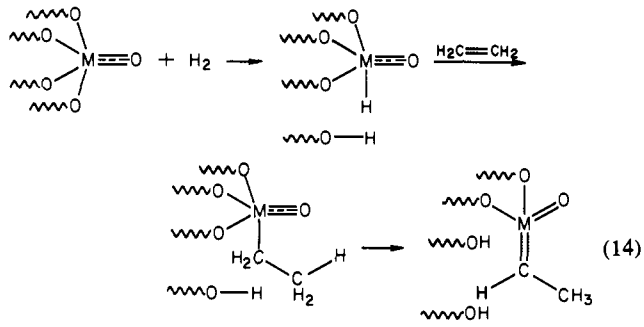
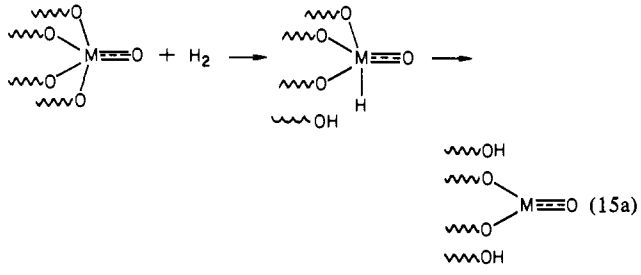
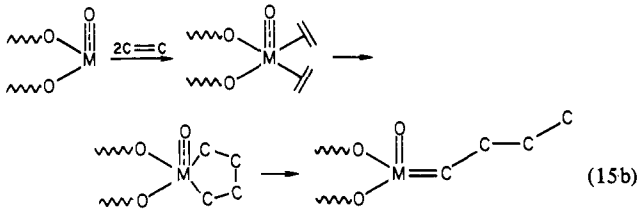


(14)

can catalyze metathesis. The second possibility (eq 15) involves an overall reduction of the metal [formally to M(IV)], (15a),



(15a)



(15b)

followed by reaction with two olefins to form a metallacyclopentane that could undergo internal α abstraction to give the oxo–alkylidene complex, (15b) The rates of these three possible initiation processes, (13), (14), and (15), should depend upon reaction conditions; each may occur in some systems. Since these processes yield different products, it should be possible to design experiments to test these predictions and to establish which occur in various circumstances.

Summary

In summary, we suggest that oxo–alkylidene complexes are the stable metathesis catalysts for high-valent Mo, W, and Re complexes and that the oxygen ligand is intimately involved in the catalytic process. Furthermore, we suggest that similar oxo–alkylidene complexes can be formed on supported catalysts and that dioxo precursors may provide a convenient route to formation of well-defined surface catalysts for olefin metathesis and oxidation reactions. The spectator oxo group is suggested to play a central role in stabilizing the critical intermediate in these reactions and may be important in other reactions of metal oxides (MnO_4^-, OsO_4, RuO_4, supported transition-metal oxides).

Acknowledgment. This research was supported in part by the National Science Foundation (Grant No. CHE-80-17774) and made use of the Dreyfus-NSF Theoretical Chemistry Computer which was funded through grants from the Camille and Henry Dreyfus Foundation, the National Science Foundation (Grant No. CHE78-20235), and the Sloan Fund of the California Institute of Technology. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research.

Registry No. 3 (M = Cr), 57414-29-6; 3 (M = Mo), 13814-75-0; 5 (M = Cr), 14977-61-8; 5 (M = Mo), 13637-68-8; 6 (M = Cr), 79899-75-5; 6 (M = Mo), 79899-76-6; 6 (M = W), 79899-77-7; 7 (M = Cr), 74670-62-5; 7 (M = Mo), 74670-63-6; 7 (M = W), 75213-82-0; 8 (M = Cr), 79899-78-8; 8 (M = Mo), 79899-79-9; 8 (M = W), 79899-80-2; (Cl_2)Ti-O, 13780-39-7; (Cl_2)Ti-CH_2, 79899-81-3; Ti-(O-*t*-Bu)$_4$, 3087-39-6; V-(O-*t*-Bu)$_4$, 10585-27-0; Cr-(O-*t*-Bu)$_4$, 10585-25-8; Ti-(O-*i*-C_3H_7)$_4$, 546-68-9; Zr-(O-*i*-C_3H_7)$_4$, 2171-98-4; Hf-(O-*i*-C_3H_7)$_4$, 2171-99-5; C_2H_4, 74-85-1.

Functionally Polymerized Surfactant Vesicles. Synthesis and Characterization

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Abstract: Bis[2-(10-undecenoyloxycarbonyl)ethyl]dimethylammonium bromide (**1**), bis[2-(10-undecenoyloxycarbonyl)-ethyl](2-hydroxyethyl)methylammonium bromide (**2**), bis[2-(10-undecenoyloxycarbonyl)ethyl]amidophosphoric acid (**3**), bis[2-(10-undecenoyloxycarbonyl)ethyl]-2-sulfoethylamine (**4**), allylbis[2-(dodecanoyloxycarbonyl)ethyl]methylammonium bromide (**5**), and dimethyl-*n*-hexadecyl[10-(*p*-vinylcarboxanilido)decyl]ammonium bromide (**6**) have been synthesized. The predominantly single compartment bilayer vesicles formed from these surfactants could be polymerized either by exposure to ultraviolet irradiation or by the use of azoisobutyronitrile (AIBN) as an initiator. The presence of vesicles (unpolymerized and polymeric) has been demonstrated by electron micrography, ^{1}H NMR, gel filtration, phase transition, turbidity changes, substrate entrapment, and permeability. Rates of light initiated polymerization of vesicles prepared from **6** have been found to be first order (k = 0.10 min^{-1} at 25 °C; [**6**] = 0.33 and 0.20 mg/1.0 mL of H_2O) and independent of the concentration of **6**. Under identical conditions, polymerization of **6** in methanol has occurred at a very much slower rate, and no polymerization has been observed at higher concentrations (2 mg of **6**/2 mL of MeOH). Polymerized vesicles are considerably more stable and less permeable and have reduced rates of turbidity changes compared to their unpolymerized counterparts.

