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ORIGINAL ARTICLE

Analytical applications of gold electrodes modified with monolayers of thiolated cyclodextrins

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Abstract The sequential method for the preparation of cyclodextrin monolayers is used to prepare modified electrodes responsive towards selected guest molecules: ferrocene, ibuprofen, methylene blue, dopamine and menadione. The inclusion into cyclodextrin cavities is monitored using cyclic voltammetry and the mediating role of the immobilized molecules towards solution species is shown on the example of dopamine oxidation.

Keywords Complex formation · Voltammetry · Cyclodextrin · Monolayer modified electrode

Introduction

Chemically modified cyclodextrins possessing thiol or disulfide anchoring groups can be used for the formation of monolayers on gold electrode surfaces [1–4]. We have applied mono(6-deoxy-6-lipoylamide)-per-2,3,6-*O*-acetyl-*β*-cyclodextrin in the stepwise self-assembly procedure of the monolayer formation on gold electrode. The removal of the protecting groups was done directly on the electrode surface. The electrochemical response of such electrode towards ferrocene was found to be highly improved when ferrocene was included in the cyclodextrin cavity [5]. The association of ferrocene with the monolayer CDs was strong and the binding constant was found to be 3.3×10^4 M^{-1}.

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The sequential self-assembly method was applied to prepare gold electrodes responsive towards ibuprofen [6]. The molecule included in the cavity of the *β*-cyclodextrin attached to the gold electrode surface can act as a mediator providing electrical contact between the electrode and the solution resident enzyme. Such behavior was noted for methylene blue and dopamine [7]. In the present paper per(6-deoxy-6-thio)α-cyclodextrin modified gold electrode with dopamine included in the cavities is used as the working electrode in the determination of dopamine.

Cyclodextrin (CD) attached to the electrode surface does not cover the electrode uniformly and bare regions of gold surface are still exposed to the solution. On the other hand, multi anchoring guest is not a dynamic structure compared to simple alkyl thiols as shown before [8], and once anchored do not reorganize to form a better packed monolayer. Therefore, Kaifer and Stoddart [2] introduced the concept of a sealing component responsible for covering the surface between the cyclodextrin molecules. The CD cavities have to be earlier blocked by a guest so that the sealing thiol does not enter the cavities during the self-assembly process. Using this approach we modified the gold electrode with mono (6-deoxy-6-lipoylamide)-per-2,3,6-*O*-acetyl-*β*-cyclodextrin. The stepwise self-assembly procedure of monolayer formation on the gold electrode allowed to prepare ferrocene responsive electrode [5]. This general procedure relies on anchoring the cyclodextrin receptor possessing one or more arms bound to the macrocycle by means of group G (Scheme 1). The terminal group of the arm is thiol or disulfide. The arm is usually 2–12 carbon atoms long. This anchoring step is performed using DMF solution containing 1 mM CD. The electrode is next cleaned and immersed to guest solution in water or

aqueous ethanol in order to form the inclusion complex. The guest is chosen to fit well to the hydrophobic cavity in order to form a strong complex. After a couple of hours, the thiol sealing component is added to the same solution, to cover the remaining bare regions of the electrode. The terminal group of the sealing thiol (denoted E in the Scheme 1) is $–CH_3$, $–NH_2$ or –COOH groups. The latter two increase the contribution of electrostatic forces in the interactions with the compounds in the solution.

