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Complexation of polyethers and pyridyl ligands with monopositive transition metal ions in the gas phase

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Abstract

The formation, ligand exchange reactions, and dissociation of various types of mixed ligand/metal complexes are studied in a quadrupole ion trap. The monopositive complexes are generated by ion-molecule association reactions between the polydentate organic ligands and laser-desorbed monopositive metal ions (M^+) and incorporate at least one polyether or at least one pyridyl ligand bound to a transition metal ion. Ligand exchange and collisional activated dissociation (CAD) techniques are used to investigate the nature of the binding interactions and the relative binding free energies of the various ligands. There are two dominant influences on the strength of the binding interactions in the complexes. First, the number of coordination sites of each ligand and its flexibility or ability to participate in cooperative binding interactions are reflected in the relative coordination capabilities of the ligands. Second, the ability of a ligand to approach the metal ion and successfully adopt a favorable binding conformation differs greatly when the metal is already bound to one versus two ligands. For example, when the metal is bound to two pyridyl ligands, the ability of a large flexible polyether with multiple oxygen binding sites to displace even one of the pyridyl ligands is greatly reduced relative to the case when the metal is only bound to a single pyridyl ligand. In addition to these two trends, the electronic configuration of the metal ion also plays a subtle role in terms of influencing the stabilities of certain monomer (pyridyl ligand + M^+) and heterodimer (pyridyl ligand + M^+ + polyether) complexes. However, the nature of the metal ion does not appear to change the trends in relative binding free energies of the various ligands; it simply influences the formation of certain types of complexes based on the optimum coordination number and favored coordination geometry of the metal ion. (Int J Mass Spectrom 176 (1998) 39–61) © 1998 Elsevier Science B.V.

Keywords: Metal complexation; Ligand exchange; Polyether; Pyridyl ligand; Transition metal

1. Introduction

Polydentate molecules, such as crown ethers or pyridyl ligands, may engage in chelation [1–2] or multisite coordination with metal ions (M^+). The coordination chemistry of these model ligands has been extensively studied in solution because fundamental aspects about metal binding, such as the influence of the size and flexibility of the ligand and its number of coordination sites, can be evaluated in detail [3–7]. In addition, binding constants can be readily measured for the metal/ligand complexes in solution [8–10], providing a quantitative means of comparing structural and electronic influences on aspects of coordination chemistry. Studies undertaken in the gas phase in a mass spectrometer provide a solvent-free environment for evaluating the intrinsic

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binding properties of chelating ligands. In the present study, we extend our ongoing investigation of multisite coordination chemistry in the gas phase to transition metal complexes that contain both polyether (L_2) and pyridyl ligands (L_1). Although relatively simple molecules, the pyridyl and polyether ligands are excellent models for studying fundamental aspects of complexation that may be relevant for understanding the behavior of biologically related receptor ligands that may participate in noncovalent binding interactions within supramolecular complexes.

There has been great interest in probing the reactions of metal ions with organic ligands in the gas phase [11–21]. The transition metal ions have partially filled d orbitals and undergo an enormous array of reactions with organic molecules in the gas phase. Molecules that have an array of identical binding sites, such as crown ethers or multidentate pyridine ligands, are especially interesting candidates for reactions with metal ions in the gas phase because multisite coordination occurs. Because size selectivity and the degree of ligand organization may play influential roles in transition metal coordination by polydentate ligands, aspects of molecular recognition are also relevant in the context of this type of complexation [22–27]. An increasing number of studies have evaluated aspects of host–guest chemistry in the gas phase [28–37], most dealing with complexation of alkali metal ions or ammonium ions by polyethers. There have been only a few gas-phase studies of the chelation of polyether or pyridyl ligands with transition metal ions [38–42]. In one recent study, gas-phase chelation reactions between an array of pyridyl ligands and a series of monopositive transition metal ions were evaluated [42]. The extent of bis- and tris-complex formation was examined, and the orders of relative transition metal ion binding free energies were measured for the series of pyridyl ligands. It was found that the extent of coordination in terms of bis vs. tris complexation correlated with the n-dentate nature of the ligand and the electronic configuration of the monopositive metal ion. In the gas phase, the order of metal binding free energies was 2,2′:6,2″-terpyridine > 1,10-phenanthroline > 2,2′-bipyridine > 4,4′-bipyridine > pyridine [42]. In another recent study from our group [40], it was found that for a series of polyether/transition metal ion complexes, collisionally activated dissociation reactions were mediated by the size of the polyether and the electronic configuration of the metal ion. These differences were rationalized based on the flexibility of the polyether and its number of coordinating sites, factors that affected the geometry during coordination of the metal ion. In a third recent study [41], the formation of dimer complexes consisting of a transition metal ion bound to two polyether ligands and then dissociation of the resulting dimer complexes was examined. The results confirmed that the more flexible polyethers had enhanced ability to fully coordinate or encapsulate the metal ion relative to the more rigid polyethers.