Completely synthetic surfactant vesicles[1] are increasingly being utilized in photochemical solar energy conversion,[2] reactivity control,[3] and drug delivery.[4] Recognizing the need for enhanced stability, Regen reported the first synthesis of a polymerized surfactant vesicle from $(CH_3)_2N^+(C_{16}H_{33})[(CH_2)_{11}OC(=O)C$-

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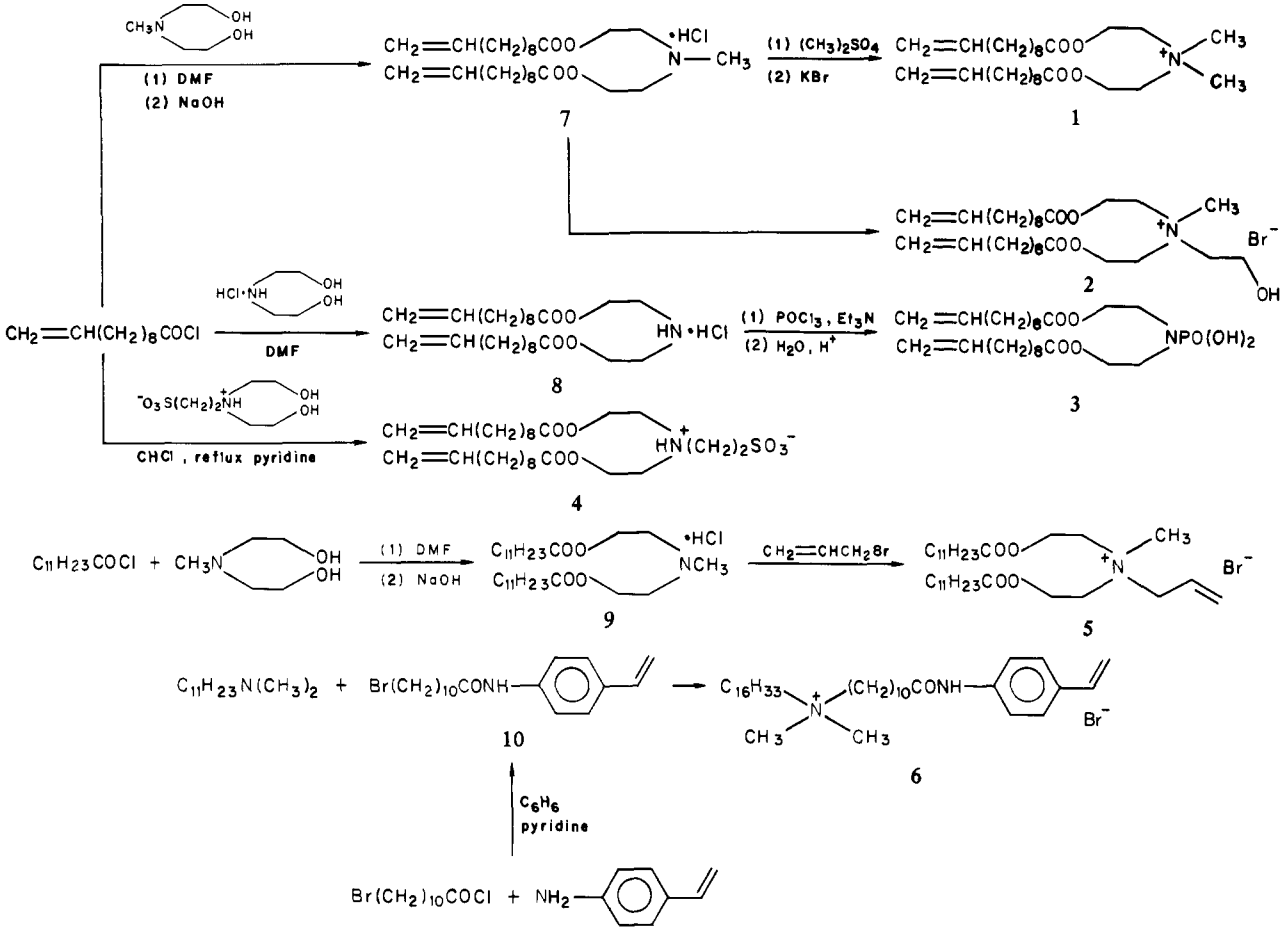
(1) Fendler, J. H. *Acc. Chem. Res.* **1980**, *13*, 7.

0002-7863/82/1504-0456$01.25/0

Scheme I



$(CH_3)_2CH_2]Br^-$.[5] More recently, formation of polymerized model membranes has been described from diacetylenes,[6] butadienes,[7] acrylates,[8] and glycolipids.[8]

This paper reports the synthesis of cationic, anionic, and zwitterionic surfactants containing carbon–carbon double bonds at the end of their hydrocarbon chains, or at their head groups, and the preparation and characterization of polymerized vesicles from these surfactants. Polymerized vesicles showed substantially enhanced stabilities while retaining their permeabilities to H^+ and OH^- and their fluidities.

Experimental Section

Scheme I shows the synthesis of surfactants **1–6**.

Bis[2-(10-undecenoyloxycarbonyl)ethyl]methylamine Hydrochloride (7·HCl). 10-Undecenoyl chloride (44.7 g, 0.22 mol) was added to a solution of 11.9 g (0.10 mol) of *N*-methyliminobis[ethanol] in 80 mL of DMF. After the solution stood for 1 h the product spontaneously crystallized; 250 mL of diethyl ether was added and the mixture was cooled at −10 °C and filtered. Subsequent recrystallization from ethyl acetate afforded 43.8 g (90% yield) of **7**·HCl: mp 108–109 °C; ^{1}H NMR ($CDCl_3$) δ 6.3 (br s, 1 H), 4.68–6.0 (m, vinyl protons, 6 H), 4.48 (t, 4 H), 3.37 (br t, 4 H), 2.87 (s, 3 H), 2.27 (t, 4 H), 2.05 (d, 4 H), 1.0–1.9 (br s, 24 H).

