	0

Anodic potential: 1.20 V *vs.* SCE. a) Conversion of anisole in the course of electrolysis. b) Ratio of *p*- to *o*-chloroanisole in the electrolysis. c) Yield of monochloroanisoles.

TABLE 2. ANODIC CHLORINATION OF ANISOLE IN THE PRESENCE OF β-CD

Expt.	Conv/%	*p*-/*o*-	Mono/%	Concn of NaCl/M	Concn of β-CD/10^3M	Included[a)] anisole/%	Temp/°C
10	8.5	3.2	85	1.0	10.0	34	20
11	7.3	3.3	82	0.5	10.0	34	20
12	7.1	3.5	88	0.1	10.0	34	20
13	3.0	3.2	82	0.1	5.0	20	20
14	5.0	2.6	74	0.1	1.0	4.8	20
15	4.0	4.1	73	0.1	10.0		0

Anode: untreated graphite electrode. Anodic potential: 1.20 V *vs*. SCE. Concentration of anisole in anolyte: 1.0×10^{-3} M. a) Calculated by using the dissociation constant of β-CD–anisole complex, 1.9×10^{-2} M.

of the anolyte became 2.0 since hydrochloric acid was generated in the course of the electrolysis.

In the Presence of β-CD. The variations in *p*-/*o*- ratios and yields of chloroanisoles in the presence of β-CD, together with the percentages of included anisole in the β-CD solution, are shown in Table 2. The table shows a slight increase in the *p*-/*o*- ratio with increasing concentration of β-CD, which indicates that the *p*-isomer was formed preferentially in the presence of β-CD in solution (expts. 12, 13, and 14). This supports the idea described above that the reagent (HOCl) can scarcely attack the *o*-positions of anisole included in β-CD.[11)] The temperature had some influence on the *p*-/*o*- ratio. When electrolysis was carried out at 0 °C, the ratio was 4.1 which was higher than the 3.5 value observed at 20 °C (expts. 12 and 15). This phenomenon may be a reflection of the thermodynamic nature in that CD includes substrate more easily at low temperatures.[15)] The yield of monochloroanisoles was low at low temperature in a similar manner as in the absence of CD (Table 1, expts. 8 and 9). As the dissociation constant of β-CD–anisole complex is 1.9×10^{-2} M,[16)] only 34% of the anisole is included in the 10^{-2} M β-CD solution which is almost the maximum concentration of β-CD in aqueous solution. This low complex formation of anisole with β-CD might be a cause for the low regioselectivity in the anodic chlorination of anisole in the presence of β-CD. The effect of the concentration of NaCl on the *p*-/*o*- ratios was small, but a slight tendency of the ratio to decrease with enhancement of the concentration of NaCl was observed (Table 2, expts. 10, 11, and 12).

In the Presence of α-CD. The results of the anodic chlorination of anisole in the presence of α-CD are given in Table 3. The electrolytic conditions were the same as those in the presence of β-CD. The *p*-/*o*- ratios became greater as the concentration of α-CD increased, *i.e.* the *p*-isomer was formed selectively at high concentrations of α-CD in solution. The yield of monochloroanisoles in the presence of α-CD was almost the same as that in the presence of β-CD, but selectivity of *p*-isomer formation was much higher. This is explained by the fact that α-CD binds anisole about 5 times stronger than β-CD. The dissociation constant of the α-CD–anisole complex is 3.75×10^{-3} M.[9)] The table also shows that the *p*-/*o*- ratio increases significantly with decreasing NaCl concentration at a constant concentration of α-CD (Table 3, expts. 16, 18, and 22). This indicates that the inhibition effect of Cl^-[17)] on the inclusion of anisole in α-CD is very great. On the other hand, the concentration of NaCl had only a small effect on the *p*-/*o*- ratios in the anodic chloriantion in the presence of β-CD (Table 2, expts. 10, 11, and 12), which is explained by the fact that Cl^- is not included in β-CD.[17)] It is also shown that the selectivities in this work in the presence of α-CD are higher than those in the homogeneous reactions reported by Breslow and Campbell (Table 4).[8)] The differences in *p*-/*o*- ratios (Table 3, expts. 16, 18, and 22) were greater than those expected from the percentages of included anisole in solution. These phenomena may reflect surface effects in which the concentrations of reagents on the graphite electrode surface are different from those in the bulk solution. The difference in the ratios in the presence of α-CD and in the presence of β-CD at the same percentage of included anisole in the bulk solution (*e.g.*, the difference between expt. 12, Table 2 and expt. 19, Table 3) may be accounted for by the following possi-

