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Role of pore size on the electrochemical oxidation of 5-hydroxytryptophan in a silica sol–gel matrix

Received: 1 October 2003 / Accepted: 7 November 2003 / Published online: 16 July 2004
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Abstract Silica sol–gels that are prepared by room-temperature processing are suited as matrices for voltammetry in the absence of a contacting liquid phase because the electrolyte encapsulated within the pore volume supports charge transport. We hypothesized that when the electrode process involves a coupled chemical reaction, the pore size can influence the product distribution. This hypothesis was tested with 5-hydroxytryptophan (5-HTPP) as the electroactive species because the cation radical formed by its oxidation can react to form a simple dione or larger dimer, trimer, and oligomer products. Microporous and mesoporous silica sol–gels, which have respective pore diameters in the Å and nm ranges, were the solid-state electrolytes. Glassy carbon (GC) electrodes were used initially; however, experiments in aqueous solution showed that passivation precluded applications in a solid electrolyte. Boron-doped diamond (BDD) electrodes yielded the same voltammetric signature as that of GC but passivated more slowly. In accord with the hypothesis, the oxidation of 5-HTPP at BDD in microporous silica yielded voltammetry suggesting that dione formation was the primary oxidation pathway. With mesoporous silica, the analogous experiment suggested dimer formation. The voltammetric interpretation was consistent with the results obtained by chemical oxidation of 5-HTPP in these matrices followed by product identification by mass spectrometry.

Keywords Voltammetry · Silica sol–gel · Nanodomains · Oxidation products · Indoles

Introduction

Silica prepared by sol–gel processing at room temperature is a rigid material with a controllable pore structure. A typical processing procedure is to prepare silica from a tetraalkyl orthosilicate sol by a sequence involving hydrolysis and condensation. The relative rates of the hydrolysis and condensation reactions influence whether the resulting gel is microporous (pore widths in the Å domain) or mesoporous (pore widths in the nm domain) [1]. The use of templating agents, such as surfactants at levels well above their critical micelle concentrations in the sol, is another route to controlling the pore size in the mesoporous domain [2].

As detailed in recent reviews, silica sol–gel materials can be utilized in electrochemical studies as binders in the preparation of ceramic electrodes [3], as a permeable support in which active reagents are doped [4, 5], and as a solid-state cell that is compatible with conventional electroanalytical methodology [6]. The ability to use silica as an electrochemical cell without a contacting liquid is possible because the pores that are present when the sol–gel is processed below the boiling point of water are filled with aqueous electrolyte.

In solid-state voltammetry, the pore size of the silica influences the apparent diffusion coefficients, D_{app} , of redox-active species encapsulated therein. For example, voltammetry of polyoxometalates in these media yield D_{app} values of 10^{-6} to 10^{-8} cm² s⁻¹ with mesoporous and microporous silica, respectively [7, 8]. Comparable results are obtained with hexacyanoferrate [9, 10] and with ferrocenylmethanol [11] as dopants. A second influence of the sol–gel matrix on the voltammetry of dopants is through ion-exchange interaction between the backbone and intermediates in the electrode process. An example is provided by the electrochemistry of UO_2^{2+} in silica. The UO_2^+ formed by the one-electron reduction of UO_2^{2+} interacts with the anionic silica sites, thereby increasing the rate of disproportionation of the dication [12].

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The present study was initiated as a continuation of our evaluation of the influence of the silica sol-gel matrix on the redox behavior of dopants. Of specific interest was the influence of the pore size on the products obtained from chemical reactions initiated by an electrochemical process. An indole, 5-hydroxytryptophan (5-HTPP), was selected as the test system because of the possibility that the pore size can influence the product distribution. Specifically, the reported electrochemical oxidation of 5-HTPP is a two-electron process accompanied by a loss of proton to form a cation radical that subsequently either dimerizes or reacts with water to form a dione; the pathway is detailed in Scheme 1 of [13].