Bis[2-(10-undecenoyloxycarbonyl)ethyl]amine Hydrochloride (8). 10-Undecenoyl chloride (44.7 g, 0.22 mol) was added to a solution of 14.2 g (0.10 mol) of iminobis[ethanol] hydrochloride in 80 mL of DMF. After the solution stood for 1.5 h the product spontaneously crystallized; **8** was recrystallized from this reaction mixture after addition of 100 mL of ethyl acetate. **8**: 35.6 g (75% yield); mp 104–105 °C; ^{1}H NMR ($CDCl_3$) δ 10.0 (br s, 2 H), 4.75–6.20 (m, vinyl protons, 6 H), 4.50 (t, 4 H), 3.40 (br t, 4 H), 2.45 (t, 4 H), 2.05 (d, 4 H), 1.0–1.9 (br s, 24 H).

Bis[2-(dodecyloxycarbonyl)ethyl]methylamine Hydrochloride (9·HCl). Lauroyl chloride (48.1 g, 0.22 mol) was added to a solution of 11.9 g (0.10 mol) of *N*-methyliminobis[ethanol] in 80 mL of DMF; the product crystallized immediately. After the solution stood for 0.5 h, 100 mL of ethyl acetate was added and **9**·HCl recrystallized. **9**·HCl: 49.4 g (95% yield); mp 106–107 °C; ^{1}H NMR ($CDCl_3$) δ 4.60 (t, 4 H), 3.45 (br t, 4 H), 2.45 (t, 4 H), 1.0–1.9 (br s, 36 H), 0.90 (t, 6 H).

11-Bromoundecan-*p*-vinylanilide (10). *p*-Vinylaniline[9] (1.19 g, 10 mmol) and 1.19 g (15 mmol) of pyridine in 50 mL of anhydrous ethyl ether were added to 3.40 g (12 mmol) of 11-bromoundecanoyl chloride with stirring at 0 °C. After 0.5 h the reaction mixture was washed with diluted HCl, aqueous $NaHCO_3$, and water; subsequent solvent removal gave **10**, which when crystallized from benzene–*n*-pentane gave 3.37 g (92% yield). **10**: mp 94–96 °C; ^{1}H NMR (CCl_4) δ 8.2 (br s, 1 H), 7.35 (double d, aromatic protons, 4 H), 4.95–6.85 (m, vinyl protons, 3 H), 3.30 (t, 2 H), 2.30 (t, 2 H), 1.0–2.1 (br s, 32 H).

Bis[2-(10-undecenoyloxycarbonyl)ethyl]dimethylammonium Bromide (1). **7**·HCl (4.88 g, 10 mmol) was treated with 1 N sodium hydroxide in methylene chloride. After solvent removal, the liquid amine was added to dimethyl sulfate (2.5 g, 20 mmol) and heated for 4 h at 85 °C. Ethyl ether and methylene chloride were then added and the solution extracted

(2) Escabi-Perez, J. R.; Romero, A.; Lukac, S.; Fendler, J. H. *J. Am. Chem. Soc.* **1979**, *101*, 2231. Nomura, T.; Escabi-Perez, J. R.; Sunamoto, J.; Fendler, J. H. *Ibid.* **1980**, *102*, 1484. Infelta, P. P.; Grätzel, M.; Fendler, J. H. *Ibid.* **1980**, *102*, 1479. Monserrat, K.; Grätzel, M.; Tundo, P. *Ibid.* **1980**, *102*, 5527. Pileni, M.-P. *Chem. Phys. Lett.* **1980**, *71*, 317. Tunuli, M. S.; Fendler, J. H. *J. Am. Chem. Soc.* **1981**, *103*, 2507.

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(9) *p*-Vinylaniline (mp 24 °C) was obtained by reducing the corresponding nitro derivative by stannous chloride in water:dioxane = 1:1 (v/v).[10,11]

(10) Mowry, D. T.; Renoll, M.; Huber, W. F. *J. Am. Chem. Soc.* **1946**, *68*, 1105. Wiley, R. H.; Smith, N. R. *Ibid.* **1950**, *72*, 5198.

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five times with a saturated aqueous solution of potassium bromide. The subsequent solvent removal gave **1**: 3.7 g (68% yield); mp <20 °C; ^{1}H NMR ($CDCl_3$) δ 4.7–6.0 (m, vinyl protons, 6 H), 4.48 (br t, 4 H), 3.80 (br t, 4 H), 3.30 (s, 6 H), 2.30 (t, 4 H), 2.05 (d, 4 H), 1.0–1.9 (br s, 24 H).

Bis[2-(10-undecenoyloxycarbonyl)ethyl](2-hydroxyethyl)methylammonium Bromide (2). **7** (obtained from 10 mmol of **7**·HCl by CH_2Cl_2/NaOH aq) and 1.88 g (15 mmol) of 2-bromoethanol were heated for 4 h at 85 °C. The reaction mixture was crystallized from benzene–*n*-pentane giving 4.10 g (71% yield) of **2**: mp 63–65 °C; ^{1}H NMR ($CDCl_3$) δ 4.7–6.0 (m, vinyl protons, 6 H), 4.57 (br t, 4 H), 3.7–4.3 (br m, 9 H), 3.43 (s, 3 H), 2.35 (t, 4 H), 2.05 (d, 4 H), 1.0–1.9 (br s, 24 H).