TABLE 3. ANODIC CHLORINATION OF ANISOLE IN THE PRESENCE OF α-CD

Expt.	Conv/%	*p*-/*o*-	Mono/%	Concn of NaCl/M	Concn of α-CD/10^3M	Included[a)] anisole/%
16	6.1	9.1	81	1.0	10.0	42
17	6.0	7.9		1.0	5.0	26
18	4.9	12.6	85	0.5	10.0	54
19	5.7	8.2	81	0.5	5.0	36
20	6.4	6.5	87	0.5	1.0	9.6
21	6.4	2.5	87	0.5	0.1	1.0
22	2.0	25	74	0.1	10.0	66
23	3.2	22	70	0.1	5.0	49

Anode: untreated graphite electrode. Anodic potential: 1.20 V *vs*. SCE. Concentration of anisole in anolyte: 1.0×10^{-3} M. a) Calculated by using the dissociation constant of α-CD–anisole complex, 3.72×10^{-3} M, under the consideration of the inhibition effect of Cl^-.

Table 4. Results of homogeneous chlorination of anisole in Breslow's report[8)]

p-/*o*-	Included anisole/%
3.43	20
5.49	33
7.42	43
11.3	56
15.4	64

bilities.

(1) α-CD is more strongly adsorbed on the graphite surface than β-CD at this potential.

(2) Slight movement of the included anisole in β-CD is allowed since the size of the β-CD cavity is a little larger than that of the anisole molecule; whereas, the anisole included in α-CD is not free to move.

Table 5. Anodic chlorination of anisole with α-CD-CME (*via* ether bond)

Expt.	Conv/%	*p*-/*o*-	Mono/%	Type of electrode
24	8.0	3.1	80	a)
25	4.5	1.9	75	b)
26	7.1	1.8	79	c)
27	8.9	2.1	83	a) treated with $K_2Cr_2O_7$

a) Obtained by the reaction between the tosylated graphite and α-CD. b) Obtained by the reaction between the reduced graphite and tosylated α-CD. c) Obtained by dipping the reduced graphite in α-CD aqueous solution followed by washing with water.

Anodic Chlorination with α-CD-CME. The results of the anodic chlorination with α-CD-CME (*via* ether linkage) obtained by the reaction between the tosylated graphite and α-CD (type a), by the reaction between the reduced graphite and tosylated α-CD (type b), and α-CD adsorbed graphite (type c) are given in Table 5. Type a shows a slight higher *p*-/*o*- ratio than the others, but its value is low compared with those in the presence of α-CD and on α-CD-CME (*via* ester linkage).[4)] This indicates that the surface coverage of α-CD introduced by the chemical modification was low on type a. Type b showed no selectivity. The attachment of α-CD on the graphite surface by the reaction between the reduced graphite and α-CD tosylate was very difficult. The reaction may be hindered by the intra- or intermolecular reaction of tosylated α-CD. No selectivity was also obtained on type c. The adsorbed α-CD on the reduced graphite electrode was removed by washing with water. The yields of chloroanisoles formed in the anodic chlorination with the above three types of electrodes were the same as those with unmodified electrodes. When type a was treated with $K_2Cr_2O_7$ for 1 h to remove α-CD on type a, the *p*-/*o*- ratio became lower than that of the electrode of type a not subject to the treatment.

ESCA Results. Three types of electrodes, type a, the tosylated graphite (type d), and the oxidized graphite (type e), were examined by ESCA. Fig. 1 shows wide ESCA spectra obtained. There are strong peaks of O 1s at 532 eV and C 1s at 285 eV on type e, which are almost the same as those of glassy carbon baked in the air.[18)] No peaks based either on Cr or on K of $K_2Cr_2O_7$ appears. The ESCA spectrum of type d shows small S 2s at 233 eV and S 2p at 170 eV in addition to the above peaks. These sulfur peaks originate from sulfur atoms in the tosyl group introduced on the graphite surface, and the peaks disappear with further modification with α-CD. This indicates that the tosyl group was removed by the reaction between the tosylated graphite (type d) and α-CD. Higher resolution ESCA spectra of O 1s in type a and type e are shown in Fig. 2. The peak intensity of type a is larger than that of type e and the peak is shifted toward a higher binding energy compared with that of type e. It is, however, difficult to assign the chemical shift, since various types of oxygen atoms exist on the

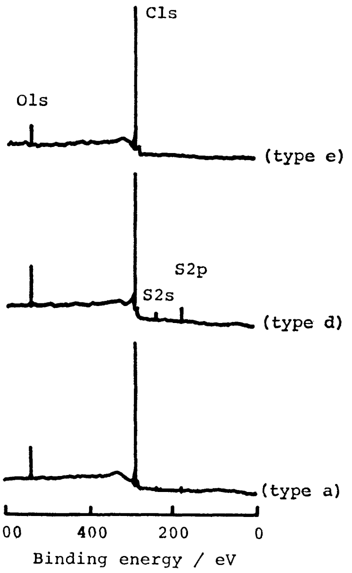


Fig. 1. ESCA spectra of the α-CD-CME (type a), the tosylated (type d), and the oxidized (type e) graphite electrodes.