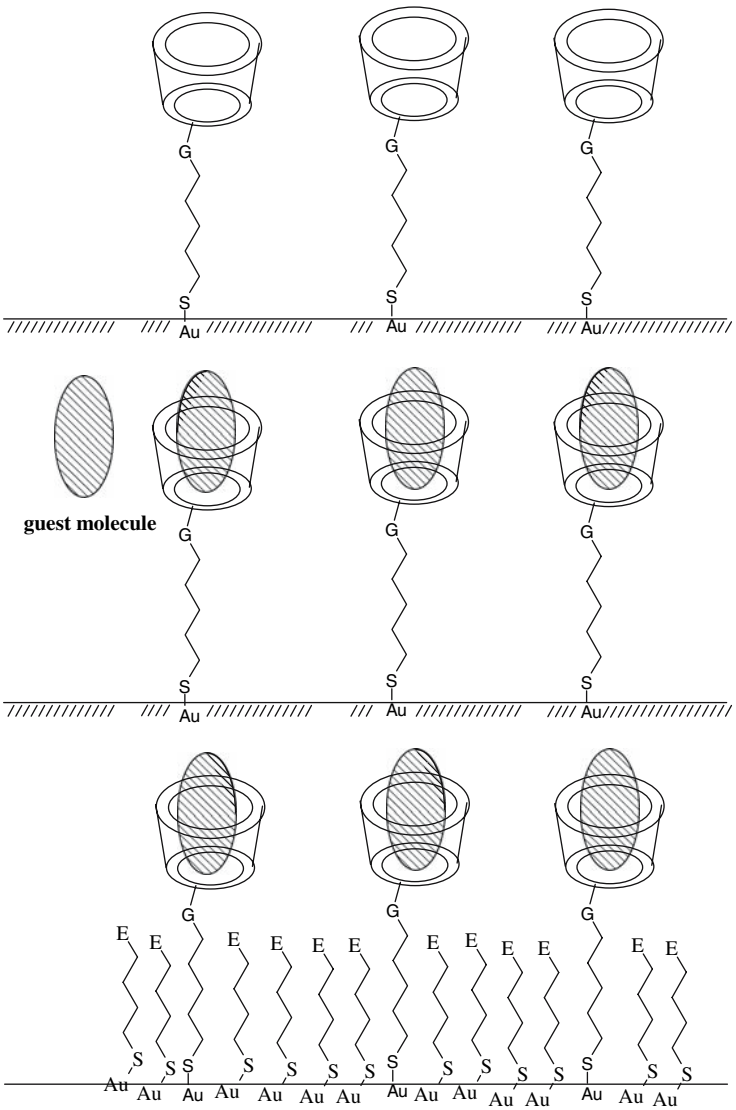
Experimental

Chemicals

Ethanol, perchloric acid and potassium hydroxide were purchased from POCh Gliwice. All other compounds used in this work were purchased from Sigma-Aldrich and Merck. Water was distilled and passed through a Milli-Q purification system. The final resistivity of water was 18.2 $M\Omega cm^{-1}$. For the Ibuprofen (racemate, SIGMA) determination 0.2 M solution of Na_2SO_4 was used as the supporting electrolyte. Methylene Blue (SIGMA) was studied in Britton-Robinson buffer solution, pH 6.6. Dopamine (SIGMA) was studied in phosphate buffer solution, pH 7.2. The synthesis of per(6-deoxy-6-thio)-α, per(6-deoxy-6-thio)-β, and per(6-deoxy-6-thio)-γ-cyclodextrins were done according to the procedure of Stoddart and coworkers [2, 9], or as described elsewhere [5].

Electrochemistry

Electrochemical experiments were carried out in three-electrode cell with SCE as a reference electrode and



Scheme 1 Schematic presentation of three-step sequential monolayer formation procedure. G denotes the group linking CD ring with anchoring spacer, E-represents functionalities responsible for electrostatic interactions with ionic species in the solution

platinum foil as a counter electrode. The supporting electrolyte was 0.1 M phosphate buffer or McIlvaine buffer. The measurements were performed using Autolab PGSTAT30. All electrochemical experiments were carried out at 25°C.

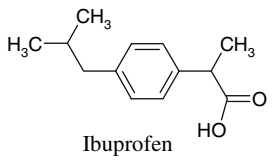
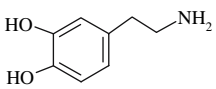
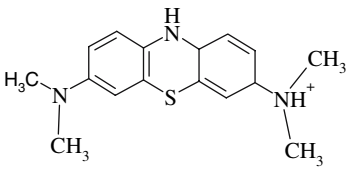
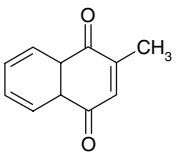
Preparation of electrodes

Monolayer modified Au(111) substrates were used as working electrodes. The substrates were 200–300 nm thick gold films evaporated onto borosilicate glass precoated with 1–4 nm underlayer of Cr (Arrandee). Before the deposition of monolayer, the substrates were cleaned by etching for 5–10 minutes in hot nitric acid, and then flame annealed until the sample glowed dark red. Self assembly procedure of the monolayers was described earlier [10, 11].