We hypothesized that performing the oxidation of 5-HTPP in a silica sol-gel in the absence of a contacting liquid phase will yield the dimer as the dominant product unless the pore size sterically hinders the coupling reaction. Previous reports suggest that the pore size can play a role in modulating the reaction pathway of dopants within sol-gels. For example, Ueda et al. [14] proposed that the pore structure influenced the photo-conversion of *trans*-4-methoxy-4'-(2-hydroxyethoxy)-azobenzene to the *cis* form. Another example is that of the electrochemical oxidation of aniline. The reaction carried out in mesoporous silica yielded polyaniline, whereas with microporous silica as the solid-state electrolyte, the dimer and other small oligomers were formed [15].

A challenge in the study of this indole in a solid-state cell was passivation of the working electrode, which was expected when conventional carbon was used [16, 17]. Because the working electrode is embedded in the sol-gel matrix during processing, restoring the surface activity by polishing was precluded. We tested two alternatives to conventional carbon electrodes. First, glassy carbon was modified with a film of mixed-valence ruthenium oxide that is stabilized with cyano crosslinks, mvRuOx [18]. This modifier is well known to promote the oxidation of biochemical compounds, including indoles [19], in liquid samples without suffering from surface passivation observed in analogous experiments with bare electrodes [20, 21, 22]. Second, boron-doped diamond (BDD) electrodes were tested. This material also is chemically stable, promotes the oxidation of certain species, and resists fouling [23, 24, 25, 26]. It was imperative to address the issue of passivation of the electrode surface in order to continue to investigate our initial hypothesis of the role of pore size on the 5-HTPP redox process.

Experimental

All chemicals were ACS reagent grade from Fisher Scientific (Fair Lawn, NJ) unless otherwise stated. The 5-hydroxy-L-tryptophan (5-HTPP) and Triton X-114 were from Sigma (St. Louis, MO). The tetramethyl orthosilicate (TMOS), 98% purity, 2,5-dihydroxybenzoate, 99%

purity, and α -cyano-4-hydroxycinnamic acid (HCA), 97% purity, were from Aldrich (Milwaukee, WI). The RuCl_3 and $\text{K}_4\text{Ru}(\text{CN})_6$ were purchased from (Alpha Aesar, Ward Hill, MA). The water was distilled in-house and was purified to a resistance greater than $17.2 \text{ M}\Omega \text{ cm}$ with a Barnstead NANOpure II system.

The glassy carbon electrodes (3 mm diameter) and the carbon fiber ultramicroelectrodes (10 μm diameter) were from Bioanalytical Systems (BAS, West Lafayette, IN). The glassy carbon electrodes were polished using 0.3- μm alumina slurry with water as the lubricant, after which they were cleaned as described by McCreery and co-workers [27]. Briefly, activated carbon (Acros Organics, New Jersey, USA) was mixed with 2-propanol in a 1:3 (v/v) ratio. After this mixture stood for 30 min, the glassy carbon electrode was placed therein and sonicated for 10 min. Finally, the electrode was transferred to water and sonicated again for 10 min.

The deposition of mvRuOx onto the glassy carbon electrode was performed by cyclic voltammetry as described previously [18, 19, 20]. The potential was cycled between 0.5 and 1.1 V (versus $\text{Ag}|\text{AgCl}$, 3 M NaCl) at a scan rate of 50 mV s^{-1} for 15 min while immersed in a solution comprising $2.0 \text{ mmol l}^{-1} \text{RuCl}_3$, $2.0 \text{ mmol l}^{-1} \text{K}_4\text{Ru}(\text{CN})_6$, $1.0 \text{ mol l}^{-1} \text{KCl}$, and $0.01 \text{ mol l}^{-1} \text{HCl}$. The plating solution was prepared at least 24 h before use.

The boron-doped diamond (BDD) electrodes, which were a gift from Michigan State University (G. Swain), were 7 mm \times 10 mm rectangles. The silicon backing of the boron-doped diamond was electrically insulated with a mixture prepared from LR White Resin-Medium Grade Acrylic Resin and LR White Accelerator (London Resin Company, Ltd., England); it was cured for 24 h. Prior to use, the BDD surface was cleaned with isopropanol.

