Chiral Separation of Arylalcohols by Capillary Electrophoresis Using Sulfonated β-Cyclodextrin and Ag Colloids as Additives

Seong-Ho Choi,* Hyen-Ju Noh,† and Kwang-Pill Lee†

*Department of Chemistry, Hannam University, Daejeon 306-791, Korea. *E-mail: shchoi@hannam.ac.kr*
†Department of Chemistry Graduate School, Kyungpook National University, Daegu 702-701, Korea
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Chiral separation of arylalcohols such as 1-phenyl-1-propanol, 1-phenyl-2-propanol, and 2-phenyl-1-propanol by capillary electrophoresis was studied using sulfonated β-cyclodextrin (CD) as a chiral selector and Ag colloids as an additive. The optimum separation condition of arylalcohols was found to be the chiral selector concentration of 6.5 mM, applied voltage of 15 kV, and pH of 7.0. In order to improve chiral separation, an Ag colloid was mixed with a running buffer. The resolution in the Ag colloid-mixed running buffer was considerably superior to that obtained with the sulfonated β-CD alone. The molar ratio of sulfonated β-CD to Ag colloid, which is one of critical parameters affecting resolution, was found to be optimum at 65 : 1. In order to elucidate the resolution mechanism, an inclusion-complex of the arylalcohols with sulfonated β-CD was prepared by mixing and shaking in solution, and then characterized by cyclic voltammetry (CV). The inclusion mechanism was also discussed using experimental results.

Key Words : Capillary electrophoresis, Ag colloid, γ-Irradiation, Sulfonated β-cyclodextrin

Introduction

Enantiomerically pure arylalcohols are applied in many fields such as enantioselective synthesis and analysis. Enantiomerical separation of arylalcohols has been performed with chromatography methods such as gas chromatography (GC)[1] and high-performance liquid chromatography (HPLC).[2] In recent years, use of chiral capillary electrophoresis (CE)[3] has grown rapidly and has proven to be a useful tool for separation of arylalcohols enantiomers. Chiral CE offers significant advantages over GC or HPLC in terms of higher separation efficiency and lower sample reagent consumption.

Cyclodextrin (CD) has been extensively used in separations due to its unique property to form inclusion-compounds with smaller hydrophobic molecules. The stability constants of the inclusion-compounds vary with the shape and the size of the smaller molecules, and thus CDs provide separation of molecules based on the shape and the size of the molecules.

There have been many publications on the chiral separation of racemic compounds by CE using CDs as chiral selectors.[4-6] In a previous investigation,[7] a CD polymer was synthesized and applied for the HPLC stationary phase in order to separate pollutants. CDs have also been used as a host-compound for preparation of inclusion complexes.[8-10]

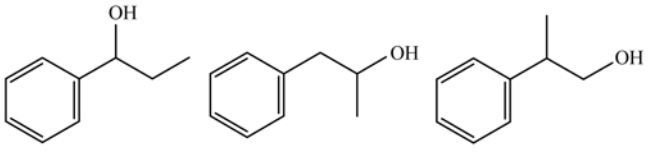
It is well known that the use of a binary selector CD, such as a mixture of a neutral CD and an ionic CD, can enhance the selectivity and resolution in chiral CE.[11,12] A combination of a CD and chiral surfactant like a bile salt was also found to be effective.[13] The application of a mixed selector of a CD and bile acid surfactant has been extended to the chiral separation of the amino acid derivatives of naphthalene-2,3-dicarboxaldehyde[14] and some drugs.[12] The chiral separation of racemic arylalcohols using a mixture of ionic CD and precious metallic colloid as additives has not been reported.

The preparation of precious metallic colloids by γ-radiation (radiolytic technique) has some advantages,[15,16] as compared to conventional chemical and photochemical techniques: (1) the reduction of metal ions can be controlled without the use of an excess of reducing agents or producing undesired oxidation by-products of the reductant. (2) the reaction rate is well-known, since the number of reducing equivalents generated by radiation is well defined. (3) radiation is absorbed regardless of the presence of light-absorbing solutes and products. (4) the reducing agent is uniformly generated in the solution.

