The structure of the $(Cu_2(m\text{-XYLpy}))^{2+}$ cation is shown in Figure 1.[24,25] It consists of two crystallographically independent cuprous ion coordination environments. Each Cu(I) is three-coordinate with ligation from two pyridine and one tertiary amino donor groups. The chelating tridentate ligands cause considerable distortions from idealized trigonal planar coordination. The *N*-amino–Cu–*N*-py angles are acute (99–105°), resulting in large *N*-py–Cu–*N*-py angles of 151.1 (4) and 150.7 (3°) for Cu1 and Cu2, respectively. Some distortion from planarity occurs with Cu1 0.131 Å out of the N1,N2,N3 plane and Cu2 0.224 Å out of the N4,N5,N6 plane. The bonding distances are typical for three-coordinate Cu(I) with nitrogen donors[15a,26] while the Cu–*N*-py distances are shorter by ~0.08 Å than the bond lengths found in the monomeric tetracoordinate Cu(I) complex containing the same tridentate ligand.[27] The cuprous ion polyhedra extend away from each other (Cu1···Cu2 = 8.940 Å) as is found in $Cu_2Cl_4(p\text{-XYLpy})$.[17]

$Cu_2(m\text{-XYLpy})(PF_6)_2$, I, is the first example of a discrete Cu(I) binuclear complex containing three-coordinate copper ions with neutral nitrogenous ligands.[15e] It possesses a number of features postulated to occur in deoxyhemocyanin. There are two distorted trigonal planar Cu(I) moieties and unsaturated pyridine nitrogen donors to model imidazole coordination in the proteins. It also has well-separated copper ion groups which could move together upon oxygenation. This latter aspect has been suggested and is an attractive proposal, considering the abundance of evidence pointing to conformation changes upon oxygen binding in hemocyanins.[1,6,13b] $Cu_2(m\text{-XYLpy})^{2+}$ is very reactive, and introduction of O_2 to its dichloromethane solution results in the high yield O_2 incorporation via hydroxylation of the benzene ring of *m*-XYLpy and formation of a phenoxy and hydroxy doubly bridged Cu(II) binuclear complex (II, R = H) where the Cu(I)···Cu(II) separation is reduced to ~3.1 Å.[28]

Thus, I appears to be a good functional model compound for the deoxy state of the copper monooxygenases in that hydroxylation of an aromatic ring is effected. Studies of Cu(I)–O_2 interactions, mechanistic investigations of O_2 "activation", and reactivity with O_2/substrate (e.g., phenols) systems are presently in progress.

I is electrochemically active, and cyclic voltammetric measurements in dimethylformamide show a quasi-reversible one-electron (per copper) oxidation wave at $E = +0.16$ V vs. NHE. Compound I also reacts with "typical" Cu(I) ligands; thus it forms adducts with CO, olefins, phosphines, and phosphites to give compounds formulated as $Cu_2(m\text{-XYLpy})L_2(PF_6)_2$. These chemical investigations will be reported separately.

Acknowledgment. We are grateful to Research Corp. (K.D.K.), National Institutes of Health (K.D.K. GM28962; J.Z. GM22566 and GM27459) and the donors of the Petroleum Research Fund, administered by the American Chemical Society (K.D.K.), for support of this work.

Registry No. I, 82731-39-3; $Cu(CH_3CN)_4PF_6$, 64443-05-6.

Supplementary Material Available: Listing of atomic coordinates and temperature factors, bond lengths, bond angles, and anisotropic temperature factors (9 pages). Ordering information is given on any current masthead page.

(24) The complex crystallizes in the space group $P\bar{1}$ with two molecules in a unit cell: $a = 11.251$ (3) Å, $b = 11.444$ (3) Å, $c = 15.721$ (4) Å; $\alpha = 95.71$ (2)°, $\beta = 102.06$ (2), $\gamma = 94.74$ (2); $\rho_{calcd} = 1.640$ g/cm^3. The positional parameters of the copper atoms were determined by the Patterson method, and the other atoms were located on difference Fourier maps. With 2761 unique observed reflections ($3° < 2\theta < 40°$, $F_o > 6\sigma(F_o)$) taken at 22 °C on a Nicolet R3m diffractometer using Mo Kα radiation, the structure was refined to a current value of 0.072 for the discrepancy index $R_1 = \sum||F_o| - |F_c||/\sum|F_o|$.

