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Poly(*N*-methylpyrrolylium) Poly(styrenesulfonate). A Conductive, Electrically Switchable Cation Exchanger That Cathodically Binds and Anodically Releases Dopamine

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ABSTRACT: A poly(*N*-methylpyrrolylium) poly(styrenesulfonate) composite was prepared by the anodic polymerization of *N*-methylpyrrole from an aqueous sodium poly(styrenesulfonate) solution. It was characterized by X-ray photoelectron spectroscopy, IR, electron microscopy, and combustion analysis. The polymer was conductive and had electrochemical properties superficially similar to those of poly(*N*-methylpyrrolylium) perchlorate. The polymer could be reduced at −0.4 V vs. SCE in aqueous NaCl, and it was shown that this process incorporated sodium ions. It was shown that reduction of the film in aqueous solutions of dopamine gave dopamine binding. The bound dopamine could be released by stepping the polymer film potential to +0.5 V.

Previous studies have shown that the properties of redox polymer films can be substantially changed by switching the film from one oxidation state to another. If the film is in an electrolyte solution and it is switched electrochemically, the process can be considered to be electrical switching of the film properties.[1] One property that will change during the redox process is the ability to bind ions. The change in the net charge on the redox polymer during reaction requires ions to flow into or out of the film and this allows the polymer film to bind and expel ions in response to the electrical signal. A particular application of interest is drug delivery, where control of the current would allow one to control the amount of ionic drug that was released from a polymer film on an electrode. This idea has, indeed, been reduced to practice for the binding and release of anions from the conducting polymers polypyrrole[2] and poly(3-methoxythiophene).[3] Conducting polymers are of particular interest because they can have a high density of redox states and their high conductivity can allow relatively thick films to be promptly switched. These factors can in principle allow binding and prompt release of relatively large quantities of the ion of interest. As an example,[2,4] a polymer film has been anodically synthesized which is composed of oxidized, cationic poly(pyrrolylium) that contains $Fe(CN)_6^{3-}$ to balance the charge. When this film (on a carbon electrode) is placed in aqueous NaCl solution the $Fe(CN)_6^{3-,4-}$ species remain strongly bound in the film unless the potential of the film is made as negative as −0.5 V. At −0.5 V $Fe(CN)_6^{4-}$ is flushed out. If the electrode potential is sequentially pulsed to −0.4 V for short times, each pulse gives release, providing increasing amounts of ferrocyanide. Thus, release can be controlled in time.

In the present study we set out to develop a new conducting polymer, which would act as a *cation* binder and releaser. Success was achieved by preparing a conducting, composite polymer, poly(*N*-methylpyrrolylium) poly(styrenesulfonate) (PMP^+PSS^-). Each component of this material was attractive for our purpose. The poly(styrenesulfonate) was expected to be strongly bound in the film and chemically inert. On the basis of literature reports of poly(*N*-methylpyrrolylium) "doped" with small anions, this polymer's electrochemical properties were appropriate, and considering the redox potentials, we expected reduced poly(*N*-methylpyrrole) to be somewhat more stable than polypyrrole in air. Importantly, a patent on poly(pyrrolylium) poly(styrenesulfonate)[6] reported reasonable stability and high conductivity for dry films. No electrochemical studies were reported.

For our drug delivery experiments, protonated dopamine was the ion of choice. Because it is a protonated amine, the binding and release of dopamine serve as a model for an extremely large class of pharmaceutically important amine and alkaloid compounds. Dopamine is a neurotransmitter and is itself of biological and medicinal interest. Furthermore, because we had previous experience with dopamine electrochemistry, this was a sensible starting point for a new venture. Previously, only two studies have described cation binding and release from electrodes. In one, several papers[8] from this laboratory described a method for covalently binding molecules (charged or neutral) into a polymer film and releasing them by cathodically cleaving the covalent bond. Dopamine was one of the molecules released that way. The other approach by Martin and co-workers[9] described cation binding and release from a poly(vinylferrocene) terpolymer based on principles very similar to those described here. The released cation was $Ru(NH_3)_6^{3+}$.