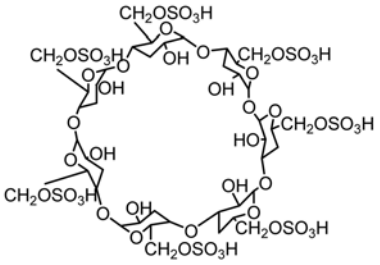
In the present work, a mixture of sulfonated β-CD (as a chiral selector) and an Ag colloid (as an additive) was employed in an attempt to improve the chiral separation of arylalcohols. The inclusion-complex of the arylalcohols with sulfonated β-CD was prepared by mixing and shaking in a solution state, and then characterized by cyclic voltammetry (CV).

Experimental Section

Chemicals. The sulfonated β-CD, 1-phenyl-1-propanol, 1-phenyl-2-propanol, and 2-phenyl-1-propanol were obtained from Aldrich Co. Scheme 1 shows the structure of arylalcohols and sulfonated β-CD used in this study. The silver nitrate ($AgNO_3$, 99.9%) was purchased from Kojima Chemicals Co., Ltd. (Japan). The poly(vinylpyrrolidone) (PVP, Mw. av. = 10,000) used as a colloid-stabilizer was obtained from Tokyo Kasei Kogyo Co., Ltd. (Japan). The 2-propanol was purchased from Tokyohasei Co. Ltd. (Japan). Other chemical reagents were used without further



1-phenyl-1-propanol 1-phenyl-2-propanol 2-phenyl-1-propanol



sulfonated β–cyclodextrin as chiral selector

Scheme 1. Structures of the arylalcohols and sulfonated β-cyclodextrin as chiral selector used in this study.

purification.

Preparation of the Ag Colloid[17] **and Running Buffer.** The Ag colloids (1.0×10^{-3} M) were prepared as follows: a mixture solution was prepared by addition of $AgNO_3$ (0.85 g), 2-propanol (30 mL) as a radical scavenger, and PVP (5.0 g) as a colloid-stabilizer in distilled water (500 mL). After the oxygen in the solution was removed by bubbling with pure nitrogen gas for 30 min, the mixture solution was irradiated by Co-60 γ-ray source. During γ-irradiation, hydrated electrons are formed as follows:

$$H_2O \rightarrow e_{aq}^-, H_3O^+, {}^{\cdot}H, H_2, {}^{\cdot}OH, H_2O_2$$

The radiation reduction of silver ions by hydrated electrons lead to the formation of Ag colloids:

$$e_{aq}^- + Ag^+ \rightarrow Ag^0$$
$$nAg^0 \rightarrow Ag_2 \rightarrow Ag_n \rightarrow Ag_{agg}$$

where n is the number of the aggregation of a few units and Ag_{agg} is the aggregate in the final stable state. The Ag colloid prepared by γ-irradiation was characterized as described earlier [18].

The running buffer was prepared by adding 0.1 M sodium phosphate buffer (20 mL) to sulfonated β-CD (*ca.* 1.3×10^{-2} mmol) and 0.2 mL Ag colloid (*ca.* 2.0×10^{-4} mmol).

Measurements. The UV spectra of the Ag colloid were recorded on a Miniature Fiber Optic UV-Vis Spectrometer (K-MAC Co. Korea). Deionized water was used as a reference material. Transmission Electron Micrographs of the samples were obtained using an Energy-Filtered Transmission Electron Microscope (EF-TEM, EM 912 Omega, Carl Zeiss, Germany) at Korea Basic Science Institute (KBSI), Korea.

CE separation was performed with a P/ACE 5500 system with a photodiode array detector (Beckman Instruments, Fullenerton, USA). An uncoated fused-silica capillary of 50 mm I.D and 57 cm (effective length of 50 cm) was used. The capillary was conditioned before each analysis by flushing successively with 0.1 M NaOH, H_2O, and buffer each for 2 min. Samples were injected with pressure at 0.5 p.s.i. for 1 s and separated at 15 kV (1 p.s.i. = 6894.76 Pa). Data in the range of 190-600 nm were acquired and processed using the P/ACE station version 1.2.

The CV-curves of the arylalcohols and inclusion complexes were obtained using a CV-50W (Bioanalytical System, Inc., Version 2.3). The platinum wire used as a counter electrode, the reference electrode (SCE), and a glass carbon electrode used as a working electrode in an electrochemical cell of a 25 mL KCl buffer solution were fabricated, and recorded after the expulsion of air by bubbling nitrogen through the solution. The scan rate was 100 mV/sec.