(25) Supplementary material.

(26) Lewin, A. H.; Michl, R. J.; Ganis, P.; Lepore, U. *J. Chem. Soc., Chem. Commun.* **1972**, 661–662.

(27) Karlin, K. D.; Hayes, J. C.; Hutchinson, J. P.; Hyde, J. R.; Zubieta, J. *Inorg. Chim. Acta* **1982**, *64*, L219–L220.

(28) Karlin, K. D.; Hayes, J. C.; Cruse, R. W.; Hyde, J. R.; Zubieta, J., to be submitted; experiments using isotopically labeled O_2 confirm incorporation of both atoms of dioxygen into II (R = H).

Electrically Stimulated Release of Neurotransmitters from a Surface. An Analogue of the Presynaptic Terminal

Larry L. Miller,* Aldrich N. K. Lau, and Essie Kariv Miller

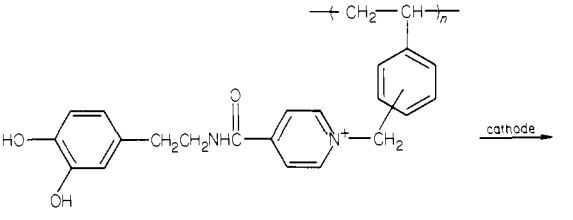
Department of Chemistry, University of Minnesota Minneapolis, Minnesota 55455

Received May 27, 1982

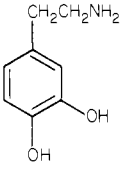
The conduction of electricity in vivo involves chemical communication between a presynaptic nerve cell and a postsynaptic nerve cell. The presynaptic terminal usually acts by liberating a transmitter substance in response to a change in its cell potential. We report that a solid electrode, modified with a thin layer of a suitable polymer, will similarly respond to a change in potential to release a neurotransmitter.

The experimental design is based upon recent work in which electrode surfaces have been modified to provide tailor-made molecular surface structures. It has been shown that polymers can be adsorbed or insolubilized onto electrodes.[1] If these polymers have suitable reducible or oxidizable groups, they are electroactive as expected. Our approach in this project was to synthesize a polymer that held a neurotransmitter via a cathodically cleavable bond. When adsorbed, this polymer could then be used to release the neurotransmitter. The controlled release of bound molecules from an electrode surface has not been previously reported. A device based upon this concept could have practical utility for the delivery of small amounts of material to specific locations at specific times.

The polymer **1** was chosen as a delivery agent for the neuro-



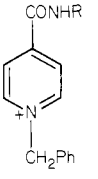
1



dopamine

transmitter, dopamine. The polymer structure includes (a) a polystyrene backbone, which provides strong adsorption to the surface, (b) an isonicotinate unit, which allows reduction at rather positive potentials, and (c) the neurotransmitter, attached via a cathodically cleavable amide bond.

It was previously demonstrated that the amide linkage of isonicotinamides would cleave upon reduction in DMF.[2] We have used aqueous solution, pH 7, to survey the reduction of several model pyridines and pyridinium salts. With use of a glassy carbon electrode, cyclic voltammetry (CV) showed that cationic *N*-alkylisonicotinamides, like compound **2**, reduced at potentials more