In this work, we evaluate the formation of various mixed ligand/metal complexes. The complexes incorporate at least one polyether or at least one pyridyl ligand bound to a transition metal ion. Ion-molecule association reactions are used to generate complexes between the polydentate organic ligands and laser-desorbed monopositive metal ions. Ligand exchange and collisional activated dissociation (CAD) techniques are used to investigate the nature of the binding interactions and the relative binding free energies of the various ligands. The ligand exchange results allow evaluation of formation of the thermodynamically favored metal complexes, whereas the CAD experiments shed light on disassembly of the dimer complexes. The primary objective is to obtain an understanding of the structural factors of the ligands that influence the stability of the complexes, and thus provide some basic information for predicting the nature of binding interactions in other types of transition metal complexes or large supramolecular assemblies that might involve an array of cooperative binding sites and in which conformational constraints must be accommodated to maximize the binding interactions. A second objective is to compare the relative metal binding free energies of the polyether versus pyridyl ligands within one-ligand and two-ligand complexes in order to obtain some basic information about how the binding free energies are altered when the metal ion becomes more fully

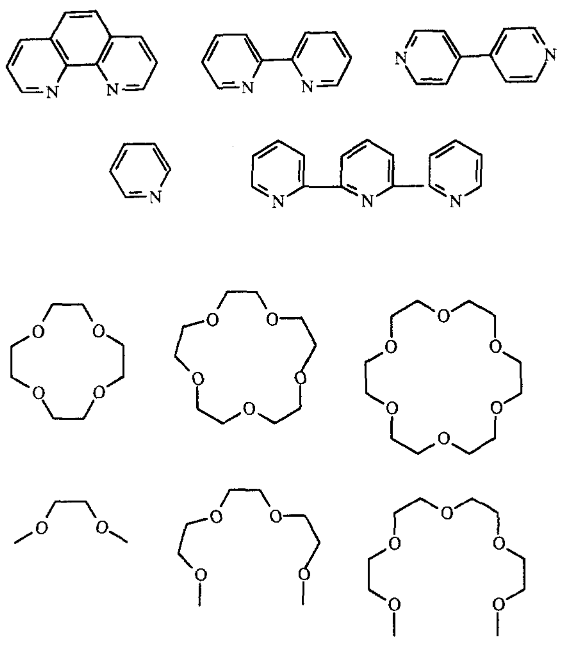

Fig. 1. Structures of ligands.

coordinated and ligand repulsions are significant. Such information could provide initial insight into how the complexation of biological ligands, such as proteins, to metal ions or polyatomic guests in the gas phase may be adequately modeled by studies involving simpler ligands, such as peptides.

The ligands of greatest interest in this study include the pyridyl molecules: 2,2′,6′,2″-terpyridine, 2,2′-bipyridine, 1,10-phenanthroline, and 4,4′-bipyridine, and the polyether molecules: 18-crown-6, 15-crown-5, 12-crown-4, triethylene glycol dimethyl ether (triglyme), dietheylene glycol dimethyl ether (diglyme), and ethylene glycol dimethyl ether (monoglyme) (Fig. 1). The heteroaromatic ligands possess from one to three nitrogen donor atoms that serve as the coordination sites for binding the transition metal ions. Three of the ligands, 2,2′,6′,2″-terpyridine, 2,2′-bipyridine, and 1,10-phenanthroline, are chelating agents because of the ability of the nitrogen atoms to cooperatively bind a metal ion. 4,4′-Bipyridine is a related model that is similar in size to 2,2′-bipyridine but is not a chelator. The crown ethers and glymes possess an array of oxygen donor atoms that may coordinate the metal ion, and they have varying degrees of flexibility that will influence the ability of the polyether to attain an optimum configuration for binding the metal ion with a maximum amount of favorable interactions and a minimum of ligand repulsions.

2. Experimental

These experiments were performed in a Finnigan MAT quadrupole ion trap mass spectrometer (ITMS) [43] equipped with a probe-mounted fiber optic laser desorption assembly [44]. Metal ions were generated by pulsed laser desorption of a metal foil applied to a Teflon sample support. A Nd:YAG laser operated in the Q-switch mode provided the desorption pulse. Transition metal ions were desorbed with a power density of 2×10^8 W/cm^2. The metal ions are stored in the ion trap and allowed to undergo reactions with neutral polyethers and pyridyl ligands for 20 to 200 ms. Each ligand was admitted through a leak valve or on a solids probe to nominally 1 to 2×10^{-6} Torr. A short electron ionization (EI) pulse (10 ms) was used to evaluate the relative amount of each reactant to avoid dependence on partial pressure readings. All EI fragments from one reactant were co-added so the overall intensity could be compared with the other reactant. Ligand concentrations were also verified by proton-transfer reactions from protonated dimethyl ether to the ligand in a short chemical ionization period. The estimated concentrations of the ligands were comparable by both methods. In either case, it is difficult to establish equal concentrations of any pair of ligands with great certainty because one ligand must always be added after the first one, and thus our efforts centered on developing a reproducible procedure that may suffer from some modest systematic errors. The metal complexes are mass-analyzed by operating the ion trap in the mass selective instability mode in which a radiofrequency (rf) voltage applied to the ring electrode is used to eject ions onto an externally located electron multiplier detector. A helium buffer gas pressure of 1 to 2 mTorr is used to assist in collisional cooling of the complexes. The

CAD spectra of the metal complexes were obtained by applying a small ac voltage (500 to 1000 $mV_{p\text{-}p}$) across the end-cap electrodes at a q_z value of 0.3 for 5–10 ms.

All polyethers, pyridyl compounds, and transition metal foils were obtained from Aldrich Chemical Company (Milwaukee, WI). All reagents were used without further purification.

