(due to vesicle lysis[16]) on the intact vesicles. In the presence of FCCP, pH gradient collapse is known to be coupled to an electroneutral countertransport of metal ions (Na$^+$ in these experiments).[16] However, the rate of gradient collapse may not only directly reflect the efficiency of the channel as a cation transporter but may also reflect the rate at which very active channels are created in the bilayer.[16]

The precise mode of action of the artificial ion channels **6ab** has yet to be established, and the design proposal of Figure 1 remains highly speculative. It is clear, however, that highly active transporters can be created by simple synthetic approaches. We look forward to reporting our further explorations of this strategy for biomimetic ion transport.

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Photodynamic Transport of Metal Ions

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The spiropyranindolines are an important class of photo- and thermochromic compounds whose unusual properties can be attributed to the equilibrium shown in Scheme I.[3] Previous work from our laboratory has demonstrated that the ca. 3 kcal/mol strain energy induced by the macrocycle shown in Scheme I leads to a dramatic shift in the spiropyranindoline = merocyanine equilibrium.[4] Replacing the macrocyclic strap with a ligating group (L) generates a new photodynamic system, **3** = **4** (Scheme II), which in the presence of an appropriate metal cation could exist as **4**, with the liberated phenolate acting as a second ligating group. Visible irradiation of **4** should then regenerate **3** with expulsion of the metal. We report herein that, using suitably substituted spiropyranindolines, *reversible* metal binding can be observed and that light-driven transport of metal ions across an organic membrane has now been achieved using the **3** = **4** system.[5,6]

While the metal ion-mediated conversion of **3a** to **4a** has been reported by Taylor,[7] the reversibility of the metal binding, a critical property for the development of a metal transport system, had not been described.[8] Reaction of **3a** with zinc (2+) salts[9] to generate **4a**, followed by irradiation with visible light, led to complete conversion of **4a** to **3a**, as determined by both NMR[10] and ultraviolet spectroscopy.[11]

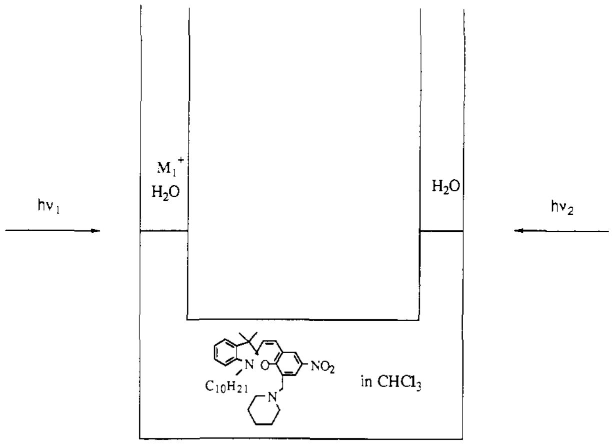


Figure 1.

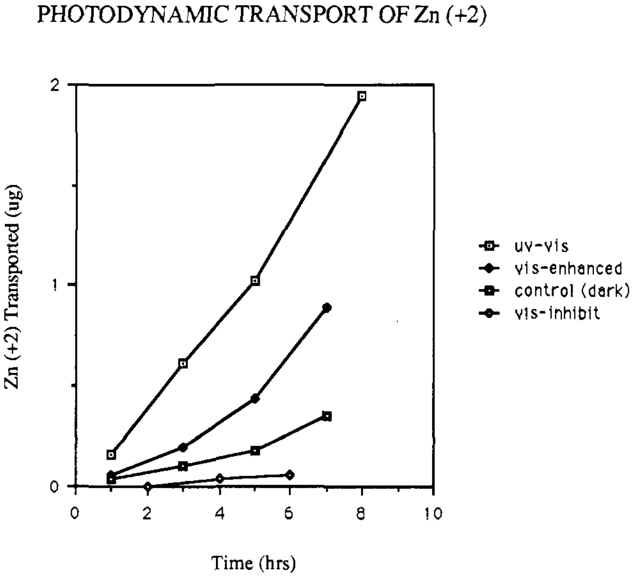
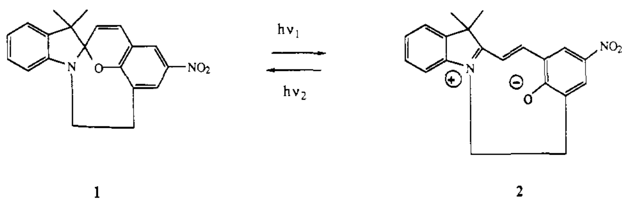
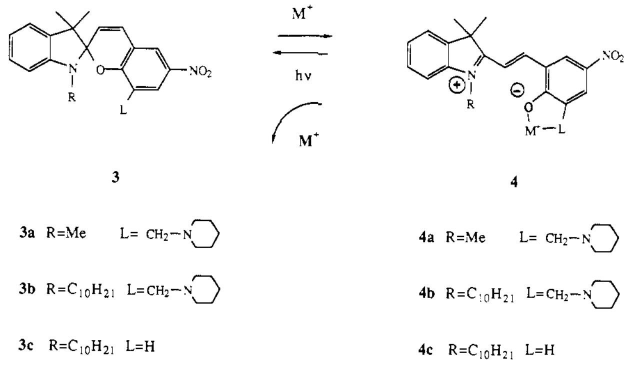