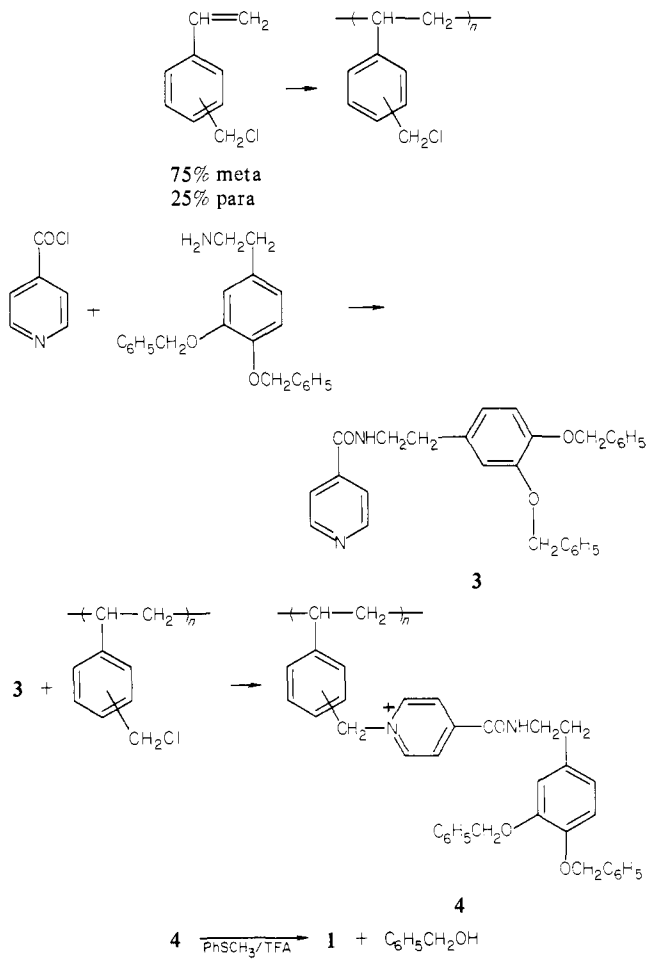
2

(1) For references to polymer modified electrodes, see, for example: (a) Fukui, M.; Kitani, A.; Degrand, C.; Miller, L. L. *J. Am. Chem. Soc.* **1982**, *104*, 28. (b) Shigehara, K.; Anson, F. C. *J. Electroanal. Chem.* **1982**, *132*, 107. (c) Bard, A. J.; Abruna, H. D. *J. Am. Chem. Soc.* **1981**, *103*, 6898. (d) Denisevich, P.; Willman, K. W.; Murray, R. W. *Ibid.* **1981**, *103*, 4727.

(2) Lund, H. *Acta Chem. Scand.* **1963**, *17*, 2325.

0002-7863/82/1504-5242$01.25/0

Scheme I



positive than −1.0 V (SCE). Gas chromatographic analysis of a preparative scale reduction in aqueous solution of *N*-benzyl-4-((butylamino)carbonyl))pyridinium demonstrated that butylamine was produced. Thus, we had hope that if suitable polymers could be synthesized and coated onto an electrode, they might serve as a controllable source of neurotransmitters. Because many neurotransmitters are amines, the method could have some generality.

The synthesis of **1** has been achieved (see Scheme I).

In the synthesis, isonicotinic acid was reacted with thionyl chloride. The resulting acid chloride was used directly in a reaction with commercial 3,4-bis(benzyloxy)-β-phenethylamine hydrochloride. With a 5-fold excess of triethylamine as an added base, the desired isonicotinamide **3**, mp 133–135 °C, was produced in 72% yield.[3] It was, in turn, reacted with previously prepared un-cross-linked poly((chloromethyl)styrene).[4] The reaction (1.0 g, 2.5 mmol of **3**, 0.34 g of polymer) took place in toluene at 80 °C over a period of 3 days. The solid product (**4**)[5] was purified, and then 1.19 g of **4** (combined from several reactions) was reacted in a mixture of 30 mL of trifluoroacetic acid and 12 mL of thioanisole for 30 h.[6] Workup gave a solid product, which was dissolved in DMF and then added dropwise to toluene for precipitation. Filtration and washing with toluene gave 0.42 g of **1** as the trifluoroacetate salt. The elemental analysis indicated that the polymer was 88% loaded, i.e., 2.1 (mmol of dopamine)/(g of polymer). The IR spectrum was consistent with expectations. The

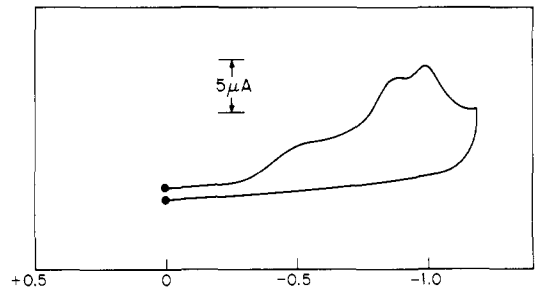


Figure 1. Cyclic voltammogram of **1** on glassy carbon: sweep rate = 100 mV s^{-1}; electrode area = 7.9 mm^2; pH 7; $\Gamma_i = 3 \times 10^{-9}$ mol cm^{-2}.