3. Results and Discussion

3.1. Formation and ligand exchange reactions of monopositive complexes

By monitoring the ligand exchange reactions of the (polyether + M^+) and (pyridyl ligand + M^+) complexes, the relative binding free energies of the ligands are elucidated. Three factors influence the experimentally measured relative binding free energies. First, the intrinsic metal binding affinities of each ligand contribute to the enthalpic term of the binding free energy. The intrinsic metal binding affinities are determined by the number and type of donor atoms, either nitrogen or oxygen atoms for the ligands in this study. Second, the degree of organization of the ligands upon metal complexation via formation of possibly several metal–ligand interactions and the concomitant loss of degrees of freedom may contribute substantially to the observed binding free energies as the entropic term. Third, the rates of the ligand exchange reactions may be influenced by steric effects because of partial or complete encapsulation of the metal ion by a ligand, referred to herein as shielding of the metal ion. Such shielding may slow down a decomplexation reaction, thus creating an activation barrier in the ligand exchange sequence. The importance of these effects can be sorted out by comparing the reactions of many types of ligands that vary in their flexibility and intrinsic binding affinity of the donor atoms. The ligand exchange reactions of the (2 × pyridyl ligand + M^+), (pyridyl ligand + M^+ + polyether), and (2 × polyether + M^+) complexes allow comparison of the binding interactions of the two ligand versus one ligand complexes, thus giving insight into the importance of steric shielding of the metal ion. Although the concentrations of the ligands could not be precisely controlled to allow equilibrium determinations, a good qualitative picture of the relative metal/ligand preferences of the binding interactions was developed from this systematic ligand exchange strategy. In addition, collisionally activated dissociation was used to evaluate the fragmentation pathways of the (L_1 + M^+ + L_2) complexes (see Table 10 later). The CAD spectra give information about the kinetically favored pathways for disassembly of the complexes, and these pathways do not necessarily correspond to the thermodynamically favored pathways for assembly of the complexes.

All monopositive complexes were formed by reactions of laser-desorbed metal ions with selected polyethers and pyridyl ligands. Because of the high energy deposition of the laser desorption event, some of the metal ions could potentially exist in excited electronic states. To probe the existence of excited states, the helium buffer gas pressure was varied from 0.5 to 2.5 mTorr, the laser power was varied from ~5 to 30 mJ/pulse, and the cooling time of the metal ions before the ion-molecule reaction period was varied from 2 to 500 ms. From these systematic studies, no evidence for the existence of excited states was found because there were no changes observed in the reactivity patterns of the metal ions as the experimental conditions were varied. Thus, for the remainder of the discussion, the issue of excited states will not be addressed.

Depending on the pyridyl and polyether ligands selected, a variety of complexes were formed, including (L_1 + M^+), (L_2 + M^+), ($2L_1$ + M^+), ($2L_2$ + M^+), and the heterodimer (L_1 + M^+ + L_2). To probe the nature of the binding interactions of these complexes, each one was isolated and then allowed to undergo ligand exchange reactions for 300 ms with neutral L_1 and L_2 ligands in the trap. These results are summarized in Tables 1 to 9. For example, the first series of experiments involved ligand exchange reactions between 18-crown-6 and 2,2′,6′,2″-terpyridine. Both 18-crown-6 and 2,2′,6′,2″-terpyridine were admitted at similar concentrations to the ion trap and allowed to react with Ni^+ ions. The (18-crown-6 +

Table 1
Product distributions after ligand exchange reactions involving 2,2′:6′,2″-terpyridine or polyether complexes with 2,2′:6′,2″-terpyridine and polyether neutrals[a]

	Products				
Selected complex	(Ether + Ni$^+$)	(2 × Ether + Ni$^+$)	(Ether + Ni$^+$ + terpyridine)	(Terpyridine + Ni$^+$)	(2 × Terpyridine + Ni$^+$)
(18-C-6 + Ni$^+$)	93	0	0	5	2
(Terpyridine + Ni$^+$)	0	0	1	64	35
(15-C-5 + Ni$^+$)	90	0	0	10	0
(Terpyridine + Ni$^+$)	0	0	0	65	35
(12-C-4 + Ni$^+$)	60	5	0	20	15
(Terpyridine + Ni$^+$)	0	0	0	65	35
(Tetraglyme + Ni$^+$)	90	0	0	8	2
(Terpyridine + Ni$^+$)	0	0	0	70	30
(Triglyme + Ni$^+$)	75	0	0	20	5
(Terpyridine + Ni$^+$)	0	0	0	70	30
(Diglyme + Ni$^+$)	20	25	1	34	20
(Terpyridine + Ni$^+$)	0	0	0	70	30
(2 × Monoglyme + Ni$^+$)	0	60	0	30	10
(Terpyridine + Ni$^+$)	0	0	0	60	40

[a] Isolation of the specific (polyether + Ni$^+$) or (2,2′:6′,2″-terpyridine + Ni$^+$) complex shown in the first column and subsequent reaction with a 1:1 mixture of polyether and 2,2′:6′,2″-terpyridine. All values ±10% based on two or three replicates; however, the values should be used only as "order-of-magnitude" indicators because of the limited ability to monitor concentrations of the ligands.

Table 2
Product distributions after ligand exchange reactions involving 2,2′:6′,2″-terpyridine or polyether complexes with 2,2′:6′,2″-terpyridine and polyether neutrals[a]

	Products				
Selected complex	(Ether + Cu$^+$)	(2 × Ether + Cu$^+$)	(Ether + Cu$^+$ + Terpyridine)	(Terpyridine + Cu$^+$)	(2 × Terpyridine + Cu$^+$)
(18-C-6 + Cu$^+$)	70	0	0	10	20
(Terpyridine + Cu$^+$)	0	0	0	50	50
(15-C-5 + Cu$^+$)	75	0	0	20	5
(Terpyridine + Cu$^+$)	0	0	0	60	40
(12-C-4 + Cu$^+$)	50	20	0	25	5
(Terpyridine + Cu$^+$)	0	0	0	70	30
(Tetraglyme + Cu$^+$)	75	0	0	20	5
(Terpyridine + Cu$^+$)	0	0	0	60	40
(Triglyme + Cu$^+$)	65	0	0	30	5
(Terpyridine + Cu$^+$)	0	0	0	70	30
(Diglyme + Cu$^+$)	10	20	0	65	5
(Terpyridine + Cu$^+$)	0	0	0	55	45
(2 × Monoglyme + Cu$^+$)	0	50	0	45	5
(Terpyridine + Cu$^+$)	0	0	0	65	35

[a] Isolation of the specific (polyether + Cu$^+$) or (2,2′:6′,2″-terpyridine + Cu$^+$) complex shown in the first column and subsequent reaction with a 1:1 mixture of polyether and 2,2′:6′,2″-terpyridine. All values ±10% based on two or three replicates; however, the values should be used only as "order-of-magnitude" indicators because of the limited ability to monitor concentrations of the ligands.