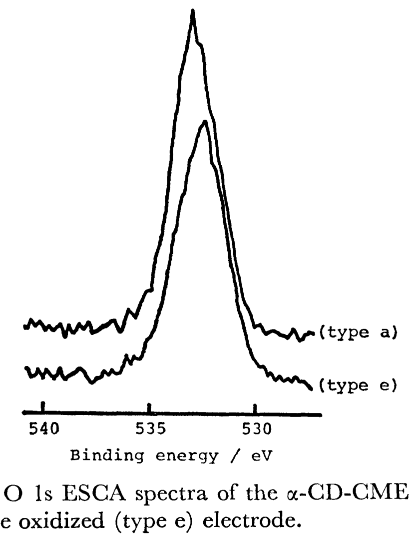


Fig. 2. O 1s ESCA spectra of the α-CD-CME (type a) and the oxidized (type e) electrode.

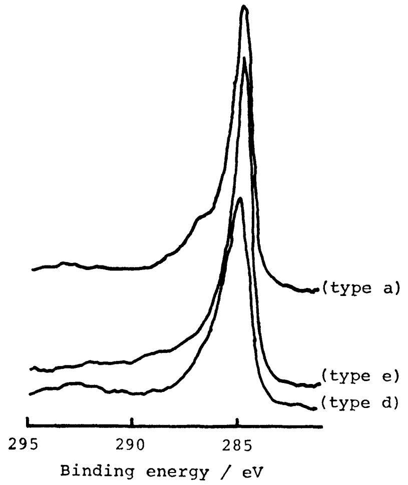


Fig. 3. C 1s ESCA spectra of the α-CD-CME (type a), the tosylated (type d), and the oxidized (type e) electrodes.

graphite surfaces. The changes in higher resolution ESCA spectra of C 1s of types a, d, and e are shown in Fig. 3. By performing chemical modification with α-CD on the graphite surface, a shoulder at the higher binding energy side of the main peak at 285 eV appeared but its height was lower than that of the previous results.[4] This shoulder may be accounted for by consideration of the charge on the carbon atoms in α-CD. All carbon atoms in α-CD adjoin oxygen atoms which have a higher electronegativity compared with the carbon atoms.[19] The surface coverage by α-CD on type a is not large because the shoulder is small. The C 1s of type d appeared at the same binding energy as type e and has no shoulder. These results also support the conclusion that the shoulder in the spectrum of type a is attributed to α-CD on the graphite surface. Fig. 4 shows S 2s ESCA spectra of types a, d, and e.

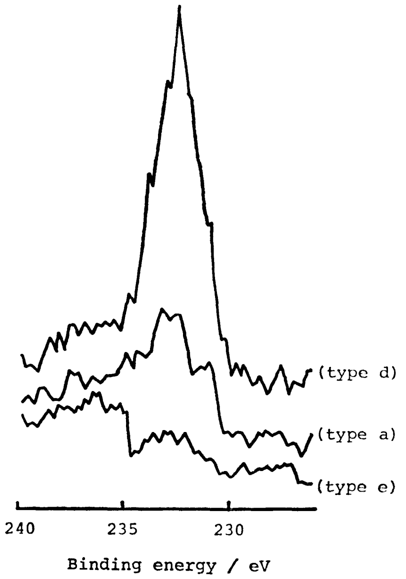


Fig. 4. S 2s ESCA spectra of the α-CD-CME (type a), the tosylated (type d), and the oxidized (type e) electrodes.

The peak of type d appeared at *ca.* 233 eV which is shifted toward the higher binding energy side compared with 229 eV, the binding energy of 2s electron in free sulfur.[20] The shift of the S 2s is in agreement with that of the S 2p of sulfonated compounds, *i.e.* the peaks of these compounds shift to a higher binding energy than those of the sulfide or disulfide compounds because the calculated charges on the sulfur atoms in sulfonated compounds are high.[19] On the other hand, the S 2s peak on type e could not be observed, which indicates that the surface is free from contamination by sulfur compounds on type e. On type a, small S 2s peak still remained. Most of tosyl group were removed by the reaction between the tosylated graphite (type d) and α-CD, but some unreacted tosyl groups remained on type a.

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