The voltammetric measurements were performed with a CH Instruments (Austin, Texas) Model 750 Electrochemical Workstation. Unless otherwise stated, the liquid-phase measurements were made and reported with $\text{Ag}|\text{AgCl}$, 3 M NaCl as the reference electrode, and the solid-state voltammetric experiments used a Pt quasi-reference electrode. Glassy carbon and Pt served as the auxiliary electrode in the liquid-phase and solid-state cells, respectively. The matrix-assisted laser desorption/ionization mass spectrometry (MALDI) experiments were run on a Bruker Reflex III instrument (Billerica, MA) with a time-of-flight mass analyzer equipped with a nitrogen gas laser (Laser Scientific, Inc., Franklin, MA) operated at 5 mW. The 337.1-nm line was used. Samples were mounted with double-sided tape, as previously reported for MALDI study of sol-gels [28].

The silica sol-gels were formed by hydrolysis and condensation of TMOS. Microporous gels were prepared by acid-catalyzed processing. Here, 1.0 ml of each of the following was combined (in the stated order): methanol, $0.05 \text{ mol l}^{-1} \text{H}_2\text{SO}_4$, $0.2 \text{ mol l}^{-1} \text{KCl}$, 0.4 mmol l^{-1} 5-HTPP, and TMOS. The mixture was

stirred for 1 h in a hood (note: vapors of TMOS may cause eye damage). For MALDI experiments and solid-state voltammetry with the BCD electrodes, the sol contained 1.0 mmol l^{-1} 5-HTPP. Other changes in preparing sols for MALDI were the following: 17.5 mg of HCA, which by efficient adsorption of the laser radiation and transfer of a proton promotes the laser desorption of the sample, was added in the processing that leads to a microporous solid; the stirring time was increased to 1.5 h; and the sol was filtered prior to use to remove any residual HCA particles.

Mesoporous materials were prepared by a template synthesis in which a surfactant, Triton X-114, at levels well above the critical micelle concentration were included in the sol to provide nanoscale assemblies around which gelation occurred [2]. For the solid-state voltammetry experiments, 0.3033 g Triton X-114, 3.0 ml methanol, 0.1 mmol l^{-1} 1.5 ml NH_4OH (pH 10), 0.75 ml H_2O , 0.75 ml 0.4 mmol l^{-1} 5-HTPP, and 3.0 ml TMOS were combined in that order and stirred for 1 h. The mesoporous sol-gels used in MALDI experiments were formed by mixing 0.3033 g Triton X-114, 3.0 ml methanol, 1.5 ml 0.05 mol l^{-1} H_2SO_4 , 1.5 ml 1.0 mmol l^{-1} 5-HTPP, and 3.0 ml TMOS. The matrix was not included in the sol. All gels were aged for at least 10 days prior to use so that the pore structure was stabilized.

The general design of the solid-state (sol-gel) voltammetric cell is that reported previously [7, 8]. A 0.5-cm length of Tygon tubing was fitted over the glassy carbon electrode that served as the auxiliary electrode and the base of the cell mold. The Pt quasi-reference electrode was inserted through the side of the tubing, and 750 μl of the sol was pipetted into the mold. The working electrode was placed into the sol during gelation. The depth was adjusted to keep the path length between the reference and working electrode at a minimum.

The MALDI experiments were performed as recently reported [29]. Briefly, the sol-gels were processed on glass slides that were pretreated with a surfactant. Sol (50–100 μl) was pipetted onto the slides. The gelation, aging, and drying was for 3 weeks, during which the indole therein was oxidized by air. The result was disks with a diameter of 2 mm and a thickness of about 0.8 mm. The matrix, which was a methanol solution of the 2,5-dihydroxybenzoate, was pipetted onto the disks 48 h before doing the MALDI analysis.

Results and discussion

Prior to studying the oxidation of 5-HTPP in silica, voltammetric experiments in aqueous solution were performed with a glassy carbon electrode. Consistent with an earlier report, the initial oxidation at 0.4 V (peak current, i_{pa}) yielded a reactive intermediate that led to the development of quasi-reversible peaks centered at -0.16 V . This process corresponds to dione/diol redox couple [13]. Because the product of the initial oxidation of 5-HTPP at 0.4 V, which has a peak current desig-

nated as i_{pa} , is not stable, the ratio of the peak current, i_{pc} , for corresponding reduction at 0.3 V to i_{pa} is less than 1.0. At a scan rate, ν , of 2 V s^{-1} , the ratio is about 0.3. A systematic study of the dependence of the peak current ratio on ν was precluded by the passivation of the electrode, which is discussed later.