^{13}C NMR spectrum was quite definitive. Although the backbone gave broad signals, the side chain, due to its more rapid motion, gave sharp ^{13}C lines. All the expected lines were present, and the chemical shifts corresponded closely to those from appropriate model compounds like **2**.

Electrodes were prepared by syringing 0.5–10-μL aliquots of a 1.0 mM solution of **1** in DMF onto the horizontal surface of a glassy carbon disk (area 7.9 mm^2) electrode. Slow evaporation of the solvent gave electrode surfaces coated with a thin layer of polymer. The amount of polymer can in this way be reproducibly controlled and varied. The amounts corresponded to 1–100 monolayers of dopamine units.

The electrochemistry of these chemically modified electrodes was studied by using aqueous 0.1 M KCl buffered at pH 7 with phosphate buffer and a saturated calomel reference electrode. In one example, an amount of **1** was added to the surface so that the initial concentration of electroactive units $\Gamma_i = 3 \times 10^{-9}$ mol cm^{-2}. The cyclic voltammogram (Figure 1) obtained by sweeping E from 0.0 to −1.2 V and back to 0.0 V showed three cathodic peaks.[7] On the return half-cycle there were no anodic peaks. A second cycle over this same E range gave much smaller peaks, and by the fourth sweep the cathodic peaks were no longer visible. The charge calculated by integrating the total, background subtracted, cathodic current was $\sim 8 \times 10^{-9}$ F cm^{-2}.

This polymer **1** also has an oxidizable hydroquinone moiety,[1a,8] and indeed, when the potential of a freshly prepared electrode was cycled from 0.0 to +0.3 V, the hydroquinone/quinone couple was evident ($E_p^a = 0.24$ V, $E_p^c = 0.14$ V). At 100 mV s^{-1} sweep rate the peak size diminished by about 10% per sweep. After sweeping cathodically to −1.2 V to cleave dopamine, the hydroquinone/quinone peaks disappeared. As expected, the hydroquinone/quinone couple was not evident when the protected polymer **4** was similarly coated onto a carbon electrode.

All these results were consistent with expectations, but the crucial experiments involved detection of dopamine in solution, which had been released from the polymeric membrane on the electrode. This was not trivial because of the small amounts involved. In one experiment, a set of 40 electrodes were prepared by dip-coating glassy carbon rods with a 0.5 mg/mL solution of **1** in DMF. Cyclic voltammetry on these rods showed peak shapes similar to those obtained by using disks. Individually, these electrodes were taken to −1.2 V so that dopamine might be discharged into a single 10-mL volume of degassed, buffered electrolyte solution. A divided cell was used to minimize anodic destruction of released dopamine. After completion of the 40 electrolyses, the catholyte was analyzed by using high-pressure liquid chromatography (HPLC). Only one peak was present in the chromatogram, and it had the same retention time (440 s) as dopamine. An ultrasphere ODS, 5 μm, 4.6 mm × 15 cm,

(3) All new compounds gave elemental analyses and IR and NMR spectra consistent with expectations. In the case of polymers **1** and **4** the elemental analyses were used to calculate the loading.

(4) Merrifield, R. B. *J. Am. Chem. Soc.* **1963**, *85*, 2149.

(5) A similar approach has been described: Endo, T.; Okawara, M. *J. Polym. Sci. Polym. Chem. Ed.* **1979**, *17*, 3667.

(6) Kiso, Y.; Ukawa, K.; Nakamura, S.; Ito, K.; Akita, T. *Chem. Pharm. Bull.* **1980**, *28*, 673.

(7) The cathodic peak shapes were sensitive to Γ_i and quite sensitive to the electrolyte composition. These changes will be described in a later publication. It may also be true that some part of the current near −0.5 V is due to oxygen reduction. Although the solutions were degassed, this is the appropriate potential region, and because the currents are small, oxygen could be involved.