Experimental Section

Commercial samples were used without purification except for *N*-methylpyrrole, which was vacuum distilled at 30–40 mmHg. It was stored under argon in the dark, and samples were removed through a septum. The sodium poly(styrenesulfonate) (100% sulfonated) from Aldrich Chemical Co. was used except where noted. Its MW was determined as 100 000 (intrinsic viscosity). The 50% and 100% sulfonated, 500 000 MW PSS^-Na^+ was from Polysciences.

Electrochemical experiments were carried out with a Princeton

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Applied Research (PAR) potentiostat, Model 173, in conjunction with PAR universal programmer Model 175 and a Houston Model 2000 recorder. The bipotentiostat was from Pine Instruments, RDE-3. XPS experiments were performed with a Physical Electronics Model 555 instrument. Characteristic peaks were C, 285 eV; N, 401 eV; S, 168 eV; Na, 1072 eV.

Polymerizations were conducted with a single-compartment cell containing a saturated calomel electrode (SCE) as a reference electrode. The counter electrode was a graphite rod. The working electrode was the glassy carbon disk (0.46 cm^2) of a ring–disk electrode from Pine Instruments that had been cleaned on a polishing cloth (Fisher) with 0.3-μm alumina (obtained from Buehler, Ltd., Evanston, Il), wiped with a tissue, and washed successively with distilled water. Polymerization at 4 mA cm^{-2} produced PMP$^+$PSS$^-$ with a combustion analysis of C, 61; N, 10.6; S, 3.7. After electroreduction, the PMP^{0}PSS$^-$,Na$^+$ gave C, 59; N, 11.3; S, 3.5%. These C and N percentages are similar to those found for other polypyrroles including PMP$^+$BF$_4^-$.[5] Infrared bands were recorded at 3413, 1540, 1300, 1164, and 1034 cm^{-1} assigned to poly(*N*-methylpyrrolylium). Other bands at 2920, 1600, 1124, 1034, and 1008 cm^{-1} were assigned to poly(styrenesulfonate). In addition, there was a broad absorption decreasing from 4000 to 1800 cm^{-1}.

Conductivity measurements were made with the four-point probe method in samples removed from the Pt electrode using an insulator tape. Conductivities for different samples of PMP$^+$PSS$^-$ were about 10^{-3} Ω^{-1} cm^{-1}.

Dopamine binding was accomplished with the same cell used for polymerization. It contained 0.1 M aqueous dopamine·HBr and was degassed with argon (glassy carbon disk holding PMP$^+$PSS$^-$ with an uncoated platinum ring). Release employed a small volume cell composed from the ring–disk electrode and a second carbon disk. A droplet of aqueous electrolyte (typically 80 μL) was syringed into the gap, covering all three electrodes. A glass capillary leading to a SCE reference was then inserted into the droplet for a reference electrode. This cell was surrounded by a glass vessel, the interior of which was lined with wet filter paper to ensure that the volume of the aqueous droplet did not diminish due to evaporation during the experiment. The use of a standard solutions containing dopamine·HBr in the droplet and CV on the ring provided a linear i_p/concentration standardization curve for dopamine analysis in the solution.

Results and Discussion

Anodic Polymerizations. Many previous reports have documented the anodic polymerization of pyrrole and N-substituted pyrroles.[5,10] Typically in these experiments an acetonitrile and Et$_4$N$^+$BF$_4^-$ solution of the monomer is oxidized on a platinum or carbon electrode. On the anode surface grows a black, conductive polymer, which has been characterized as a partially oxidized polypyrrole containing counteranions, i.e., BF$_4^-$. Typically, there is one BF$_4^-$ to balance a cationic charge delocalized over four or five pyrrole units.