Results and Discussion

In order to find an optimum CE conditions for separation of arylalcohols, the effects of the applied voltage, pH, and concentration of sulfonated β-CD (a chiral selector) were examined. The optimum conditions were the separation voltage of 15 kV on pH = 7.0 and in 6.5 mM sulfonated β-CD in the absence of Ag colloid in this study (see, Fig. 1, 2, and 3).

The surface of precious metallic nanoparticles interacts with organic molecules containing various functional groups such as -SH, $-NH_2$, and -COOH. In a previous investigation,[18,19] the interaction between thiol group of the cysteine and surface of Ag colloid prepared by γ-irradiation was examined. It was found that the intensity of the circular discrimination spectra was increased by the addition of Ag colloid. The Ag colloid is expected to affect the CE resolution, because the Ag colloids interact with chiral selector (such as sulfonated β-CD) or analytes (such as arylalcohols). However, the Ag colloid as an additive has not been applied in CE so fa.. In order to improve the chiral CE separation of arylalcohols, the Ag colloid was mixed with a running buffer. The interaction of inclusion complex and colloid particle affected changing the electrophoretic mobility and is not much affected on EOF.

Figure 1 shows a TEM image and UV/VIS spectra of PVP-stabilized Ag colloid prepared by γ-irradiation. The Ag nanoparticles have the size of *ca*. 21 nm by the TEM images. In Figure 1, a characteristic UV/VIS band of the Ag colloid appears at 407 nm due to the function of the size properties of particles. The UV/VIS band of a particle is generally referred to as the plasomon resonant band.[20] It is noted that that such an absorption band was not observed before γ-irradiation.

Figure 2 shows the chiral separation of 1-phenyl-1-propanol with sulfonated β-CD in the absence of Ag colloid (a) and in the presence of Ag colloid (b). In the absence of the Ag colloid, the retention times (t_r) were 7.78 and 7.95 min, respectively, and the resolution (R_s) was *ca.* 0.18. In the presence of the Ag colloid, t_r's were 19.99 and 21.07 min,

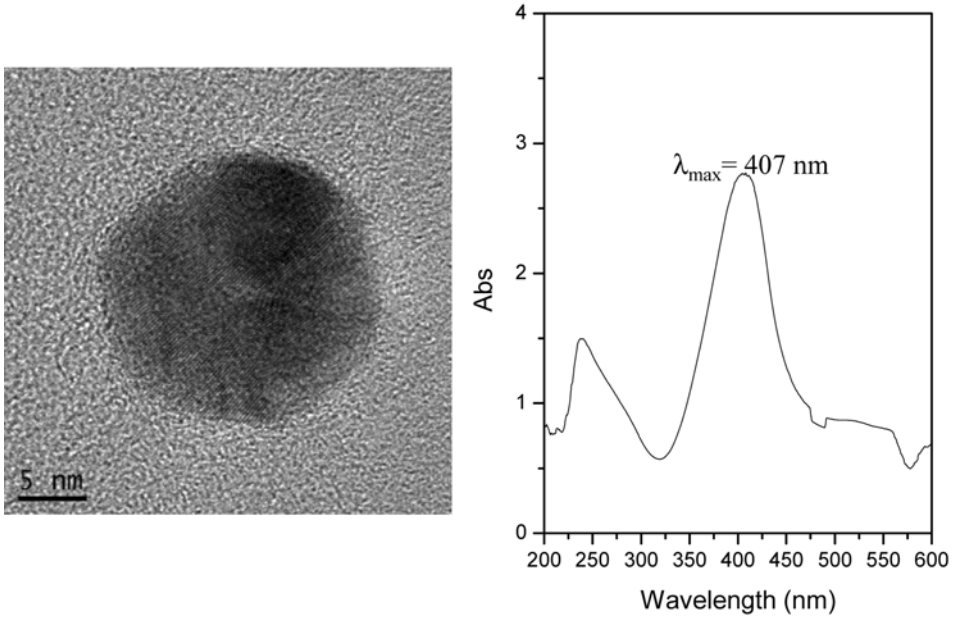


Figure 1. TEM images and UV spectra of PVP-stabilized Ag colloids prepared by γ-irradiation.