Table 3
Product distributions after ligand exchange reactions involving 2,2′:6′,2″-terpyridine or polyether complexes with 2,2′:6′,2″-terpyridine and polyether neutrals[a]

	Products				
Selected complex	(Ether + Co^+)	(2 × Ether + Co^+)	(Ether + Co^+ + Terpyridine)	(Terpyridine + Co^+)	(2 × Terpyridine + Co^+)
(18-C-6 + Co^+)	90	0	10	0	0
(Terpyridine + Co^+)	20	0	35	20	25
(2 × Terpyridine + Co^+)	0	0	0	0	100
(18-C-6 + Co^+ + Terpyridine)	0	0	85	0	15
(15-C-5 + Co^+)	60	0	30	0	10
(Terpyridine + Co^+)	0	0	40	30	30
(2 × Terpyridine + Co^+)	0	0	0	0	100
(15-C-5 + Co^+ + Terpyridine)	0	0	70	0	30
(12-C-4 + Co^+)	40	20	10	20	10
(Terpyridine + Co^+)	0	0	20	30	50
(2 × Terpyridine + Co^+)	0	0	0	0	100
(12-C-4 + Co^+ + Terpyridine)	0	0	60	0	40
(Tetraglyme + Co^+)	85	0	15	0	0
(Terpyridine + Co^+)	0	0	40	15	45
(2 × Terpyridine + Co^+)	0	0	0	0	100
(Tetraglyme + Co^+ + terpyridine)	0	0	85	0	15
(Triglyme + Co^+)	50	0	30	10	10
(Terpyridine + Co^+)	0	0	50	40	10
(2 × Terpyridine + Co^+)	0	0	0	0	100
(Triglyme + Co^+ + terpyridine)	0	0	80	0	20
(Diglyme + Co^+)	40	30	10	15	5
(2 × Diglyme + Co^+)	0	90	0	10	0
(Terpyridine + Co^+)	0	0	30	50	20
(2 × Terpyridine + Co^+)	0	0	0	0	100
(Diglyme + Co^+ + terpyridine)	0	0	90	0	10
(2 × Monoglyme + Co^+)	0	60	10	30	0
(Terpyridine + Co^+)	0	0	10	30	60
(2 × Terpyridine + Co^+)	0	0	0	0	100
(Monoglyme + Co^+ + terpyridine)	0	0	60	0	40

[a] Isolation of the specific (polyether + Co^+) or (2,2′:6′,2″-terpyridine + Co^+) complex shown in the first column and subsequent reaction with a 1:1 mixture of polyether and 2,2′:6′,2″-terpyridine. All values ±10% based on two or three replicates; however, the values should be used only as "order-of-magnitude" indicators because of the limited ability to monitor concentrations of the ligands.

Ni^+) complex was isolated and allowed to react with neutral 2,2′,6′,2″-terpyridine and 18-crown-6. The product distribution after 300 ms consists of 93% of the original precursor complex (18-crown-6 + Ni^+), 5% (2,2′,6′,2″-terpyridine + Ni^+), and 2% (2 × 2,2′,6′,2″-terpyridine + Ni^+), as listed in Table 1. Next the (2,2′,6′,2″-terpyridine + Ni^+) complex was isolated and allowed to react with 18-crown-6 and 2,2′,6′,2″-terpyridine. The resulting product distribution consists of 1% (18-crown-6 + Ni^+ + 2,2′,6′,2″-terpyridine), 64% of the original precursor complex (2,2′,6′,2″-terpyridine + Ni^+), and

Table 4
Product distributions after ligand exchange reactions involving 2,2′-bipyridine or polyether complexes with 2,2′-bipyridine and polyether neutrals[a]

	Products				
Selected complex	(Ether + Ni$^+$)	(2 × Ether + Ni$^+$)	(Ether + Ni$^+$ + 2,2′-bipyridine)	(2,2′-Bipyridine + Ni$^+$)	(2 × 2,2′-Bipyridine + Ni$^+$)
(18-C-6 + Ni$^+$)	50	0	50	0	0
(2,2-Dipyridine + Ni$^+$)	40	0	25	5	30
(2 × 2,2′-Dipyridine + Ni$^+$)	0	0	0	0	100
(18-C-6 + Ni$^+$ + 2,2′-Dipyridine)	0	0	75	0	25
(15-C-5 + Ni$^+$)	40	0	50	0	10
(2,2′-Dipyridine + Ni$^+$)	15	0	25	20	40
(2 × 2,2′-Dipyridine + Ni$^+$)	0	0	0	0	100
(15-C-5 + Ni + 2,2′-Dipyridine)	0	0	70	0	30
(12-C-4 + Ni$^+$)	30	20	40	0	10
(2,2′-Dipyridine + Ni$^+$)	0	0	70	10	20
(2 × 2,2′-Dipyridine + Ni$^+$)	0	0	0	0	100
(12-C-4 + Ni$^+$ + 2,2′-dipyridine)	0	0	70	0	30
(Tetraglyme + Ni$^+$)	45	0	50	0	5
(2,2′-Dipyridine + Ni$^+$)	30	0	30	5	35
(2 × 2,2′-Dipyridine + Ni$^+$)	0	0	0	0	100
(Tetraglyme + Ni$^+$ + 2,2′-dipyridine)	0	0	70	0	30
(Triglyme + Ni$^+$)	40	0	40	0	10
(2,2′-Dipyridine + Ni$^+$)	15	0	45	10	30
(2 × 2,2′-Dipyridine + Ni$^+$)	0	0	0	0	100
(Triglyme + Ni$^+$ + 2,2′-dipyridine)	0	0	70	0	30
(Diglyme + Ni$^+$)	25	20	35	0	20
(2 × Diglyme + Ni$^+$)	0	70	30	0	0
(2,2′-Dipyridine + Ni$^+$)	0	0	35	10	55
(2 × 2,2′-Dipyridine + Ni$^+$)	0	0	0	0	100
(Diglyme + Ni + 2,2′-dipyridine)	0	0	70	0	30
(2 × Monoglyme + Ni$^+$)	0	55	30	0	15
(2 × 2,2′-Dipyridine + Ni$^+$)	0	0	0	0	100
(Monoglyme + Ni$^+$ + 2,2′-dipyridine)	0	0	60	0	40