The present study used a polymeric anion, poly(styrenesulfonate) (0.1 M) in aqueous solutions of *N*-methylpyrrole (0.05 M). The anode was usually a glassy carbon disk, the cathode was a carbon rod, and the reference electrode for measuring the disk potential was saturated calomel (SCE). Most experiments used 100% sulfonated polystyrene (PSS$^-$). The polymerizations were performed with either constant current or constant potential. With the latter approach and an anode potential of 0.7 V a black, conductive film could be obtained. It was found, however, that at 0.7 V the current dropped rather rapidly. Film growth, therefore, took a long time. This behavior, documented by the chronoamperogram of Figure 1, contrasts with the typical behavior for polypyrrole in which there is an initial period with low currents (while the film nucleates) followed by large currents.

With constant-current electrolysis, the current can of course be kept arbitrarily high. It was, therefore, easier to get thick films of polymer. A typical constant-current synthesis used 0.05 M *N*-methylpyrrole, 0.03 M PSS$^-$, and a current of 4.4 mA cm^{-2}. Under these conditions, the disk potential varied by less than 30 mV. Typically, after 300 s the process was complete.

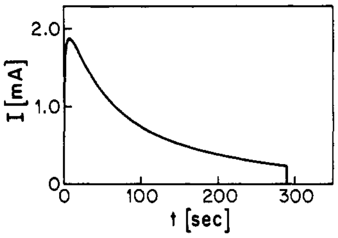


Figure 1. Chronoamperogram for the polymerization of *N*-methylpyrrole (0.05 M) and poly(styrenesulfonate) (0.03 M) at 0.70 V (SCE).

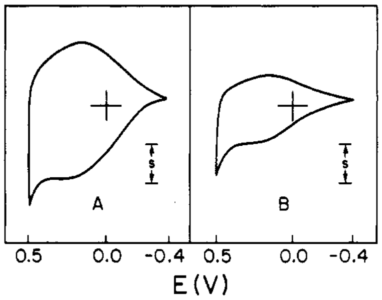


Figure 2. Cyclic voltammograms for PMP$^+$PSS$^-$ in aqueous 0.1 M LiClO$_4$. Sweep from −0.4 to 0.5 V and return: (A) 1 V s^{-1}, *s* = 0.5 mA; (B) 10 mV s^{-1}, *s* = 50 μA.

We propose that the film is a composite of partially oxidized poly(*N*-methylpyrrolylium) (PMP$^+$) and PSS$^-$. In the following paragraphs, we primarily describe electrochemical results using these new, composite filmed electrodes and also report spectroscopic studies on films that had been removed from the underlying carbon or platinum electrode. These studies characterize the structure of the oxidized and reduced polymers, PMP$^+$-PSS$^-$ and PMP^0/PSS$^-$Na$^+$ and show that it can bind and release cations.

Characterization of PMP$^+$/PSS$^-$ and PMP^0/PSS$^-$,Na$^+$. After film preparation, electrodes were removed from the preparation medium, washed with water, and studied electrochemically with an aqueous solution containing 0.1 M LiClO$_4$ as supporting electrolyte. Cyclic voltammograms (CV) were run from −0.4 to +0.5 V using sweep rates of 10–100 mV s^{-1}. Figure 2 shows the voltammograms, which have a broad anodic peak around 0.3 V and a corresponding cathodic peak near 0.15 V.

It is instructive to compare voltammograms of PMP$^+$-PSS$^-$ with those of PMP$^+$BF$_4^-$, which were previously measured with CH$_3$CN and Et$_4$N$^+$BF$_4^-$ as the electrolyte giving $E°$ = 0.45 V vs. SSCE.[5] ($E°$ is presumably the center of the anodic and cathodic CV peak positions.) Under these conditions, PMP$^+$PSS$^-$ gives $E°$ = 0.55 V vs. SCE in CH$_3$CN and 0.2 V in aqueous LiClO$_4$ and a very similarly shaped voltammogram. This suggests that PSS$^-$ is incorporated into a poly(*N*-methylpyrrole) (PMP) film during polymerization, just like BF$_4^-$. At −0.4 V, where the voltammetric sweep begins, the PMP$^+$ is nearly completely reduced to its neutral form, PMP^0. The anodic voltammogram current then corresponds to reoxidation of the PMP^0 to PMP$^+$. The cathodic current gives PMP$^+$ → PMP^0. Thus, there is a chemically reversible change induced as the potential is cycled between −0.4 and 0.5 V.