Bis[2-(10-undecenoyloxycarbonyl)ethyl]amidophosphoric Acid (3). **8** (4.75 g, 10 mmol) and 12.1 g (120 mmol) of triethylamine in 70 mL of chloroform were added to 4.6 g (30 mmol) of phosphorus oxychloride with stirring in an ice bath.[12] After 10 h at 0 °C a few milliliters of water were added for hydrolyzing the excess phosphorus oxychloride and the reaction mixture was washed at pH 3 with diluted HCl. The organic phase was dried, the solvent removed, and **3** crystallized from benzene–*n*-pentane. **3**: 2.80 g (54% yield); mp 100–101 °C; ^{1}H NMR ($CDCl_3$) δ 10.1 (br s, 2 H), 2.8–6.1 (m, vinyl protons, 6 H), 4.53 (t, 4 H), 3.40 (br se, 4 H), 2.47 (t, 4 H), 2.10 (d, 4 H), 1.0–1.9 (br s, 24 H).

Bis[2-(10-undecenoyloxycarbonyl)ethyl]-2-sulfoethylamine (4). 10-Undecenoyl chloride (4.47 g, 22 mmol), 2.13 g (10 mmol) of *N*-(2-sulfoethyl)iminobis[ethanol], and 3.2 g (40 mmol) of pyridine in 30 mL of anhydrous chloroform were refluxed overnight. The solvent was removed and the solid **4** was crystallized from methanol. **4**: 4.63 g (85% yield); mp 99–100 °C; ^{1}H NMR ($CDCl_3$) δ 4.7–6.1 (m, vinyl protons, 6 H), 4.48 (br t, 4 H), 3.1–4.0 (br m, 9 H), 2.40 (t, 4 H), 2.05 (d, 4 H), 1.1–1.9 (br s, 24 H).

Allylbis[2-(dodecanoyloxycarbonyl)ethyl]methylammonium Bromide (5). **9**·HCl (5.20 g, 10 mol) was treated with 1 N NaOH in methylene chloride. After solvent removal, the liquid amine was refluxed with an excess (5 mL) of allyl bromide for 3 h. After the removal of the unreacted halide, **5** was crystallized from ethyl acetate. **5**: 5.14 g (85% yield); mp 77–78 °C; ^{1}H NMR ($CDCl_3$) δ 5.6–6.1 (m, vinyl protons, 3 H), 4.3–4.8 (m, 6 H), 4.05 (br t, 4 H), 3.44 (s, 3 H), 2.30 (t, 4 H), 1.1–1.9 (br s, 36 H), 0.90 (t, 6 H).

Dimethyl-*n*-hexadecyl[10-(*p*-vinylcarboxanilido)decyl]ammonium Bromide (6). **10** (3.66 g, 10 mmol) and 3.24 g (12 mmol) of *N,N'*-dimethyl-*n*-hexadecylamine[13] were heated for 12 h at 65 °C. After cooling, the reaction product was crystallized from a few drops of methylene chloride and *n*-pentane. **6**: 5.79 g (91% yield) of **6**; mp 69–70 °C; ^{1}H NMR ($CDCl_3$) δ 9.35 (br s, 1 H), 7.50 (double d, aromatic protons, 4 H), 5.0–7.0 (m, vinyl protons, 3 H), 3.70 (br m, 10 H), 2.50 (t, 2 H), 1.0–2.1 (br s, 44 H), 0.90 (t, 3 H).

All other reagents used were of reagent grade and were used without further purification. Water was purified by deionization and subsequent distillation in an all-glass apparatus.

Typical vesicle formation involved sonicating between 5 and 20 mg of surfactant in 4 mL of water at 60 °C using the microprobe of a Bransonic 1510 sonifier set at 70 W. An optically clear solution was obtained in about 5–20 min.

Vesicles were polymerized by two distinct procedures. In one procedure, 3 mg of free radical initiator azoisobutyronitrile, AIBN (Aldrich), was cosonicated for 4 min at 60 °C with 4 cm^3 of vesicle solution prepared as stated above. Usually a clear to slightly opaque solution was obtained after sonication. This solution was then placed in a paraffin oil bath thermostated to 80 °C for 6 h. The resulting solution is much clearer than the starting vesicle solution. All six compounds were polymerized in this manner. Alternatively, in procedure B, polymerization was accomplished by irradiation by an Oriel 450 W xenon lamp source. The distance between the source and the Quartz cuvette was 18 in. The time required for polymerization varied for each sample. For example, compound **6** required just 40 min and other compounds required between 8 and 10 h. Compounds **2**, **5**, and **6** were polymerized by light. Polymerizations were monitored by ^{1}H NMR using a Varian XL-200 spectrometer in D_2O (Aldrich, 99.8% D) performing 50 000 to 100 000 scans. Disappearance of the vinyl protons in the region 4.5–6.5 ppm was followed at ambient temperature using sodium 2,2-dimethyl-2-silapentane-5-sulfonate, DSS, as an internal standard.