[a] Isolation of the specific (polyether + Ni$^+$) or (2,2′-bipyridine + Ni$^+$) complex shown in the first column and subsequent reaction with a 1:1 mixture of polyether and 2,2′-bipyridine. All values ±10% based on two or three replicates; however, the values should be used only as "order-of-magnitude" indicators because of the limited ability to monitor concentrations of the ligands.

35% (2 × 2,2′,6′,2″-terpyridine + Ni$^+$), as listed in Table 1.

3.2. Ligand exchange reactions for monopositive complexes

3.2.1. 2,2′,6′,2″-Terpyridine

Because 2,2′,6′,2″-terpyridine is the largest pyridyl ligand and the only tridentate one, its metal coordination abilities are expected to be greatest. The results for the ligand exchange experiments involving 2,2′,6′,2″-terpyridine and the polyethers are summarized in Tables 1 to 3. In general, the results confirm that 2,2′,6′,2″-terpyridine binds Co$^+$, Cu$^+$, or Ni$^+$ ions more strongly than any of the polyethers. After isolation of each (polyether + Cu$^+$) or (polyether + Ni$^+$) complex in the presence of neutral 2,2′,6′,2″-terpyridine and polyether molecules, the direct formation of (2,2′,6′,2″-terpyridine + M$^+$) and (2 ×

Table 5
Product distributions after ligand exchange reactions involving 2,2′-bipyridine or polyether complexes with 2,2′-bipyridine and polyether neutrals[a]

	Products				
Selected complex	(Ether + Cu$^+$)	(2 × Ether + Cu$^+$)	(Ether + Cu$^+$ + 2,2′-Bipyridine)	(2,2′-Bipyridine + Cu$^+$)	(2 × 2,2′-Bipyridine + Cu$^+$)
(18-C-6 + Cu$^+$)	70	0	25	0	5
(2,2′-Dipyridine + Cu$^+$)	40	0	25	5	30
(2 × 2,2′-Dipyridine + Cu$^+$)	0	0	5	0	95
(18-C-6 + Cu$^+$ + 2,2′-Dipyridine)	5	0	75	0	20
(15-C-5 + Cu$^+$)	30	0	30	0	40
(2,2′-Dipyridine + Cu$^+$)	20	0	10	20	50
(2 × 2,2′-Dipyridine + Cu$^+$)	0	0	0	0	100
(15-C-5 + Cu$^+$ + 2,2′-Dipyridine)	0	0	50	0	50
(12-C-4 + Cu$^+$)	40	10	35	0	15
(2,2′-Dipyridine + Cu$^+$)	0	0	45	10	45
(2 × 2,2′-Dipyridine + Cu$^+$)	0	0	0	0	100
(12-C-4 + Cu$^+$ + 2,2′-Dipyridine)	0	0	50	0	50
(Tetraglyme + Cu$^+$)	60	0	35	0	5
(2,2′-Dipyridine + Cu$^+$)	35	0	20	5	40
(2 × 2,2′-Dipyridine + Cu$^+$)	0	0	2	0	98
(Tetraglyme + Cu$^+$ + 2,2′-dipyridine)	3	0	70	0	27
(Triglyme + Cu$^+$)	30	0	50	0	20
(2,2′-Dipyridine + Cu$^+$)	15	0	25	10	50
(2 × 2,2′-Dipyridine + Cu$^+$)	0	0	0	0	100
(Triglyme + Cu$^+$ + 2,2′-dipyridine)	0	0	50	0	50
(Diglyme + Cu$^+$)	20	15	40	0	25
(2,2′-Dipyridine + Cu$^+$)	0	0	50	10	40
(2 × 2,2′-Dipyridine + Cu$^+$)	0	0	0	0	100
(Diglyme + Cu$^+$ + 2,2′-dipyridine)	0	0	60	0	40
(2 × Monoglyme + Cu$^+$)	0	25	50	0	25
(2 × 2,2′-Dipyridine + Cu$^+$)	0	0	0	0	100
(Monoglyme + Cu$^+$ + 2,2′-dipyridine)	0	0	50	0	50

[a] Isolation of the specific (polyether + Cu$^+$) or (2,2′-bipyridine + Cu$^+$) complex shown in the first column and subsequent reaction with a 1:1 mixture of polyether and 2,2′-bipyridine. All values ±10% based on two or three replicates; however, the values should be used only as "order-of-magnitude" indicators because of the limited ability to monitor concentrations of the ligands.