The initial solid-state voltammetry experiments used a carbon fiber as the working electrode in mesoporous silica that was doped with 5-HTPP. A typical result is shown in Fig. 1. The initial oxidation peak was at the same potential as that observed in solution, 0.4 V. Consistent with other studies of voltammetry in mesoporous silica [7, 8], the shape of the voltammogram at 0.5 V s^{-1} is that for a mix of hemispherical and planar diffusion. In this medium physical diffusion is the main component of D_{app} [8]; in such a case, the reverse currents are known to be severely attenuated at a micron-scale electrode.

When the solid-state voltammetry was repeated using microporous silica as the electrolyte, the reversal of the oxidation of 5-HTPP was observed (Fig. 2). Here, $i_{\text{pa}}/i_{\text{pc}}$ approached 1.0, which signifies that the cationic product of the oxidation of 5-HTPP not only is stable but also, unlike with the mesoporous silica cell, does not diffuse away from the electrode surface. Because physical diffusion is restricted in microporous relative to mesoporous silica [7, 8], this result is not surprising. For a surface-confined process, coincidental peak potentials are expected. The observed peak separation at 0.1 V s^{-1} was 30 mV. This small, albeit significant, peak split may be caused by quasi-reversible electron transfer and/or the fact that in a solid state system a significant uncompensated resistance is present, which can give an

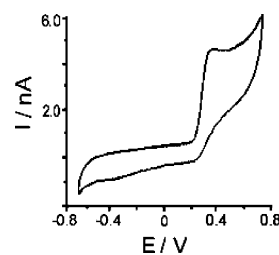


Fig. 1 Solid-state voltammetry of 1.0-mmol dl^{-3} 5-HTPP doped in a mesoporous silica sol-gel, Working electrode, glassy carbon fiber (10 μm diameter); scan rate, 0.5 V s^{-1} . The potentials are measured versus a Pt quasi-reference electrode

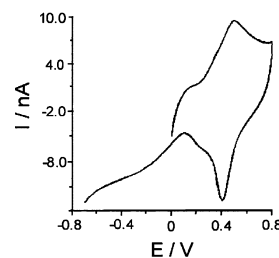


Fig. 2 Solid-state voltammetry of 0.4-mmol dl^{-3} 5-HTPP doped in a microporous silica sol-gel. Conditions are those in Fig. 1

ohmic shift in potentials even at the low currents observed at a fiber electrode.

A contributing factor to the resistance of the system is that the oxidation of 5-HTPP at carbon electrodes leads to passivation of the surface. Voltammograms of 0.5 mmol l^{-1} 5-HTPP in 0.1 mol l^{-1} KNO_3 (aqueous solution) at a glassy carbon electrode of conventional size (3-mm diameter) were obtained at 0.5 V s^{-1} (Fig. 3). Unlike voltammetry at a fiber electrode, the reverse processes are observed. The data demonstrate that the electrode becomes passivated after ten scans. This factor limited our attempts to perform quantitative diagnostic tests on the voltammetry of 5-HTPP in silica at a carbon electrode. Indeed, in the solid electrolyte the carbon fiber was passivated after three or fewer scans.