Figure 2.

Scheme I



Scheme II



The ability of **3b**[12] to mediate metal-ion transport across an organic membrane was examined using the apparatus which is

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(10) NMR experiments were performed using 3 mM solution of the spiropyranindoline with 1 equiv of metal perchlorate in deuteriochloroform., Spectra were recorded at 500 MHz.

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Table I. Rate of Ion Transport

	k_{rel}		k_{rel}
Hg^{2+}	200.0	Cu^{2+}	0.4
Zn^{2+}	1.0	Ca^{2+}	0.1
Cd^{2+}	1.0		

outlined in Figure 1. A barrier was placed between the arms of a water-jacketed U-tube, with a 100-W sun lamp (visible light source) on one side and a 350-W medium pressure mercury lamp on the other, immersed in a visible light filter solution that would cut off light with $\lambda > 350$ nm,[13] ensuring the maintenance of constant temperature while the two interfaces were separately exposed to either visible, ultraviolet, or no irradiation ($h\nu_1$ and $h\nu_2$). Four experiments were performed,[14] which are summarized in Figure 2: the metal solution–chloroform interface was irradiated with UV light, and the chloroform–H_2O interface was irradiated with visible light (UV–vis); only the chloroform–H_2O interface was irradiated with visible light (vis-enhanced); the metal solution–chloroform interface was irradiated with visible light (vis-inhibit); and no irradiation at either interface (control). Both aqueous layers had samples removed periodically, which were assayed for metal content by using atomic absorption spectroscopy. As indicated in Figure 1, the rate of transport varied from 0.005 μg/h, when visible light is used to retard metal uptake, to 0.25 μg/h when metal uptake is stimulated with UV irradiation and metal release is induced by visible light irradiation, representing a 50-fold irradiation-dependent variation in transport rate.[15]

These results are consistent with the known effect of visible and ultraviolet irradiation on the concentration of the zwitterionic species in the **3** = **4** equilibrium.[3] Irradiation of the metal solution–chloroform interface with ultraviolet light ($h\nu_1$) increases the concentration of the zwitterionic species so that more metal can be transported across the interface, while irradiation at the same interface with visible light decreases the concentration of the zwitterionic species, and even less metal is transported into the chloroform phase than in the control experiment, in which there is no irradiation at either interface. When the chloroform–water interface is irradiated with visible light ($h\nu_2$), however, the transport rate increases because visible irradiation causes release of the bound metal. The importance of the bidentate zwitterion in achieving the metal ion transport was clearly demonstrated by repeating the zinc transport experiment with **3c**, which lacks the piperidomethyl appendage on the spiropyranindoline. In this experiment, no transport was observed under any of the irradiation conditions.