2,2′,6′,2″-terpyridine + M$^+$) is observed. For isolation and reaction of the (polyether + Co$^+$) complexes, the formation of heterodimer (polyether + Co$^+$ + 2,2′,6′,2″-terpyridine) complexes is observed along with the occurrence of (2,2′,6′,2″-terpyridine + Co$^+$) and (2 × 2,2′,6′,2″-terpyridine + Co$^+$) complexes. The heterodimer (polyether + Co$^+$ + 2,2′,6′,2″-terpyridine) complexes react exclusively by replacement of the polyether ligand by a second 2,2′,6′,2″-terpyridine ligand. These results illustrate that the 2,2′,6′,2″-terpyridine ligand is capable of displacing the polyether ligand from each of the (polyether + M$^+$) or (polyether + M$^+$ + 2,2′,6′,2″-terpyridine) complexes, thus indicating that 2,2′,6′,2″-terpyridine has the greatest metal binding free energy of all the ligands in the study.

Stable heterodimer complexes, (2,2′:6′,2″-terpyridine + M$^+$ + polyether), are never observed for any of the Cu$^+$ and Ni$^+$ ligand exchange reactions, regardless of whether the (2,2′:6′,2″-terpyridine + M$^+$) or (polyether + M$^+$) complexes are first isolated and allowed to react with neutral ligands. This result

Table 6
Product distributions after ligand exchange reactions involving 2,2′-bipyridine or polyether complexes with 2,2′-bipyridine and polyether neutrals[a]

	Products					
Selected complex	(Ether + Co$^+$)	(2 × Ether + Co$^+$)	(Ether + Co$^+$ + 2,2′-Bipyridine)	(2,2′-Bipyridine + Co$^+$)	(2 × 2,2′-Bipyridine + Co$^+$)	(3 × 2,2′-Bipyridine + Co$^+$)
(18-C-6 + Co$^+$)	50	0	40	0	10	0
(2,2′-Dipyridine + Co$^+$)	35	0	30	5	25	5
(2 × 2,2′-Dipyridine + Co$^+$)	0	0	0	0	50	50
(18-C-6 + Co$^+$ + 2,2′-Dipyridine)	0	0	70	0	30	0
(15-C-5 + Co$^+$)	30	0	50	0	20	0
(2,2′-Dipyridine + Co$^+$)	10	0	35	10	35	10
(2 × 2,2′-Dipyridine + Co$^+$)	0	0	0	0	70	30
(15-C-5 + Co$^+$ + 2,2′-Dipyridine)	0	0	50	0	30	20
(12-C-4 + Co$^+$)	30	5	40	0	20	5
(2,2′-Dipyridine + Co$^+$)	0	0	50	5	35	5
(2 × 2,2′-Dipyridine + Co$^+$)	0	0	0	0	70	30
(12-C-4 + Co$^+$ + 2,2′-Dipyridine)	0	0	30	0	40	30
(Tetraglyme + Co$^+$)	55	0	40	0	5	10
(2,2′-Dipyridine + Co$^+$)	10	0	40	5	40	5
(2 × 2,2′-Dipyridine + Co$^+$)	0	0	0	0	60	40
(Tetraglyme + Co$^+$ + 2,2′-dipyridine)	0	0	60	0	40	20
(Triglyme + Co$^+$)	40	0	30	0	20	10
(2,2′-Dipyridine + Co$^+$)	5	0	35	10	40	10
(2 × 2,2′-Dipyridine + Co$^+$)	0	0	0	0	70	30
(Triglyme + Co$^+$ + 2,2′-dipyridine)	0	0	50	0	30	20
(Diglyme + Co$^+$)	20	5	35	0	35	5
(2,2′-Dipyridine + Co$^+$)	0	0	25	25	40	10
(2 × 2,2′-Dipyridine + Co$^+$)	0	0	0	0	70	30
(Diglyme + Co$^+$ + 2,2′-dipyridine)	0	0	50	0	30	20
(2 × Monoglyme + Co$^+$)	0	25	45	0	25	5
(2,2′-Dipyridine + Co$^+$)	0	0	0	40	50	10
(2 × 2,2′-Dipyridine + Co$^+$)	0	0	0	0	70	30
(Monoglyme + Co$^+$ + 2,2′-dipyridine)	0	0	30	0	50	20

[a] Isolation of the specific (polyether + Co$^+$) or (2,2′-bipyridine + Co$^+$) complex shown in the first column and subsequent reaction with a 1:1 mixture of polyether and 2,2′-bipyridine. All values ±10% based on two or three replicates; however, the values should be used only as "order-of-magnitude" indicators because of the limited ability to monitor concentrations of the ligands.

Table 7
Product distributions after ligand exchange reactions involving 4,4′-bipyridine or polyether complexes with 4,4′-bipyridine and polyether neutrals[a]

	Products				
Selected complex	(Ether + Ni^+)	(2 × Ether + Ni^+)	(Ether + Ni^+ + 4,4′-bipyridine)	(4,4′-Bipyridine + Ni^+)	(2 × 4,4′-Bipyridine + Ni^+)
(18-C-6 + Ni^+)	100	0	0	0	0
(2 × 4,4′-Dipyridine + Ni^+)	70	0	0	0	30
(15-C-5 + Ni^+)	100	0	0	0	0
(2 × 4,4′-Dipyridine + Ni^+)	40	0	0	0	60
(12-C-4 + Ni^+)	60	10	30	0	0
(2 × 4,4′-Dipyridine + Ni^+)	0	0	60	0	40
(12-C-4 + Ni^+ + 4,4′-Dipyridine)	0	0	100	0	0
(Tetraglyme + Ni^+)	100	0	0	0	0
(2 × 4,4′-Dipyridine + Ni^+)	70	0	0	0	30
(Triglyme + Ni^+)	100	0	0	0	0
(2 × 4,4′-Dipyridine + Ni^+)	30	0	0	0	70
(Diglyme + Ni^+)	70	10	18	0	2
(4,4′-Dipyridine + Ni^+)	10	0	50	20	20
(2 × 4,4′-Dipyridine + Ni^+)	0	0	45	0	55
(Diglyme + Ni^+ + 4,4′-dipyridine)	0	2	98	0	0
(2 × Monoglyme + Ni^+)	0	54	45	0	1
(Monoglyme + Ni^+)	20	50	30	0	0
(2 × 4,4′-Dipyridine + Ni^+)	0	1	60	0	39
(Monoglyme + Ni^+ + 4,4′-dipyridine)	0	0	98	0	2