This change from PMP$^+$ to PMP^0 must be accompanied by counterion movement. Anions must leave the film or cations enter the film during reduction. Our postulate was that the polymeric anions would remain and cations would

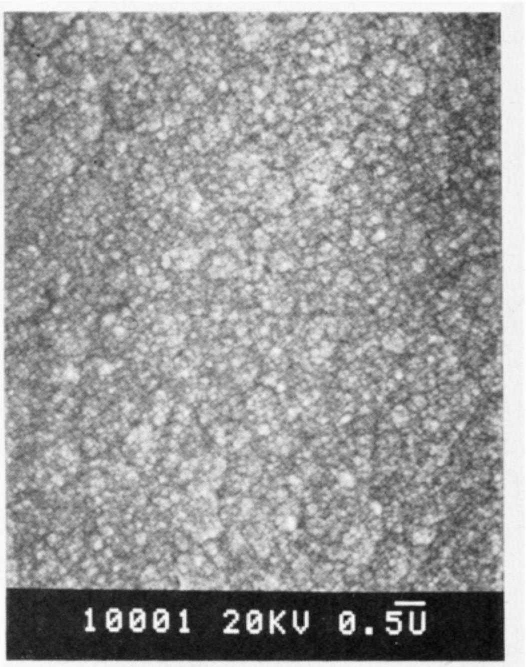


Figure 3. Scanning electron micrograph of PMP^0/PSS^-.

be incorporated. This was substantiated by X-ray photoelectron spectroscopy (XPS). The spectra of films grown as indicated above gave peaks for C, N, and S. No Na signal was seen unless the sample was first sputter etched with an argon beam. Then, typically, a trace of Na could be detected. This suggests that the original, oxidized film (PMP^+PSS^-) is charge balanced with one SO_3^- moiety for each cation site on the PMP^+, but without further evidence this must be taken with some reservation.

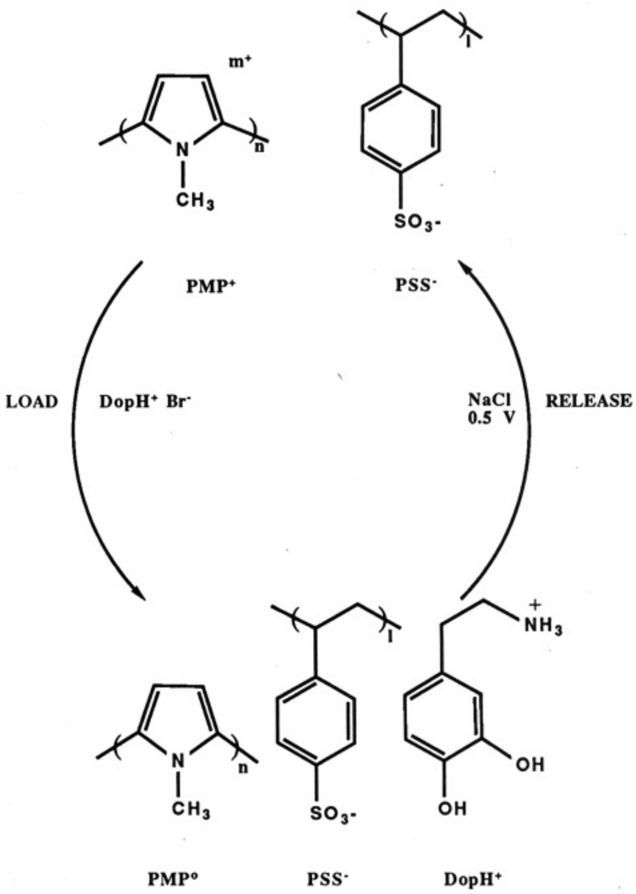
Reduced films were produced for XPS by potentiostating them at −0.6 V in 0.1 M NaCl for a period of time until the electrolysis current leveled off. After the film soaked 0.5 h and underwent an intensive rinse with degassed H_2O, it was dried overnight and placed in the spectrometer. XPS analysis showed that sulfur was still present in about the same amount and that Na was incorporated as we had expected. Sputtering with an argon beam increased the Na signal by a factor of 3. Simply soaking an oxidized electrode in aqueous 0.1 M NaCl gave only a trace Na signal. These results demonstrate that PSS^- remains in the film during reduction and Na^+ is incorporated during that process.