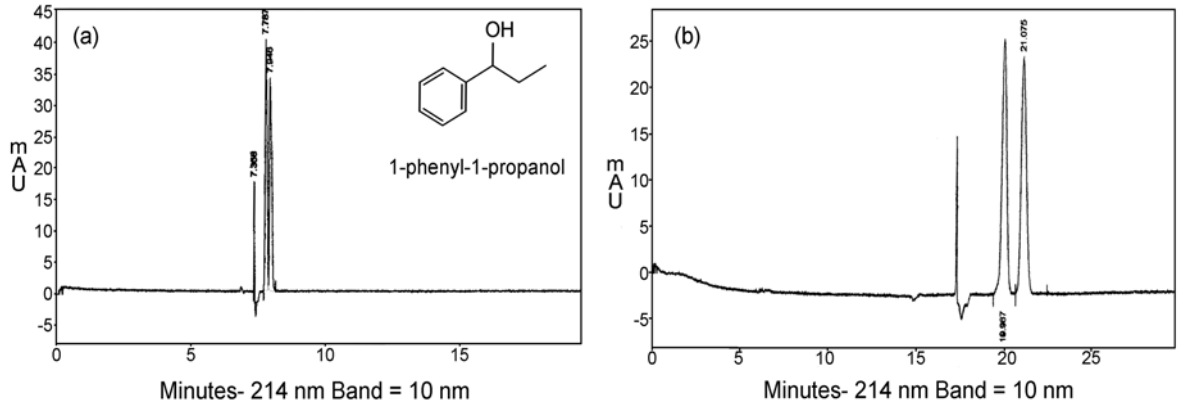


Figure 2. Chiral separation of the 1-phenyl-1-propanol in the presence of sulfonated β-cyclodextrin in the absence of Ag colloids (a) and in the presence of Ag colloids (b) as additives. Buffer, 10 mM phosphate at pH 7.0; separation voltage 15 kV; capillary, 57 cm × 50 mm (I.D.); effective length = 50 cm; detection, UV at 214 nm.

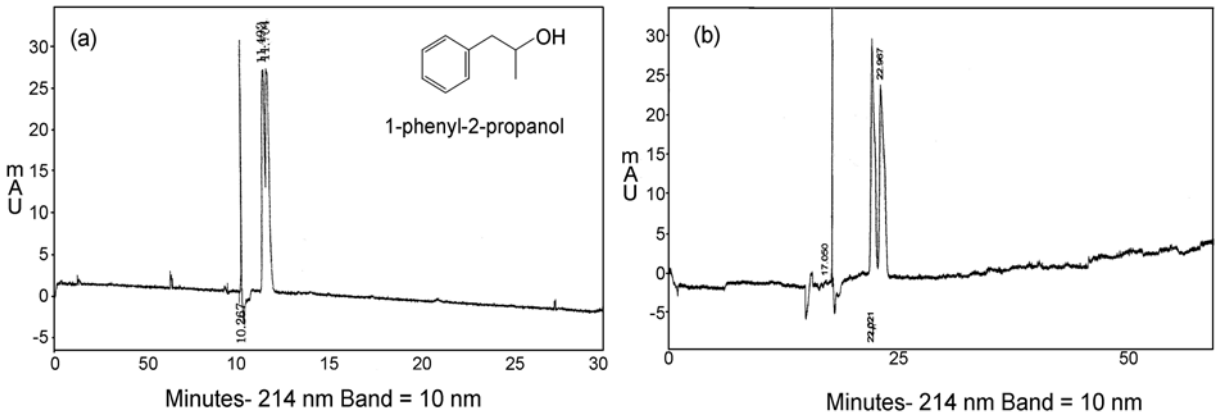


Figure 3. Chiral separation of the 1-phenyl-2-propanol in the presence of sulfonated β-cyclodextrin in the absence of Ag colloids (a) and in the presence of Ag colloids (b). Buffer, 10 mM phosphate at pH 7.0; separation voltage 15 kV; capillary, 57 cm × 50 mm (I.D.); effective length = 50 cm; detection, UV at 214 nm.