Results

For the electrodes modified with monolipoamide derivatives of β-CD (receptor 1 and 2, Scheme 2) ferrocene was used as the guest and octanethiol as sealing component. This electrode was used to determine the drug ibuprofen. The determination was indirect based on the substitution of ferrocene by ibuprofen in the cavities, hence the voltammetric peaks corresponding to the electrode processes of ferrocene decreased. The ibuprofen molecule is nonelectroactive, however, based on the decreasing peak current of ferrocene bound to the β-CD, the calibration plots and the association constant of the Ibu @ $CD_{surface}$ system could be evaluated (Fig. 1). Figure 1 presents the peak current–ibuprofen concentration plots for receptor 1 and receptor 2 (Scheme 2).

Scheme 2 Guest molecules together with cyclodextrin host receptors used for the modification of the gold surfaces

Guest	Host	
 Ibuprofen	mono(6 deoxy-6-lipoylamide)-β-cyclodextrin	**Receptor 1**
	mono(6 deoxy-6-lipoylamide)-per-2,3,6-O-methyl-β-cyclodextrin	**Receptor 2**
 Dopamine	per(6-deoxy-6-thio)-α-CD	**Receptor 3**
 Methylene Blue	per(6-deoxy-6-thio)-β-CD	**Receptor 4**
 Menadion	per(6-deoxy-6-thio)-γ-CD	**Receptor 5**

The guest molecule included in the cavity may act as a mediating unit, transmitting electrons between the electrode and the solution species. This function of the CD complex is especially important in case of electro- and bioelectrocatalysis. In the latter case, the CD monolayer separates mechanically the biomolecules e.g., redox enzymes from the electrode surface thus preventing their denaturation or conformational changes. Methylene Blue (Scheme 2) is an efficient mediator for the reduction of oxygen catalyzed by redox enzyme—laccase. Methylene Blue (MB) placed in the CD cavity retains its mediating role while the molecule of enzyme is kept isolated from the electrode surface. The voltammetric behavior of MB included in per(6-deoxy-6-thio 2,3 di-O-Me) β-CD on the electrode surface is shown in Fig. 2. The reversibility of the system is clearly seen by the small separation of the cathodic and anodic signals corresponding to the reduction and oxidation of surface immobilized compound.

Neurotransmitter, dopamine (DA) forms a stable inclusion complex with α-CD. The electrooxidation of dopamine is accompanied with chemical side reactions complicating its determination. In the presence of mercaptopropionic acid as the sealing compound, the interference of chemical reactions is eliminated [10]. The voltammograms of dopamine included into the cavities is shown in Fig. 3. With increasing time dopamine is slowly removed to the buffer solution not containing DA. Figure 3 presents the 5th–10th scans. The voltammetric curves for increasing concentrations of dopamine in the solution recorded using the α-CD modified electrode are shown in Fig. 4. The catalytic

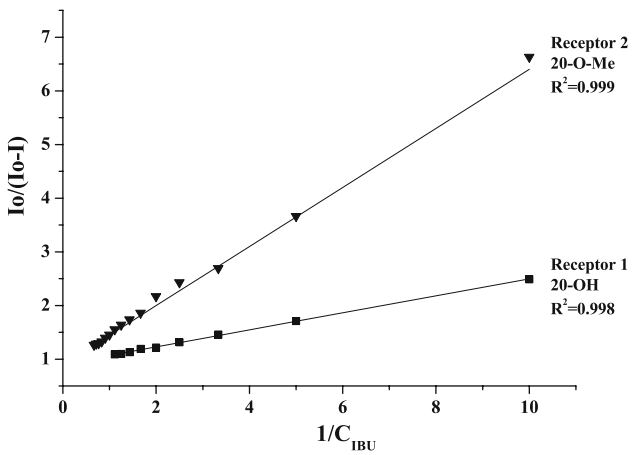


Fig. 1 Calibration lines for ibuprofen obtained using gold electrodes modified with *mono*(6-deoxy-6-lipoylamido)-β-cyclodextrin (receptor 1) and its per methylated analogue *mono*(6-deoxy-6-lipoylamide-*per*-*O*-methyl)-β-cyclodextrin (receptor 2) complexed with ferrocene