In an attempt to electrolyze 5-HTPP in a silica sol-gel, electrodes other than bare carbon were investigated. The desired behavior was to have the same voltammetric pathway at the selected electrode as that at carbon but to retain activity during electrolysis. Two alternatives to bare carbon were tested, a glassy carbon electrode that was modified with a film of mRuOx and a BDD electrode. The selection of the mRuOx -modified electrode was based on reports that it resists passivation during the oxidation of a wide range of biochemical compounds [19, 20, 21, 22]. The cyclic voltammetry of 5-HTPP at a mRuOx -modified glassy carbon electrode is characterized by a direct oxidation at 0.8 V and a mediated oxidation at 0.95 V [19]. In contrast to the data in Fig. 3, the anodic peak current for the mediated oxidation of 5-HTPP persists during continuous scanning; however, a 20% diminution of the current at 0.8 V was observed. The product of the oxidation was not the dione; the development of quasi-reversible peaks centered at -0.16 V , which correspond to the dione/diol couple, that are observed at bare carbon electrodes (Fig. 3) were not developed at the mRuOx -modified electrode. Because of this change in the electrode process, the mRuOx -modified electrode was not suited to testing our hypothesis regarding the role of the matrix on the solid-state electrochemistry of 5-HTPP.

Boron-doped diamond electrodes also are reported to resist passivation. For example, they remain active during the voltammetry of compounds such as amines that are known to be problematic at conventional sur-

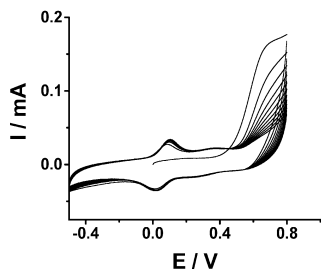


Fig. 3 Cyclic voltammetry of 0.4-mmol dl^{-3} 5-HTPP in 0.1-mol dl^{-3} KNO_3 at a 3-mm (diameter) glassy carbon electrode. Scan rate, 0.5 V s^{-1} ; initial potential, 0.0 V ; initial scan, positive-going. The potentials are measured versus a Pt quasi-reference electrode

faces [24, 25]. A typical cyclic voltammogram for 5-HTPP at BDD is shown in Fig. 4. The general features are the same as at the glassy carbon electrode. From the difference in the peak potentials, the redox couple at 0.3 V in Fig. 4 corresponds to the dione/diol couple. The value differs from that of the corresponding process in Fig. 3 because a quasi-reference electrode was used in the experiment illustrated in Fig. 4. The BDD retained some activity during continuous scanning. After 36 scans at 0.05 V s^{-1} in a 0.4-mmol l^{-1} 5-HTPP solution, anodic peak at 0.7 V decreased by about 50%.

Cyclic voltammetry of 5-HTPP in microporous silica was performed using a BDD working electrode (Fig. 5). Because of the electrode size, the peak currents were in the μA range. In this medium such currents distort the voltammograms because of ohmic losses. Nevertheless, it is apparent that the pathway is different from that in aqueous solution. The primary evidence is that a cathodic process corresponding to the initial oxidation of 5-HTPP in microporous silica at a carbon micro-electrode is developed, which is in marked contrast to voltammetry in a liquid phase. Secondary evidence is that there is some indication of a quasi-reversible redox process with an average peak potential of about 0.05 V . The difference between that value and the onset of the initial oxidation at about 0.4 V is within 0.1 V of the difference between the formal potential for the dione/diol couple and the potential for the oxidation of 5-HTPP observed in the well-characterized liquid-phase system (Fig. 3). However, this secondary point can be questioned because of the low signal to background ratio in the region near zero volts. Because of passiv-

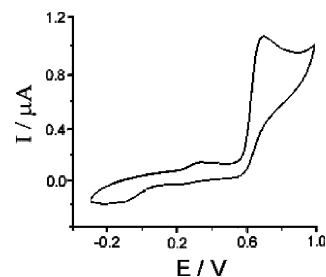


Fig. 4 Cyclic voltammetry of 0.4-mmol dl^{-3} 5-HTPP at the boron-doped diamond working electrode (0.07 cm^{-2}). Conditions are those in Fig. 3 except the scan rate is 0.05 V s^{-1}

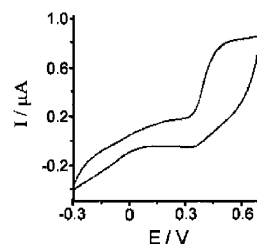


Fig. 5 Solid-state voltammetry of 1.0-mmol dl^{-3} 5-HTPP with the 0.07-cm^{-2} boron-doped diamond electrode in a microporous silica sol-gel. Scan rate, 0.025 V s^{-1} . The potentials are measured versus a Pt quasi-reference electrode

ation of the BDD electrode in the microporous silica, experiments to clarify the voltammetry in the region near zero volts were not successful. In this regard, after about six scans, the current at 0.5 V in Fig. 5 was attenuated by a factor of 0.5. With that degree of attenuation, redox currents, if any, near zero volts would not be measurable after a few scans; hence, attempts to clarify the voltammetry in this region failed.