[a] Isolation of the specific (polyether + Ni^+) or (4,4′-bipyridine + Ni^+) complex shown in the first column and subsequent reaction with a 1:1 mixture of polyether and 4,4′-bipyridine. In some cases, small amounts of (3 × 4,4′-bipyridine + Ni^+) were observed, but the percentage was <5%. All values ±10% based on two or three replicates; however, the values should be used only as "order-of-magnitude" indicators because of the limited ability to monitor concentrations of the ligands.

indicates that the heterodimer (2,2′:6′,2″-terpyridine + M^+ + polyether) complexes are less stable than the (2,2′:6′,2″-terpyridine + M^+) or (2 × 2,2′:6′,2″-terpyridine + M^+) dimer complexes, and probably represents a situation in which the polyether ligand has a sufficiently lower binding free energy relative to 2,2′:6′,2″-terpyridine that it cannot compete effectively for coordination of the metal ion compared with 2,2′:6′,2″-terpyridine. A second 2,2′:6′,2″-terpyridine ligand can attach to the (2,2′:6′,2″-terpyridine + Ni^+) and (2,2′:6′,2″-terpyridine + Cu^+) complexes, indicating that a second ligand with an equally large binding free energy can successfully attach to the metal ion, in spite of the steric constraints caused by the first bulky 2,2′:6′,2″-terpyridine ligand bound to the metal ion. This latter result proves that steric hindrance caused by the complexation of the metal ion by the bulky 2,2′:6′,2″-terpyridine, thus creating an insurmountable activation barrier, is not the sole reason that the other polyether ligands do not attach to the complex; the difference in binding free energies of the competing ligands plays the dominant role.

In contrast to the lack of heterodimers formed for the Ni^+ and Cu^+ reactions, the reactions of the (2,2′,6′,2″-terpyridine + Co^+) complexes with each of the polyethers reveal that attachment of a polyether ligand to the (2,2′,6′,2″-terpyridine + Co^+) complex is a favorable process (although in fact the polyether ligand is eventually displaced by a second 2,2′,6′,2″-terpyridine ligand if the ligand exchange period is extended). The difference in the ligand exchange behaviors of the (2,2′,6′,2″-terpyridine + Co^+) versus (2,2′,6′,2″-terpyridine + Ni^+), and (2,2′,6′,2″-terpyri-

Table 8
Product distributions after ligand exchange reactions involving 4,4′-bipyridine or polyether complexes with 4,4′-bipyridine and polyether neutrals[a]

	Products				
Selected complex	(Ether + Cu$^+$)	(2 × Ether + Cu$^+$)	(Ether + Cu$^+$ + 4,4′-bipyridine)	(4,4′-Bipyridine + Cu$^+$)	(2 × 4,4′-Bipyridine + Cu$^+$)
(18-C-6 + Cu$^+$)	100	0	0	0	0
(4,4′-Dipyridine + Cu$^+$)	45	0	0	5	50
(2 × 4,4′-Dipyridine + Cu$^+$)	85	0	0	0	15
(15-C-5 + Cu$^+$)	100	0	0	0	0
(4,4′-Dipyridine + Cu$^+$)	30	0	0	40	30
(2 × 4,4′-Dipyridine + Cu$^+$)	50	0	0	0	50
(12-C-4 + Cu$^+$)	30	25	45	0	0
(4,4′-Dipyridine + Cu$^+$)	20	0	20	20	40
(2 × 4,4′-Dipyridine + Cu$^+$)	0	0	60	0	40
(12-C-4 + Cu$^+$ + 4,4′-dipyridine)	0	0	100	0	0
(Tetraglyme + Cu$^+$)	100	0	0	0	0
(4,4′-Dipyridine + Cu$^+$)	45	0	0	5	50
(2 × 4,4′-Dipyridine + Cu$^+$)	60	0	0	0	40
(Triglyme + Cu$^+$)	100	0	0	0	0
(4,4′-Dipyridine + Cu$^+$)	45	0	0	10	45
(2 × 4,4′-Dipyridine + Cu$^+$)	30	0	0	0	70
(Diglyme + Cu$^+$)	72	1	25	0	2
(4,4′-Dipyridine + Cu$^+$)	5	0	35	20	40
(2 × 4,4′-Dipyridine + Cu$^+$)	0	0	3	0	97
(Diglyme + Cu$^+$ + 4,4′-dipyridine)	2	0	78	0	20
(2 × Monoglyme + Cu$^+$)	0	60	30	0	10
(Monoglyme + Cu$^+$)	45	35	20	0	0
(2 × 4,4′-Dipyridine + Cu$^+$)	0	0	5	0	95
(Monoglyme + Cu$^+$ + 4,4′-dipyridine)	0	0	40	0	60

[a] Isolation of the specific (polyether + Cu$^+$) or (4,4′-bipyridine + Cu$^+$) complex shown in the first column and subsequent reaction with a 1:1 mixture of polyether and 4,4′-bipyridine. All values ±10% based on two or three replicates; however, the values should be used only as "order-of-magnitude" indicators because of the limited ability to monitor concentrations of the ligands.

dine + Cu$^+$) complexes, in terms of the formation of heterodimer complexes, is rationalized later.