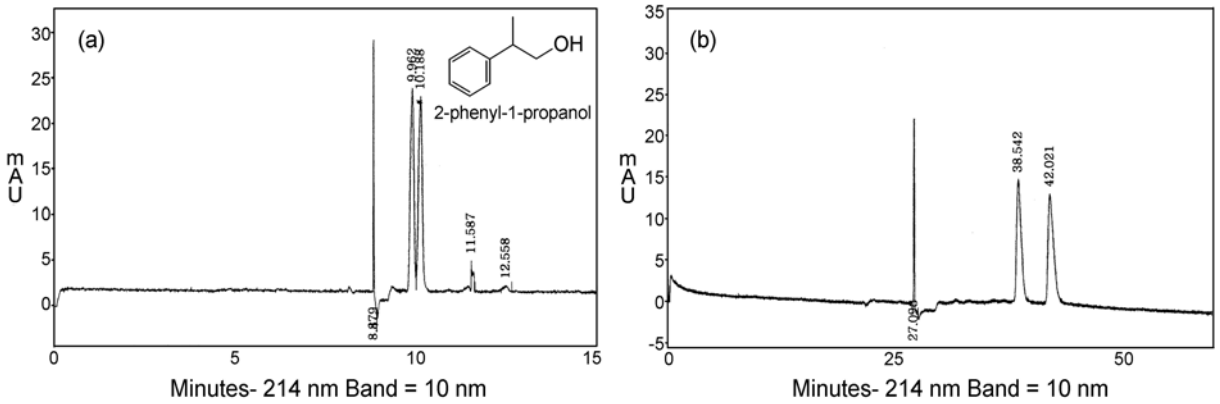


Figure 4. Chiral separation of the 2-phenyl-1-propanol in the presence of sulfonated β-cyclodextrin in the absence of Ag colloids (a) and in the presence of Ag colloids (b). Buffer, 10 mM phosphate at pH 7.0; separation voltage 15 kV; capillary, 57 cm × 50 mm (I.D.); effective length = 50 cm; detection, UV at 214 nm.

respectively, and R_s was *ca.* 2.18.

Figure 3 shows the chiral separation of 1-phenyl-2-propanol. In the absence of the Ag colloid, the retention times (t_r) were 11.49 and 11.70 min, respectively, and the resolution (R_s) was *ca.* 0.16. In the presence of the Ag colloid, t_r's were 22.02 and 22.97 min, respectively, and R_s was *ca.* 1.00.

Figure 4 shows the chiral separation results of 2-phenyl-1-propanol. In the absence of the Ag colloid, the retention times (t_r) were 9.96 and 10.19 min, respectively, and the resolution (R_s) was *ca.* 0.17. In the presence of the Ag colloid, t_r's were 38.54 and 42.02 min, respectively, and R_s was *ca.* 8.70.

From Figures 2, 3, and 4, the separation-degree of arylalcohols is in the following order: 2-phenyl-1-propanol > 1-phenyl-1-propanol > 1-phenyl-2-propanol, which indicates that: (1) The steric effects of 2-phenyl-1-propanol and 1-phenyl-1-propanol are higher than that of 1-phenyl-2-propanol because of the phenyl group, which is presented beside the chiral center, (2) The methyl group, which is beside the chiral center in 2-phenyl-1-propanol, has greater hydrophobic properties than the alcohol group, which is beside the chiral center in 1-phenyl-1-propanol, therefore, the 2-phenyl-1-propanol was inserted deeper in the cavity of sulfonated β-CD than 1-phenyl-1-propanol.

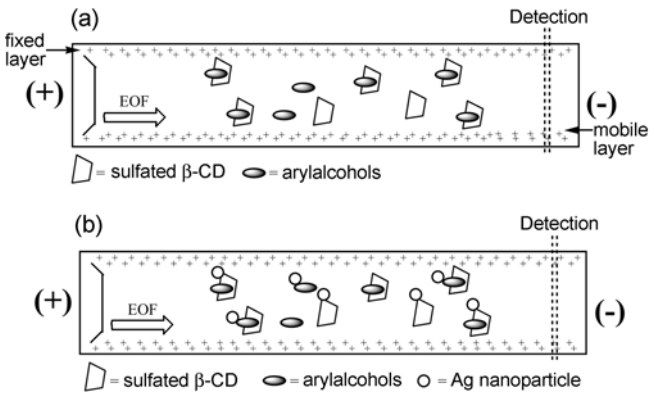


Figure 5. Schematic representation of chiral separation of arylalcohols with sulfonated β-CD in the absence of Ag colloids (a) and in the presence of Ag colloids (b).

Figure 5 shows the schematic representation of chiral separation of arylalcohols with sulfonated β-CD in the absence of Ag colloids (a) and in the presence of Ag colloids (b). As shown in Figure 5(a), the arylalcohols, sulfonated β-CD, and the complex in running buffer at pH = 7 migrate down by the electrophoretic and electroosmotic flow (EOF). In Figure 5(b), the surface of the Ag nanoparticles interact with sulfonated β-CD, arylalcohols, or the complex in running buffer at pH = 7. These interactions may be affected by EOF. The enantio-separation of arylalcohols in the presence of the Ag particles was improved entirely due to slower EOF.