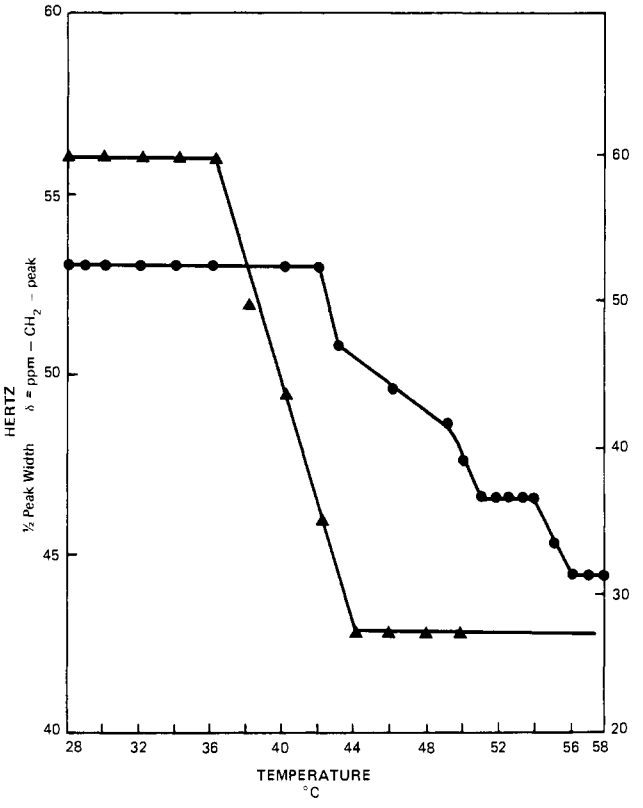

Figure 1. Plots of the alkyl CH_2 ^{1}H NMR half-line width (at 1.38 ppm from DSS) for AIBN polymerized (▲) and unpolymerized (●) vesicles prepared from **6** as functions of temperature.

Polymerization rates for **6** were determined by following the absorption changes at 282 nm as a function of irradiation time. Irradiations of thermostated (25 °C) vesicle solutions were carried out by a 450 W xenon lamp. The lamp intensity was determined to be 7×10^{13} photons per cm^2 per s at the position of irradiation by means of a ferrioxalate chemical dosimeter.[15]

Samples for electron microscopy were prepared by mixing equal volumes of the polymerized vesicle solution (**1**–**6**) with a 5% uranyl acetate solution. This solution was then placed on the copper grid for 1–2 min. Times over 3 min seemed to cause clumping of the polymerized vesicles. Electron micrography was performed on a Hitachi HU-11E electron microscope.

Entrapment of either 2-aminopyridine·HCl (Aldrich) or 1-pyrenesulfonic acid (Aldrich) was performed by sonicating (70 W at 60 °C) equal volumes of a 0.57 mM solution of 2APHCl (pH 4.6) in the case of compounds **1**, **2**, **5**, **6** or an equal volume of a 0.97 mM 1-pyrenesulfonic acid in the case of compounds **3** and **4**. The resulting solutions were then divided. Half were polymerized by addition of AIBN (and resonication at 70 W, 60 °C) or using light (450 W xenon lamp) and the other half were not polymerized. Both solutions (immediately after vesicle formation or polymerization) were passed through a Sephadex column (Sigma G-50-80, 20.80 μm, 16 × 178 mm) using water an as eluent to separate bound from free 2APHCl or 1-pyrenesulfonic acid. Once entrapped, these probes remained in the vesicle interiors for days. Fluorescence measurements were made on a SPEX Fluorolog spectrofluorometer in the E/R model. Generally, 2.5-mm slits with a 5-nm band path were used. All fluorescence measurements were determined in air-saturated solutions.

Stabilities of vesicles to ethanol were investigated by adding 0.1-mL aliquots of methanol (Fisher) to 2 cm^3 of the vesicle or polymerized vesicle solutions (as prepared above), then mixing the resulting solutions and measuring the absorbance change at 400 nm using a Cary 118C spectrophotometer. The equation

$$A_{corr} = A_{obsd}\frac{\text{mL of vesicle + mL of alcohol}}{\text{mL of vesicle}}$$

was used to correct for absorbance change due to dilution.[5]

Turbidity changes were followed by injecting 0.1 mL of 3.0 M NaCl solution into 3.0-mL vesicles containing 1.7×10^{-3} M stoichiometric

(12) Eibl, H.; Arnol, D.; Werlzleen, H. U.; Westphal, O. *Justus Liebigs Ann. Chem.* **1967**, *709*, 226.

(13) *N,N'*-Dimethyl-*n*-hexadecylamine (bp 140–142 °C; 0.4 torr) was obtained from *N,N'*-dimethylpalmitoylamide by reduction in THF.[14]

(14) Staudinger, H.; Roessler, K. *Chem. Ber.* **1936**, *69*, 61. Raltson, A. W.; Eggenberger, D. N.; Harwood, H. J.; DuBrow, P. L. *J. Am. Chem. Soc.* **1947**, *69*, 2095.

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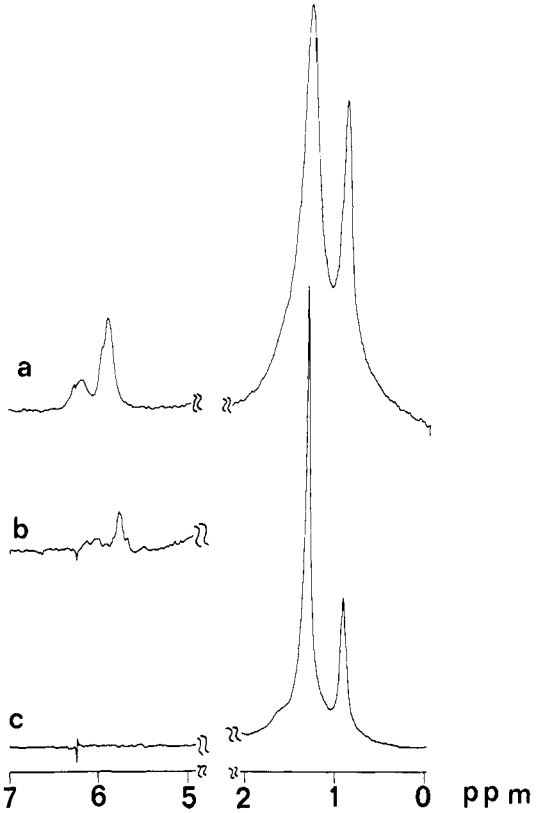