(8) Degrand, C.; Miller, L. L. *J. Am. Chem. Soc.* **1980**, *102*, 5728. Ueda, C.; Tse, D. C.-S.; Kuwana, T. *Anal. Chem.* **1982**, *54*, 850. Jaegfeld, H.; Torstensson, A. B. C.; Gorton, L. G. O.; Johansson, G. *Anal. Chem.* **1981**, *53*, 1979.

column was used with 0.05 M phosphate buffer, pH 2.3, as solvent. The amount detected was 3.8×10^{-8} mol. A very approximate electrical yield based on the integrated current was 30%. The solution could also be directly analyzed electrochemically, taking advantage of the hydroquinone group on dopamine. This was accomplished by using a clean carbon disk. Cyclic voltammetry or differential pulse voltammetry showed the expected response due to dissolved dopamine. A control experiment consisted of soaking 40 coated electrodes in electrolyte for a equivalent time with no electrolysis. No dopamine could be detected in the solution.

Similar experiments have shown that only very small amounts of dopamine are released under any circumstances yet investigated. For example, an electrode with $\Gamma_i = 3 \times 10^{-9}$ mol cm^{-2} released only a 10% coulometric yield of dopamine. Studies in progress are aimed at developing electrodes that are capable of promptly releasing larger amounts of neurotransmitter and demonstrating that such released neurotransmitters have an effect on neurons.

Acknowledgment. This work was supported by the National Science Foundation. Stimulating discussions of neurophysiology were held with many people, including David Samuel and Stuart Taylor.

Registry No. 3, 82741-47-7; dopamine, 51-61-6; isonicotinic acid, 55-22-1; thionyl chloride, 7719-09-7; isonicotinoyl chloride, 14254-57-0; 3,4-bis(benzyloxy)-β-phenethylamine HCl, 1699-56-5; poly((chloromethyl)styrene), 9080-67-5.

Selective Preparation of Catalytically Active Zeolite-Encapsulated Rhodium Complexes

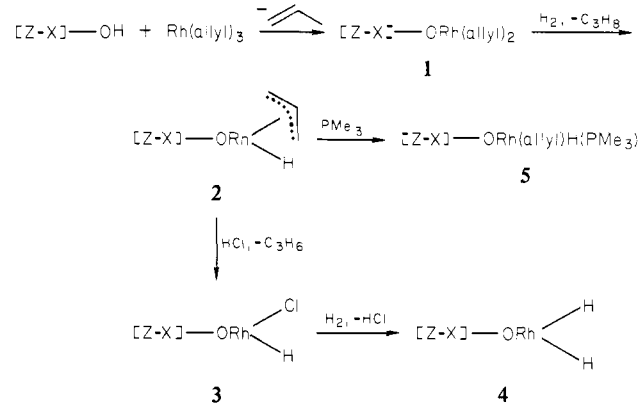
Tai-Nang Huang and Jeffrey Schwartz*

Department of Chemistry, Princeton University
Princeton, New Jersey 08544

Received May 3, 1982

Metal-containing zeolite materials have long been of significance as catalyst systems; however, little is known concerning specific deposition of metal complexes *inside* preformed zeolite cavities: due to size restrictions of the zeolite channels and to the distribution of potentially ligating sites on the particle surface or in the channels as well as in the cavity, it is difficult to introduce metals selectively into zeolite cavities via their "inorganic" compounds by conventional ion-exchange methods. Indeed, it has been found to be advantageous in a practical sense to cocrystallize an "inorganic" metal complex and the zeolite to obtain a desired species.[1] Procedures for activation of such materials as catalysts can often lead to migration of metallic centers to the external surface of the zeolite and, since activation is usually performed under strongly reducing conditions, to their aggregation to metal particles. Specific preparation of catalytically active, zeolite-encapsulated metal species, therefore, can be difficult; this in turn hampers rational development of this class of species as selective catalysts. We have recently reported the synthesis and several reactions of families of oxide-bound rhodium hydride complexes, for example, [Si]-ORh(allyl)H,[2] formed by protolytic deposition of a soluble organorhodium species onto an hydroxylated metal oxide. These complexes can be studied on the "molecular level" and have been proven useful as catalysts for hydrogenation of olefins and arenes. We have now demonstrated that this deposition technique using a soluble organometallic complex can be implemented with use of partially proton-exchanged zeolites (for example, those with "super cages" >10 Å in diameter) and have demonstrated the *selective entrapment* of the transition metal inside the "supercage". A zeolite-encapsulated catalyst species can thus exhibit properties different from those of simple oxide-bound ones: such modification can derive from the "molecular sieve" property of the zeolite microcrystals and from the possibility that "three-dimensional" environmental aspects of the supercage can influence substrate-catalyst interactions.