In order to elucidate the separation mechanism in detail, complexes of the arylalcohols with sulfonated β-CD were prepared in the absence and in the presence of the Ag colloid. The prepared complexes were then characterized by CV in the solution state.

Figure 6 shows the cyclic voltammograms of the 1-phenyl-1-propanol (a), 1-phenyl-2-propanol (b), and 2-phenyl-1-propanol (c) in the presence of Ag colloid: **1** Ag colloid; **2** pure arylalcohols; **3** arylalcohols in Ag colloid; and **4** the complex of arylalcohols and sulfonated β-CD in Ag colloid. In all cases, CV of the Ag colloid (0.54 mg in a 25 mL KCl buffer solution) obtained with the glass carbon electrodes as working electrodes exhibited one reduction and two oxidation peaks. In Ag colloid, the oxidation peaks at +87 mV and +75 mV were recorded as to $Ag^0 \rightarrow Ag^+$ and $Ag^+ \rightarrow Ag^{2+}$, respectively. In Figure 6(a), the oxidation peak of 1-phenyl-1-propanol was determined at –73 mV due to oxidation of the 1-phenyl-2-propanol. The oxidation peak of 1-phenyl-1-propanol in Ag colloid was at +25 mV due to complexation of 1-phenyl-1-propanol with surface of Ag nanoparticles. These results clearly indicate that the 1-phenyl-1-propanol interact with the surface of the Ag nanoparticles. On the other hand, the oxidation peak of the complex of 1-phenyl-1-propanol with sulfonated β-CD and Ag colloid was at 132 mV. From these results, the new complex due to 1-phenyl-1-propanol, sulfonated β-CD, and

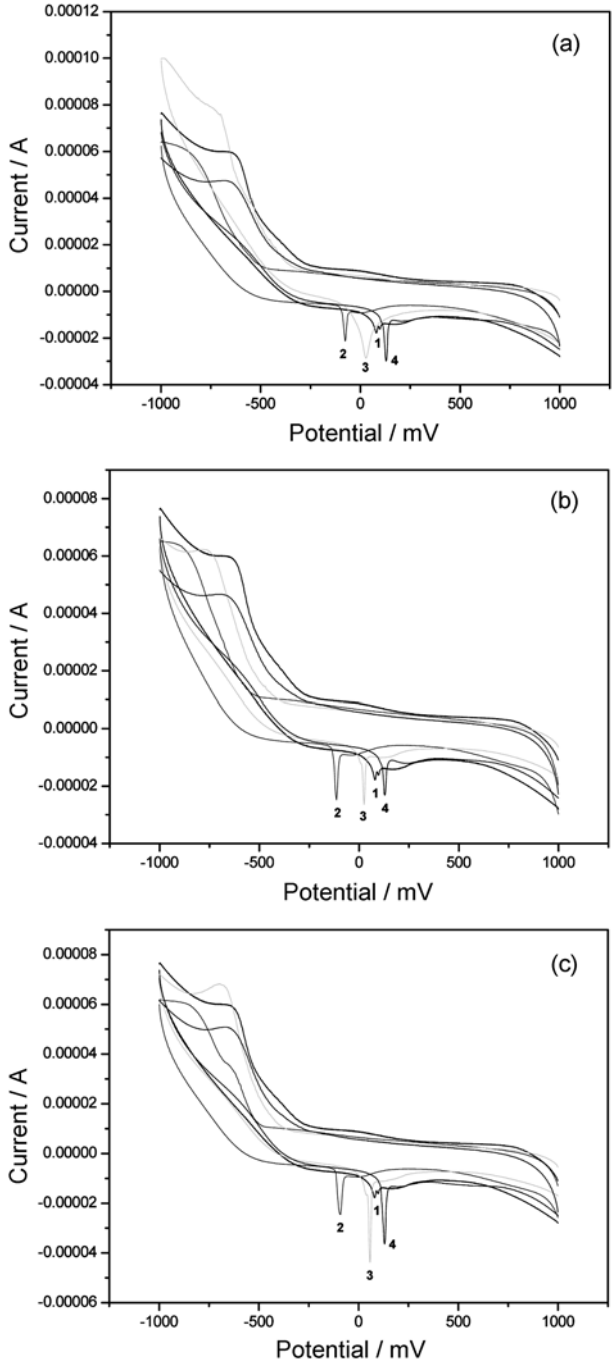


Figure 6. Cyclic voltamograms of the 1-phenyl-1-propanol (a), 1-phenyl-2-propanol (b), and 2-phenyl-1-propanol (c). 1, Ag colloids; 2, arylalcohols; 3, arylalcohols in Ag colloids; 4, the complex in Ag colloids.