Figure 2. (a) ^1H NMR spectrum of sonicated (25 mg/4 mL of D_2O, sonicated at 70 W) nonpolymerized surfactant vesicles, prepared from **5**. (b) Vinyl protons of **5** subsequent to partial polymerization of already formed vesicles (AIBN added to the outside of sonicated **5**). (c) ^1H NMR spectrum of sonicated, completely polymerized (by UV light) surfactant vesicles prepared from **5**. Complete loss of vinyl protons is clearly seen. Chemical shifts were recorded on a Varian XL 200 MHz instrument at ambient temperature relative to sodium 2,2-dimethyl-2-silapentane-5-sulfonate, DSS (~100 000 scans).

surfactant (i.e., final electrolyte gradient between inside and outside of vesicle = 0.10 M). Changes of time-dependent absorbances, at 400 nm, were monitored to calculate initial rates of turbidity changes.[16]

Results and Discussion

Vesicle Formation. All the surfactants, with the exception of **1**, were found to be completely insoluble in water. They could be dispersed, however, by ultrasonic irradiation. Increasing the sonication time resulted in an exponential decrease of turbidity (monitored at 400 nm) down to a plateau value. Further sonication did not appreciably alter the turbidity. Each surfactant was sonicated as long a time as it took to reach the beginning of the plateau value in the turbidity–time plots. These "well-sonicated" surfactants have been considered to contain reasonably uniformly sized single compartment surfactant vesicles.[1,17,18]

Vesicle formation has been substantiated by ^1H NMR spectroscopy, substrate entrapment, and gel filtration, as well as by observing thermotropic phase transitions and turbidity changes. Thus, incompletely sonicated surfactants showed extremely broad ^1H NMR signals. Conversely, well-sonicated surfactants gave well-resolved ^1H NMR spectra with discrete magnetic resonances corresponding to the chemical shifts of the surfactants in $CDCl_3$ (see Experimental Section). The presence of intact vinyl protons was clearly seen in all spectra.

2-Aminopyridine hydrochloride was entrapped in surfactant vesicles prepared from **1**, **2**, **5**, and **6** in 1%, while 1-pyrenesulfonic acid was incorporated into **3** and **4** in 0.01%. Gel filtrations on Sephadex G-25 were used to quantify the extents of entrapment.

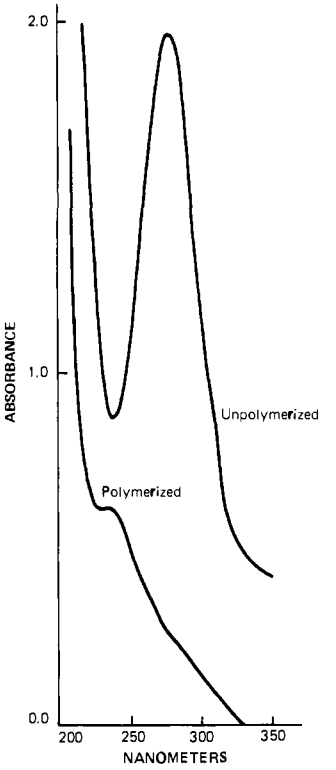

Figure 3. Absorption spectra of vesicles prepared from **6** prior and subsequent to polymerization by a 450 W xenon lamp.

The appearance of some of these probes in the void volume is only explicable in terms of their association with the surfactant vesicles.

Phospholipid vesicles undergo distinct structural changes at a certain temperature, the phase transition temperature, when heated or cooled.[19] Below the phase transition temperature lipids in the bilayers are in highly ordered "gel" states, with their alkyl chains in all-trans conformations. Above the phase transition temperature lipids become "fluid" as the consequence of gauche rotations and kink formation. The observation of distinct phase transition temperatures for completely synthetic surfactant vesicles[1,17,18] confirmed the similarity between liposomes and surfactant vesicles.[1] Vesicles prepared from **1**, **2**, **4**, **5**, and **6** all showed temperature-dependent phase transitions (Table I) as determined by following changes in the turbidity or in ^1H NMR line widths (Figure 1).

Electrolyte induced turbidity change is also an inherent property of lipid vesicles.[20] Surfactant vesicles investigated in the present work like those examined previously[18] also undergo turbidity changes. They shrink in hyperosmolar and swell in hypoosmolar solutions.

Surfactant vesicles prepared from **1**, **2**, and **4** were found to be stable for weeks. Those prepared from **3**, **5**, and **6** were stable only for hours. Interestingly, vesicles prepared from **2**, **4**, and **5** could not be destroyed by the addition of 9%, 13%, and 5% ethanol, respectively. Additional alcohol destroyed these vesicles, of course.

Vesicle Polymerization. Polymerized vesicles were obtained either by heating the surfactant with AIBN or by exposing them to ultraviolet irradiation (see Experimental Section).

Polymerization of vesicles prepared from **1**, **2**, **3**, **4**, and **6** results in "zipping-up" each half of the bilayer separately or cross-linking them. Polymerization of vesicles prepared from **5** offers the possibility of "zipping-up" separately either the inner or the outer surface. Alternately both surfaces may be polymerized. Ultraviolet irradiation of vesicles prepared from **5** resulted in the complete loss of vinyl protons (Figure 2c) indicating the cross-linkage of both the inner and outer surfaces. Conversely, addition