Scheme I. Formation and Reactions of Zeolite-Supported Rhodium Hydrides[a]



[a] [Z-X] = zeolite; [Z-X]-OH = hydroxyl group inside the supercage.

Triallylrhodium reacts with surface hydroxyl groups (Brønsted acid sites), particularly those located within the zeolite cavities of partially proton-exchanged X-type zeolites ([Z-X]-OH), under mild conditions to form the supported diallylrhodium complex [Z-X]-ORh(allyl)$_2$, **1** (see Scheme I). In a typical experiment a solution of 85 mg (0.38 mmol) of Rh(allyl)$_3$ in 5 mL of octane was added to a slurry (in 20 mL of octane) of 1.6 g of partially (15%) proton-exchanged Linde 13X molecular sieve at room temperature. Propylene evolved during deposition (50 h) was identified by GC/MS and was determined quantitatively by using a calibrated PV manometer; on average, 2 equiv of rhodium were deposited per unit cell of the zeolite. Subsequent treatment of **1** with H_2 (1 atm, room temperature, 48 h) led to the formation of dark gray zeolite-bound rhodium hydride **2** (ν_{Rh-H} = 2010 cm^{-1}) with concomitant evolution of 1 equiv of propane. In contrast to its silica-supported analogue,[2] no bridging hydride ligands could be detected by IR analysis; this suggests a distribution of mononuclear complexes in the zeolite cage. The remaining allylic group of **2** could be removed either via slow hydrogenolysis (>10 days, 1 atm, room temperature) or by reaction with gaseous HCl (24 h, 1 atm, room temperature); this latter process gave propene (0.34 equiv), propane (0.46 equiv), and hexane (0.06 equiv).[2] Zeolite-supported rhodium hydridochloride species (**3**) is likely formed.[2] Treating **3** with H_2 gave **4**; two Rh-H bands of equal intensity were observed by IR analysis (ν_{Rh-H} = 2098, 2029 cm^{-1}). No bridging hydride ligands could be detected.[3,4]

Silica-supported rhodium hydride complexes catalyze hydrogenation of variously substituted olefins with relative rates depending solely on local steric congestion about the double bond.[2] In contrast, whereas **2** did exhibit high catalytic activity for olefin hydrogenation, size/shape selectivity for the substrate (attributed to the "molecular sieve" nature of the zeolite support) was also noted. With **2**, linear uptake of H_2 was observed in catalyzed hydrogenation experiments for all olefins studied (Figure 1). However, *rates* (at 1 atm) *for hydrogenation of olefinic substrates larger than cyclohexene were negligible*, demonstrating that the catalytically reactive center is located *within* the intracrystalline volume of the zeolite: transport restrictions preclude hydrogenation of molecules of sizes unable to pass through the crystalline channels. Thus, with [Si]-ORh(allyl)H, rates for catalyzed hydrogenation of 1-butene, 1-hexene, and 1-octene are comparable

(1) Weisz, P. B.; Firilette, V. J.; Maatman, R. W.; Mower, E. B. *J. Catal.* **1962**, *1*, 307.
(2) Ward, M. D.; Schwartz, J. *J. Mol. Catal.* **1981**, *11*, 397. Ward, M. D.; Schwartz, J. *J. Am. Chem. Soc.* **1981**, *103*, 5253.
(3) According to this stoichiometry, [Z-X]-ORhCl$_2$ is likely formed too. It would not be possible to detect this species directly by using spectroscopic techniques available to us. The dichloride should, however, be converted to **3**, and thence to **4**, under the hydrogenation reaction conditions.[2,4]
(4) Ward, M. D.; Schwartz, J. *Organometallics* **1982**, *1*, 1030.

0002-7863/82/1504-5244$01.25/0