Conductivity measurements on dry films of PMP^+PSS^- were made with the four-point probe method. As previously reported,[6] the conductivities were high. Different samples, all of which were dried 2–3 h in air, gave $\sigma = 10^{-3}$ Ω^{-1} cm^{-1}. This can be compared to the literature value for $PMP^+BF_4^-$ of 10^{-2} Ω^{-1} cm^{-1}.[5]

Additional structural information about PMP^+PSS^- was provided by IR spectroscopy. As expected there was a featureless absorption decreasing in intensity from 4000 to 1800 cm^{-1}, which is quite similar to that of polypyrrole. In addition, strong peaks at 1124, 1034, and 1008 cm^{-1} were present which are characteristic of SO_3^-.

Scanning electron microscopy was performed to investigatge the film morphology. As one looks at either the surface formed next to the electrode or the surface formed on the solution side, a similar amorphous, granular structure is observed. Reduced films showed an identical morphology. The grain size appeared to be on the order of 0.1 μm (Figure 3). This contrasts with anodically grown poly(pyrrolylium) perchlorate, which shows large hemispherical particles on its outer surface and a very close packed structure on the inner surface.

Scheme I



Dopamine Binding and Release. The principal goal of this study was to demonstrate that organic cations could be bound into the reduced film, i.e., PMP^0/PSS^-M^+, and released by oxidizing the polymer film. For initial studies we chose protonated dopamine as the cation of interest. The idea can be illustrated as shown in Scheme I.

Since many drugs are in fact protonated amines like dopamine, success would indicate that the method would be applicable to a large class of medicinal compounds. Dopamine also offered the practical advantage that it is electroactive. The hydroquinone moiety is converted anodically to the corresponding quinone and this provides a convenient analytical tool. A particular disadvantage is that anodic dopamine release demands careful potential control to avoid the formation of dopaquinone. Specifically, it was necessary to limit the anodic potential of the film to $E \leq 0.60$ V to avoid oxidation (and partial destruction) of dopamine during anodic release.

Consider now the binding and release experiment in detail. PMP^+PSS^- films were grown on glassy carbon electrodes as above (NaPSS MW = 500 000) at a constant current of 4.4 mA cm^{-2} until 0.6 C was passed. The filmed electrode was washed and then placed in water containing 0.1 M dopamine hydrobromide. The electrode potential was stepped to −0.60 V until the cathodic current dropped to small values to bind dopamine. The electrode was removed, washed, and placed in 0.1 M aqueous NaCl. If a cyclic voltammogram was then run on the film the resulting voltammogram showed peaks attributable to dopamine. Figure 4 shows a CV of dopamine on clean glassy carbon and a CV of the PMP^0/PSS^- dopamine film. After the film was briefly potentiostated at 0.5 V, a second CV scan on the film gave a smaller dopamine peak, indicating that it had been released.