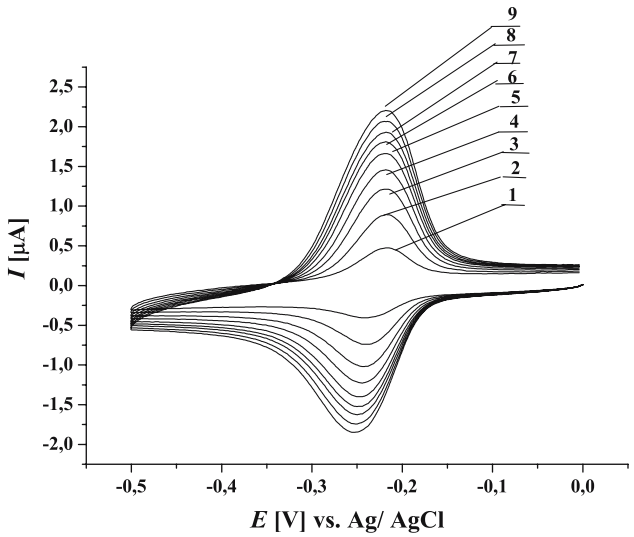


Fig. 2 Cyclic voltammograms for Au electrode modified by SAM film with MB@β-CD (receptor 4) complex with octanethiol as the sealing component. Curves recorded for increasing concentration, 1–12 μM MB in solution, under Ar atmosphere, scan rate 500 mV/s

shape of the curves recorded at slow scan rate (5 m V/s) indicates that DA present in the cavities catalyzes oxidation of the solution dopamine and improves the sensitivity of the determination. For the smallest concentration of DA used (line 1 Fig. 4) the oxidation potential is more positive since it corresponds to the DA included in the cavities of adsorbed α-CD. In this case the electrode is covered with two component monolayer with dodecanethiol as the

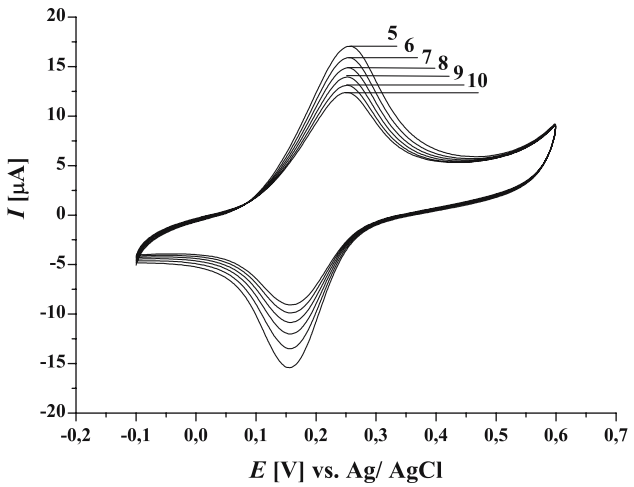


Fig. 3 Multicyclic voltammetric curves (5th–10th scan) recorded for an Au disk electrode modified by SAM film of DA@α-CD (receptor 3) complex with mercaptopropionic acid as the sealing component. Curves recorded in the pure supporting electrolyte solution (20 mM phosphate buffer, pH 7.2) under Ar atmosphere, scan rate 50 mV/s

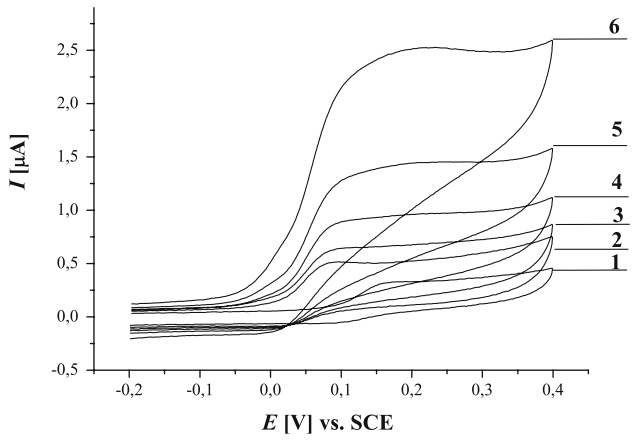


Fig. 4 Cyclic voltammetry curves for the Au electrode modified by SAM containing DA@α-CD and dodecanethiol as the sealing component. Curves recorded for increasing concentrations of DA in phosphate buffer (pH 7.0): (1) 1, (2) 2, (3) 5, (4) 10, (5) 20, (6) 50 10^{-6}M. Scan rate: 5 mV/s