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(17) Lim, Y. Y.; Fendler, J. H. *J. Am. Chem. Soc.* **1979**, *101*, 4023.
(18) Kano, K.; Romero, A.; Djermouni, B.; Ache, H. J.; Fendler, J. H. *J. Am. Chem. Soc.* **1979**, *101*, 4030.
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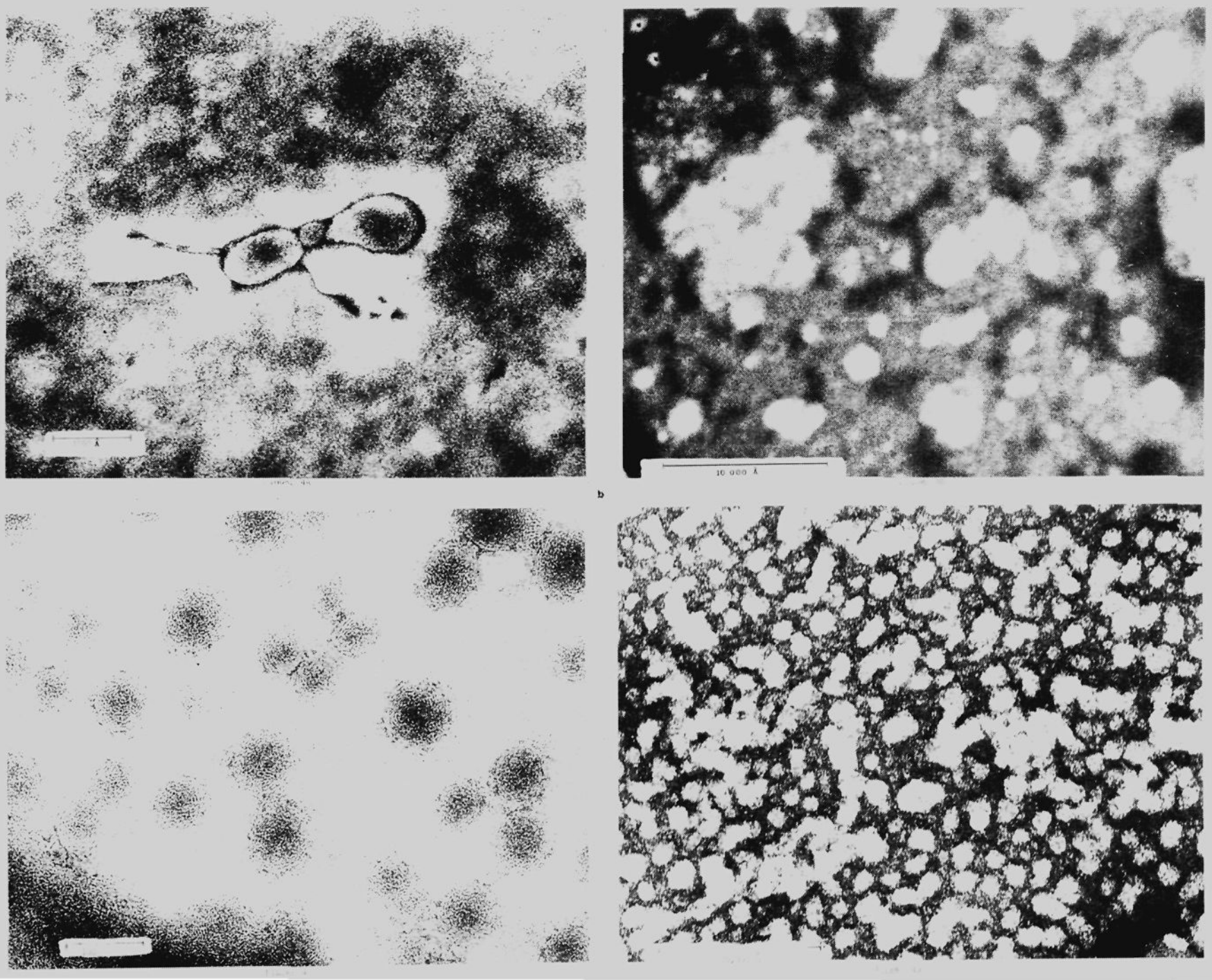

Figure 4. Electron micrographs of uranyl acetate stained polymerized surfactant vesicles prepared by adding AIBN to the outside of already sonicated **5** (a), by cosonicating AIBN with **6** (b), by cosonicating AIBN with **3** (c), and by UV light polymerizing **6** (d).

Table I. Properties of Unpolymerized and Polymeric Vesicles

vesicle	stability to EtOH, %	phase transition temp, °C	rates of turbidity changes, s^{-1}	hydroxide ion permeability time
1 unpolymerized	0	32		I[a]
1 polymeric	25			>1 h
2 unpolymerized	9	44		I[a]
2 polymeric	12			~10 min
3 unpolymerized	0		2×10^{-2}	
3 polymeric	0		2×10^{-4}	
4 unpolymerized	13	47	$\sim 10^{-2}$	
4 polymeric			1.4×10^{-4}	
5 unpolymerized	5	31		I[a]
5 polymeric	10			~20 min
6 unpolymerized	0	41	2×10^{-2}	I[a]
6 polymerized	33	40	4.7×10^{-4}	~30 min

[a] Instantaneous.

of AIBN to *already sonicated* **5** and subsequent heating caused incomplete loss of the vinyl protons (Figure 2b). Integration of the vinyl proton regions (δ 5.5–6.1) with respect to CH_3N of the surfactant showed approximately 60% polymerization. This corresponds to "zipping-up" only the outer surface of vesicles prepared from **5**. Figure 3 shows changes in the absorption of **6** accompanying polymerization.

Rates of polymerization of vesicles prepared from **6** were found to be independent of the stoichiometric surfactant concentrations. The first-order rate constants at 25.0 °C, obtained from good linear plots covering 85–90% reactions for the polymerization of sonicated vesicles prepared from 0.20 mg of **6** in 1 mL of water and 0.33 mg of **6** in 1 mL of water, were found to be 0.10 min^{-1} and 0.10 min^{-1}, respectively. Significantly, polymerization rates of 0.2 mg of **6** in 2.0 mL of methanol, where no aggregates could be present, were very much smaller ($t_{1/2} \approx 50$ min), and no observable polymerization occurred upon the overnight irradiation of 2 mg of **6** in 2 mL of methanol. These results show the need for proper alignments of surfactants for polymerization and provide additional evidence for the presence of vesicles.

Characterization of Polymerized Vesicles. Polymerized vesicles are considerably more stable than their unpolymerized counterparts. They show no sign of fusion or deterioration over months. They have also improved stabilities against lysing by alcohol (Table I).