When the solid electrolyte was mesoporous silica, the only redox process observed at the BDD electrode was the oxidation of 5-HTPP. This result, when considered with the voltammetric behavior in microporous silica, is consistent with our hypothesis; that is, in mesoporous silica the electrolytically formed cation radical reacts rapidly to form a dimer that is not electrochemically active whereas in microporous silica, not only is the reaction between water and the cation radical slowed enough to see the reduction of the initial oxidation product, but also the steric factor provided by the microporous environment favors the formation of the dione over the dimer as the primary product.

The definitive test of this hypothesis is to determine the products after bulk electrolysis. Because of the nearly immediate passivation of the carbon electrodes and the gradual loss of activity of the BDD electrode, electrolysis of 5-HTPP in the sol-gel failed. As an alternative, chemical oxidation was performed. Silica was prepared on treated glass slides from 50–100- μ l aliquots of indole-doped sol as described in the Experimental section. The resulting wafers had thicknesses of about 0.8 mm, which is a dimension that can be permeated throughout by a gas in minutes. They were exposed to air for 3 weeks, under which conditions the 5-HTPP is oxidized. The oxidation of the indole in the microporous sol-gel results in a brown color that is characteristic of the dione. In contrast, the mesoporous sol-gel remains colorless. Because the dimer is colorless, this visual data supports the hypothesis, but further evidence was obtained by employing a mass spectrometry technique in order to investigate the products found inside the pores of the sol-gel.

This evidence that dimerization is the preferred pathway in the mesoporous silica was supported by MALDI data. With the mesoporous sol-gel, the peak at 451.3 m/z agreed to within 0.15% of that expected for the 5-HTPP dimer, presuming addition of an oxygen atom and loss of two hydrogen atoms. When the microporous sol-gel was used, a peak at 234.9 m/z was observed, which is within 0.04% of the mass of the dione plus a hydrogen atom. Details on the MALDI study of the products of the chemical oxidation of 5-HTPP in silica are reported elsewhere [29].

Conclusions

The cyclic voltammetry of the indole, 5-HTPP, in silica sol-gels was dependent on the pore size of this solid-

state electrolyte. When it was microporous, the cation radical that is produced by the oxidation of 5-HTPP was sufficiently stable to observe its reduction at a scan rate of 50 mV s^{-1} , but subsequent chemical reaction to yield a secondary dione product occurred. When the medium was mesoporous silica, the cation radical reacted rapidly with water. The hypothesis that the product was in fact the dimer rather than the dione was supported by the color of the indole-doped sol-gels and mass spectrometric identification of the products after air oxidation. A possible complicating factor in this interpretation is that the pH of the mesoporous silica used for the solid-state voltammetry experiments is higher than that of the other sol-gels in this study. However, the pathways for the conversion of the cation radical to the dimer relative to the dione both involve loss of a proton [13], so neither will become strongly preferred by a change of pH.

Carbon electrodes were used for most of this electrochemical study; however, because they rapidly passivate during the voltammetry of 5-HTPP, typical diagnostic steps such as a study of the influence of scan rate on peak current could not be performed. A preliminary investigation of BDD electrodes for the oxidation of 5-HTPP showed less tendency to passivate and the same general oxidation pathway relative to a carbon surface, but a significant loss of activity with cycle number in a continuous scanning experiment was still seen. We are further investigating BDD as a working electrode for solid-state voltammetry in silica. Of importance is that micron-scale BDD electrodes are now available for such work.

Acknowledgements This work was supported by donors to the Petroleum Research Foundation of the American Chemical Society through grant PRF 33863-AC5 to JAC. The Miami University Summer Scholars program partially supported JLC. The boron doped diamond electrodes were a gift from GM Swain, Michigan State University.

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