Ag colloids were formed. The new complex of 1-phenyl-1-propanol was formed by addition of Ag colloid. On the other hand, an oxidation peak of 1-phenyl-1-propanol in sulfonated β-CD was not observed. In Fig. 6(b), the oxidation peak (**2**) of 1-phenyl-2-propanol was observed at –118 mV due to oxidation of 1-phenyl-2-propanol. The oxidation peak (**3**) of the 1-phenyl-2-propanol was observed at +20 mV due to complexation of 1-phenyl-2-propanol with

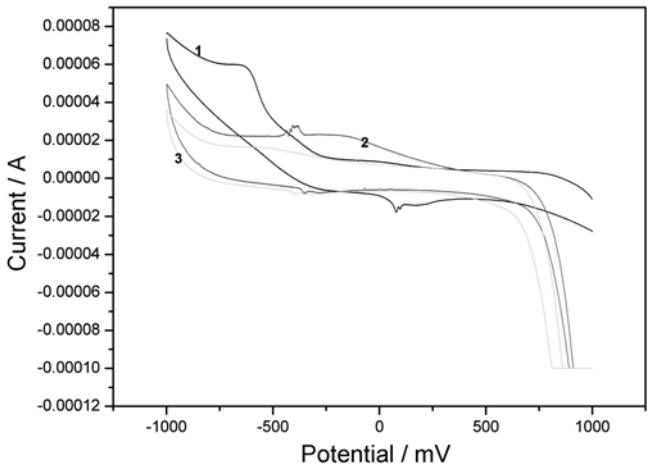


Figure 7. Cyclic voltamograms of the Ag colloids (**1**), sulfated β-CD (2), and sulfated β-CD in Ag colloids (**3**).

the surface of Ag nanoparticles. On the other hand, the oxidation peak (**4**) of the 1-phenyl-2-propanol with sulfonated β-CD in the presence of Ag colloid was at +132 mV due to the complexation of the 1-phenyl-2-propanol with sulfonated β-CD and Ag colloid. In Figure 6(c), the oxidation peak (**2**) of 2-phenyl-1-propanol was at –96 mV, the oxidation peak (**3**) of 2-phenyl-1-propanol in Ag colloids was at +60 mV, and the oxidation peak (**4**) of 2-phenyl-1-propanol in the presence of sulfonated β-CD and Ag colloid was at +132 mV. Again, these results indicate the surface of Ag nanoparticles interact with 2-phenyl-1-propanol and sulfonated β-CD.

In order to compare the interaction of arylalcohols and sulfonated β-CD with Ag colloid, the CV analysis of the sulfonated β-CD was performed in the absence and in the presence of Ag colloid. Figure 7 shows the cyclic voltammograms of Ag colloid (**1**), pure sulfonated β-CD, and sulfonated β-CD in Ag colloid (**3**). The small oxidation peak (**2**) of sulfonated β-CD found at –350 mV is due to oxidation of sulfonated β-CD. The small oxidation peak (**3**) of sulfonated β-CD in Ag colloid found at –385 mV is due to complexation of sulfonated β-CD with the surface of Ag nanoparticles. From these results, the surface of Ag nanoparticles interact more with arylalcohols than with sulfonated β-CD.

Conclusions

Chiral CE separation of arylalcohols (1-phenyl-1-propanol, 1-phenyl-2-propanol, and 2-phenyl-1-propanol) was studied with sulfonated β-cyclodextrin (CD) as a chiral selector and Ag colloid as an additive. In summary,

(1) The optimum CE condition is the chiral selector concentration of 6.5 mM, the applied voltage of 15 kV, and pH of 7.0.

(2) Addition of Ag colloid to the running buffer improves the resolution significantly.

(3) The molar ratio of the sulfonated β-CD to Ag colloid, which is one of the most critical factors affecting separation,

was found to be optimum at 65 : 1.

(4) The inclusion-complex of arylalcohols with sulfonated β-CD in the solution state was characterized by CV.

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