The presence of closed vesicles with average diameters of 1000 Å was established by their electron micrographs (Figure 4).

^1H NMR line broadening (Figure 1) and turbidity measurements indicated thermotropic phase transition for polymeric **6**. Unfortunately, under the conditions used (AIBN polymerization), ^1H NMR line broadening could not be used for determining temperature dependencies on the line broadening. It should be remembered that phase transition temperatures and the ranges of transition depend somewhat on the measurements utilized. Indeed no transition was observed for polymeric surfactant vesicles prepared from phosphatidylcholine–diacetylene vesicles.[21]

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Rates of turbidity changes of polymeric vesicles are appreciably smaller than those for their unpolymerized counterparts (Table I).

Proton and hydroxide ion permeabilities in polymerized vesicles are much slower than those in their unpolymerized analogues. Permeabilities of these ions in dimethyldioctadecylammonium chloride surfactant vesicles are instantaneous.[1] Conversely, hydroxide ion permeates into polymerized surfactant vesicles with half lives ranging from 5–20 min (Table I). Significantly, permeation into completely polymerized vesicles of **5** is slower than that into vesicles of **5** "zipped-up" only on their outer surfaces.

Polymerization of surfactant vesicles provides convenient permeability control and allows the creation of pH gradients in addition to enhancing stabilities. Importantly, beneficial properties (ability to compartmentalize substrates in different microenvironments, presence of high-surface potential, charge density, and phase transition) remain unaffected. Further characterization and exploitation of these and related surfactant vesicles are under active investigation in our laboratories.

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Registry No. 1, 79898-71-8; 1 polymeric, 79899-59-5; **2**, 79898-72-9; **2** polymeric, 79899-60-8; **3**, 79898-73-0; **3** polymeric, 79899-61-9; **4**, 79898-74-1; **4** polymeric, 79899-62-0; **5**, 79898-75-2; **5** polymeric, 79899-64-2; **6**, 79898-76-3; **6** polymeric, 79899-65-3; **7** HCl, 79919-75-8; **8** HCl, 79898-77-4; **9** HCl, 79898-78-5; **10**, 79898-79-6; 10-undecenoyl chloride, 38460-95-6; *N*-methyliminobis[ethanol], 105-59-9; iminobis-[ethanol] HCl, 14426-21-2; lauroyl chloride, 112-16-3; *p*-vinylaniline, 1520-21-4; 11-bromoundecanoyl chloride, 15949-84-5; 2-bromoethanol, 540-51-2; phosphorus oxychloride, 10025-87-3; *N*-(2-sulfoethyl)iminobis[ethanol], 10191-18-1; allyl bromide, 106-95-6; *N,N*-dimethyl-*n*-hexadecylamine, 112-69-6.

Nucleoside Complexing: A ^{13}C NMR Spectroscopic Study of Binding of Metal Ions to Guanosine and Related Nucleosides in Solution. Evidence for O-6 Binding under Basic Conditions

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Abstract: The influence of hard and soft metals on the ^{13}C NMR spectrum of guanosine and inosine under both neutral and basic conditions in Me_2SO has been determined. Several related molecules also studied include 2′-deoxyguanosine, 1-methylguanosine, and N^2,N^2-dimethylguanosine. Under neutral conditions, hard metal species such as $Ba(NO_3)_2$ and $Pr(NO_3)_3$ do not perturb the ^{13}C NMR spectrum of guanosine, but under basic conditions (in the presence of the amine base triethylamine) a considerable change in the ^{13}C NMR spectrum is observed. An analogous effect is observed for N^2,N^2-dimethylguanosine, but is absent for 1-methylguanosine. Under neutral conditions, soft metal species such as $HgCl_2$ bind readily to guanosine, 1-methylguanosine, and N^2,N^2-dimethylguanosine, but in the presence of the amine base triethylamine, $HgCl_2$ binds only to guanosine. Triethylamine alone does not significantly perturb the ^{13}C NMR spectrum of guanosine or its derivatives, and these results suggest that metals do promote deprotonation at N(1). The shifts observed are best interpreted as resulting from the binding of the hard metal species to O(6) of guanosine when N(1) is deprotonated and the binding of the soft metal species to N(1) after deprotonation. The influence of metal ions on the ^{13}C NMR shifts with 1-methylguanosine and N^2,N^2-dimethylguanosine is consistent with these binding site assignments.

Since the discovery of the effectiveness of certain platinum(II) antitumor agents,[1] which are generally believed to function by binding to nucleic acids in the tumor cells,[2] there has been increased research focused at understanding the interactions of metals with nucleic acid derivatives.[3] In particular, the antitumor agent *cis*-$[Pt^{II}(NH_3)_2Cl_2]$ is known to interact with guanine[4] or at least at the GC pair,[5] and may interact with the 6-oxo group promoting deprotonation at N(1).[6-9] Such deprotonation could lead to the mispairing of guanosine with thymine, and eventually cell death.[2] Such mispairing also bears directly on metal mutagenicity. However, virtually all attempts to demonstrate the binding of Pt(II) complexes and many other metal species with O(6) have proved unsuccessful although very weak binding has been demonstrated in the solid state for a few special cases.[6,10-13] One impediment to the definitive evaluation of the importance of such binding in solution is the lack of effective spectroscopic criteria for its assessment.[14]

We believe that N(9)-alkylated guanines (Figure 1; when S = D-ribose the molecule is named guanosine) can be viewed as having three likely metal binding regions. Region K, involving the N(7) site of the five-membered ring, is the *kinetically* favored site since it is not protonated under neutral conditions. Region T, involving the N(1) site, is the *thermodynamically* favored binding site for softer metal species (Hg(II), Pt(II), Pd(II), etc.). However, this site is protonated under neutral conditions and is

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