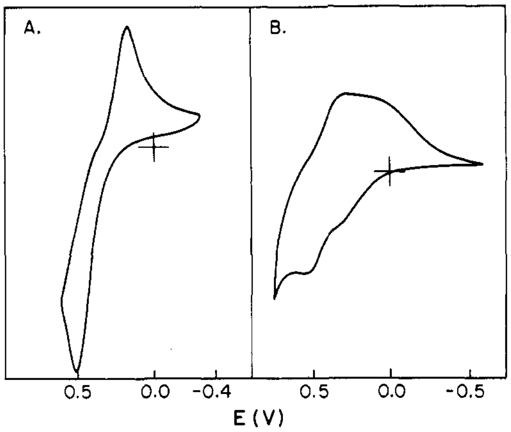


Figure 4. Cyclic voltammograms at 100 mV s^{-1} in 0.1 M $LiClO_4$ of (A) dopamine hydrobromide; (B) PMP^0/PSS^- dopamine H^+.

Definitive results on dopamine release were obtained with a small-volume cell. This device has been described.[2,4] The electrode surface area/solution volume ratio is large, giving a relatively large concentration of dopamine in solution to facilitate analysis, which is performed on a third electrode in contact with the solution using CV. A calibration curve of current peak heights on the third electrode is used to measure the concentration. In practice this device is composed of a commercial ring–disk electrode (a Pt ring surrounds a carbon disk) and an auxiliary carbon disk electrode. The disk of the ring–disk is coated with PMP^+PSS^- and loaded with dopamine. The ring is used for the analysis of released dopamine.

The polymer film was oxidized by stepping the potential to 0.5 V for 30 s and then the droplet was analyzed for released dopamine. Dopamine was identified by its characteristic CV peaks and quantified by the peak currents. A set of three experiments gave anodic peak currents of 14.4 ± 1.4 A. This translates to a solution concentration of 0.63 mM and to a surface concentration of dopamine, which had been in the film, of 1.1×10^{-7} mol cm^{-2}.

Further experiments using similarly prepared films showed that a single pulse to 0.5 V for 1 min was sufficient. Repetitive pulses did not increase the dopamine concentration in solution. It was also shown that anodic pulses to 0.6 V were less effective because they oxidized dopamine and produced decomposition products indentifiable by CV. Interestingly, a potential pulse to 0.3 V did not release any substantial quantity of dopamine. In this light, it is worth remarking that ion exchange will slowly release small quantities of dopamine (over 8 min, an amount equivalent to about 16% of that from anodic release). When 50% sulfonated polystyrene was used instead, the ion exchange could be substantially suppressed; i.e., no dopamine leakage could be detected in the first 8 min of contact with 0.1 M $LiClO_4$ aqueous solution. In this case, the average release amount (9.6 ± 0.8 μA) was somewhat lower.

Conclusions

The initial goals of this study were (1) to prepare a composite of a cationic, conducting redox polymer and a polymeric polyanion on an electrode; (2) to show that upon cathodic reduction this polymer film would incorporate cations; (3) to demonstrate that a protonated amine of biomedical importance could be cathodically bound and anodically released into aqueous solution. These goals were accomplished. The method is far more effective than our previous approach for dopamine release, which used covalent binding and cathodic release[8] because (1) it does not involve a complicated, many-step polymer synthesis; (2) it releases larger quantities (100 × as much cm^{-2}); (3) in principle the PMP^+PSS^- film can be reloaded.

It should be emphasized that these experiments all employed aqueous solution, which puts the materials to a severe test. The many previous studies of polymer-modified electrodes[1] have usually employed solvents like acetonitrile. This is important because swelling of the polymer film increases the rate of ion diffusion in the film and, therefore, the rate of the redox process. Furthermore, in water many electroactive groups are unstable in one redox form or the other.

On the positive side, all this went as predicted, and, because there is little precedent for our observations, this makes the work of some importance. To express our reservations, it should be acknowledged that we have not learned to control the release rate, and we do not understand the structure of the polymer or the details of binding and release in the way that they should be understood. Further studies should improve on our knowledge and our practical abilities to deliver interesting chemicals on call at a predetermined rate.

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