The transport of other metal ions using **3b** = **4b** was examined, and the results are summarized in Table I. No transport was observed with solutions of Fe^{3+}, Co^{2+}, Ni^{2+}, or Li^{1+}, indicating that group Ib and IIb metal cations are best suited for transport using this system. While Cd^{2+} gave very similar results to those obtained with Zn^{2+}, the results obtained with Hg^{2+} were very different. Not only was the rate of transport much faster with Hg^{2+} than with other ions, but, in contrast to the zinc result described above, the rate of mercury transport was insensitive to UV irradiation at the interface of the chloroform–metal solution ($h\nu_1$). To test whether the same mode of metal binding by **3b** was operational with Hg^{2+} and Zn^{2+}, the mercury experiment was repeated with **3c**, the spiropyranindoline lacking the attached ligating group. While no transport of Zn^{2+} had been observed with **3c**, the rate of transport of Hg^{2+} with **3b** and **3c** were the same, indicating that the binding of mercury by **3b** was different than the other group IIb metal cations, possibly via a π complex, which dissociates on irradiation.[16]

In conclusion, we have demonstrated photodynamic ion transport using spiropyranindoline **3a** and the chloride salts of zinc(II), copper(II), and cadmium(II). Changes in transport rate of an order of magnitude were observed. Further studies directed toward increasing the rate of transport and the development of photodynamic active transport of metal ions across a concentration gradient are currently underway in our laboratory.

Acknowledgment. We thank Professor Brice Bosnich for valuable discussions and Dr. Andrew Davis for invaluable assistance in obtaining the atomic absorption data. Support from the Office of Naval Research and the Dow Chemical Company is gratefully acknowledged. The NMR instruments used were funded in part by the NSF Chemical Instrumentation Program and by the NCI via the University of Chicago Cancer Research Center (CA 14599).

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(11) Ultraviolet spectra of a 5×10^{-5} M solution of spiropyranindoline in 1:1 acetone/ethanol in the presence of 50 equiv of metal chloride or perchlorate were monitored at 520 nm, the λ_{max} of the zwitterionic form **4** (ref 3 and 4).

(12) It was necessary to employ the decyl chain on the indoline nitrogen to prevent the zwitterionic form, **4**, from forming emulsions at the chloroform–water interface.

(13) Sunamoto, J.; Kiyoshi, K.; Yukio, M.; Tetsumi, K. *J. Am. Chem. Soc.* **1982**, *104*, 5502.

(14) The experiments were performed by charging the U-tube with 4 mL of 50 mM $ZnCl_2$, 7 mL of 3 mM spiropyranindoline in chloroform, and 4 mL of H_2O.

(15) Starting with equal concentrations of metal ion in both aqueous phases in the apparatus described in Figure 1 should result in photodynamic transport across the organic membrane, producing an increased metal ion concentration on one side and a diminished one on the other side. However, the rates of transport described in Figure 1 (μg Zn[2+]/hr) are too slow to permit the photodynamic transport of metal ion across a concentration gradient to be accurately measured using the present analytical method.

(16) For a discussion of the reversibility of the mercuration of alkenes, see: Halpern, J.; Tinker, H. B. *J. Am. Chem. Soc.* **1967**, *89*, 6427.

Heteronuclear Three-Dimensional NMR Spectroscopy. Natural Abundance ^{13}C Chemical Shift Editing of ^1H–^1H COSY Spectra

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Homonuclear three-dimensional (3D) NMR spectroscopy has been shown to be an effective means of resolving spectral overlap observed in two-dimensional (2D) NMR experiments.[1-4] By combining two proton 2D NMR experiments in which the detection period of the first experiment serves as the evolution period of the second, a proton that is frequency labeled in t_1 can be correlated to a second proton (t_2) and further correlated to a third (t_3) by using similar or different types of experiments.[2-4] We have recently shown[5] that this same principle can be applied to produce a heteronuclear 3D NMR experiment by combining a heteronuclear shift correlation and a homonuclear 2D NMR experiment (e.g., COSY, NOESY). As previously demonstrated[5] with a uniformly ^{15}N-labeled peptide, homonuclear COSY and NOESY spectra can be simplified with this technique by editing with respect to the heteronuclear chemical shifts in a third dimension. Since a large heteronuclear J coupling is involved in one of the coherence transfer steps, heteronuclear 3D NMR spectroscopy appears particularly promising in structural studies of large, isotopically labeled biomolecules.

In this communication we demonstrate that heteronuclear 3D NMR spectroscopy can also be effectively applied to small molecules with ^{13}C at natural abundance. The approach is illustrated for a 78 mM solution of the aminoglycoside, kanamycin A (structure shown in Figure 1). As for most saccharides, the

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