monolayer ''sealing component''. This allows to eliminate the contribution of DA oxidation on the uncovered gold surfaces, mentioned in our earlier paper [10]. Menadione (Scheme 2) may be also used as the mediator of dopamine oxidation. The sensitivity is similar but the mediator signals do not decrease with time indicating very stable binding to the γ-CD cavities (receptor 5).

The dodecanethiol sealing component decreases the background currents. In common physiological samples dopamine appears together with ascorbic acid, the latter usually in large excess. When the sealing unit is cysteamine [10], the determination of DA together with the ascorbate is made possible since the ascorbate processes take place at more negative potentials and in addition—polar ascorbate does not show affinity towards the hydrophobic CD cavity. Electrodes covered with per (6-deoxy-6-thio) α-CD (receptor 3) with cysteamine sealer are useful for the determination of DA in large excess of ascorbates and the oxidation peaks are separated by more than 100 mV.

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References

1. Ferancova, A., Labuda, J.: Cyclodextrins as electrode modifiers. Fresenius J. Anal. Chem. **370**, 1–10 (2001)
2. Rojas, M.T., Königer, R., Stoddart, J.F., Kaifer, A.E.: Supported Monolayers Containing Preformed Binding Sites. Synthesis and Interfacial Binding Properties of a Thiolated β-Cyclodextrin Derivative. J. Am Chem. Soc. **117**, 336–343 (1995)
3. Maeda, Y., Fukuda, T., Yamamoto, H., Kitano, H.: Regio- and Stereoselective Complexation by a Self-Assembled Monolayer of Thiolated Cyclodextrin on a Gold Electrode. Langmuir **13**, 4187–4189 (1997)
4. Fukuda, T., Maeda, Y., Kitano, H.: Stereoselective Inclusion of DOPA Derivatives by a Self-Assembled Monolayer of Thiolated Cyclodextrin on a Gold Electrode. Langmuir **15**, 1887–1890 (1999)
5. Chmurski, K., Temeriusz, A., Bilewicz, R.: β-Cyclodextrin-Based Ferrocene-Imprinted Gold Electrodes. Anal. Chem. **75**, 5687–5691 (2003)
6. Chmurski, K., Temeriusz, A., Bilewicz, R.: Measurement of drug binding to mixed monolayers containing β-cyclodextrin active sites. J. Incl. Phen. Macroc. Chem. **49**, 187–191 (2004)
7. Chmurski, K., Koralewska, A., Temeriusz, A., Bilewicz, R.: Catalytic Au Electrodes Based on SAMs of per(6-deoxy-6-thio-2,3-di-O-methyl)- β-Cyclodextrin. Electroanalysis **16**, 1407–1412 (2004)
8. Choi, S.-J., Park, S.-M.: Electrochemical characterization of nanosized electrode arrays prepared from nanoporous self-assembled monolayers. Bull. Korean Chem. Soc. **23**, 699–704 (2002)
9. Ashton, P.R., Königer, R., Stoddart, J.F.: Amino Acid Derivatives of β-Cyclodextrin. J. Org. Chem. **61**, 903–908 (1996)
10. Majewska, U.E., Chmurski, K., Biesiada, K., Olszyna, A., Bilewicz, R.: Per(6-deoxy-6-thio)-α-Cyclodextrin monolayer Modified Gold Electrode. Electroanalysis **18**, 1463–1470 (2006)
11. Bilewicz, R., Chmurski, K.: Cyclodextrin and Their Complexes. In Dodziuk, H. (ed.) Cyclodextrin and Their Complexes, Ch. 10.5, pp. 298–318. Wiley-VCH Weinheim (2006)