As the size of the polyether increases in the (polyether + M$^+$) complexes (i.e. from 12-crown-4 to 15-crown-5 to 18-crown-6), the rate of formation of (2,2′:6′,2″-terpyridine + M$^+$) via the ligand displacement process decreases, as determined by monitoring the extent of ligand exchange process at several intervals. Two factors may contribute to this size-dependent trend. The larger size of the polyether gives it more flexibility in orienting its oxygen dipoles to optimally bind the metal ion and may allow involvement of more binding sites, thus increasing the binding enthalpy of the larger polyether and giving the resulting complex greater thermodynamic stability. As the cavity size of the crown ether increases, the metal ion may be more fully encapsulated, thus causing steric hindrance that results in an activation barrier to extraction of the metal ion by 2,2′:6′,2″-terpyridine.

One notable difference between the ligand exchange reactions involving 2,2′:6′,2″-terpyridine and the Cu$^+$ and Ni$^+$ ions versus the Co$^+$ ions is that heterodimer complexes (2,2′:6′,2″-terpyridine + Co$^+$

Table 9
Product distributions after ligand exchange reactions involving 4,4′-bipyridine or polyether complexes with 4,4′-bipyridine and polyether neutrals[a]

	Products				
Selected complex	(Ether + Co^+)	(2 × Ether + Co^+)	(Ether + Co^+ + 4,4′-bipyridine)	(4,4′-Bipyridine + Co^+)	(2 × 4,4′-Bipyridine + Co^+)
(18-C-6 + Co^+)	100	0	0	0	0
(4,4′-Dipyridine + Co^+)	70	0	0	5	20
(2 × 4,4′-Dipyridine + Co^+)	70	0	0	0	30
(15-C-5 + Co^+)	100	0	0	0	0
(4,4′-Dipyridine + Co^+)	65	0	0	25	10
(2 × 4,4′-Dipyridine + Co^+)	60	0	0	0	40
(12-C-4 + Co^+)	20	20	60	0	0
(2 × 4,4′-Dipyridine + Co^+)	0	0	60	0	40
(12-C-4 + Co^+ + 4,4′-Dipyridine)	0	0	100	0	0
(Tetraglyme + Co^+)	100	0	0	0	0
(4,4′-Dipyridine + Co^+)	70	0	0	5	25
(2 × 4,4′-Dipyridine + Co^+)	70	0	0	0	30
(Triglyme + Co^+)	100	0	0	0	0
(4,4′-Dipyridine + Co^+)	60	0	0	30	10
(2 × 4,4′-Dipyridine + Co^+)	40	0	0	0	60
(Diglyme + Co^+)	20	50	30	0	0
(2 × Diglyme + Co^+)	0	90	10	0	0
(2 × 4,4′-Dipyridine + Co^+)	0	0	40	0	60
(Diglyme + Co^+ + 4,4′-dipyridine)	0	0	100	0	0
(2 × Monoglyme + Co^+)	0	60	30	0	10
(2 × 4,4′-Dipyridine + Co^+)	0	0	20	0	80
(Monoglyme + Co^+ + 4,4′-dipyridine)	0	0	60	0	40

[a] Isolation of the specific (polyether + Co^+) or (4,4′-bipyridine + Co^+) complex shown in the first column and subsequent reaction with a 1:1 mixture of polyether and 4,4′-bipyridine. All values ±10% based on two or three replicates; however, the values should be used only as "order-of-magnitude" indicators because of the limited ability to monitor concentrations of the ligands.

+ polyether) are observed for the Co^+ reactions, whereas they were never formed for the Ni^+ and Cu^+ reactions. This result highlights another difference in the coordination behaviors of Co^+ ($3d^8$) versus Cu^+ ($3d^{10}$) and Ni^+ ($3d^9$). The different electronic configuration of Co^+ relative to those of Ni^+ and Cu^+ promotes a striking contrast in the stabilities of the heterodimer complexes. From our earlier study of the gas-phase chelation reactions between metal ions and pyridyl-type ligands [42], it was noted that Co^+ but not Cu^+ nor Ni^+ formed trimer complexes with the bidentate 2,2′-bipyridine and 1,10-phenanthroline ligands. This contrast signaled some sort of intrinsic difference in the coordination ability of Co^+ relative to Ni^+ and Cu^+, and it probably causes the same difference in this study with respect to forming heterodimers.

We speculate that there are three feasible explanations for the contrast between the Co^+ versus Ni^+ and Cu^+ complexation reactions. First, Co^+ might promote slightly weaker binding interactions compared with Ni^+ or Cu^+, thus resulting in the least selective complexation behavior, alleviating ligand repulsions as the ligands crowd around the metal ion, and allowing heterodimers to survive in the trap without undergoing rapid displacement of the polyether ligands by the 2,2′,6′,2″-terpyridine molecules. These factors presumably would give the heterodimer

(2,2′,6′,2″-terpyridine + Co^+ + polyether) complexes a chance to survive on the timescale of the ion trapping experiment. However, previous measurements of the binding energies of Co^+, Cu^+, and Ni^+ ions to organic ligands via dative bonds have not indicated a large difference in the magnitudes of the bond energies [18], and thus there is little experimental evidence to support this idea. Second, the Co^+ ion may exhibit less intrinsic selectivity in its preference for coordination to nitrogen versus oxygen donors because it is a slightly "harder" acid than Ni^+ or Cu^+ [19,45]. Because ethers are recognized as harder bases than pyridine-type ligands [46], Co^+ could initially show less selectivity when binding to the polyethers versus pyridyl ligands. In this situation, the polyethers have enhanced binding free energies to the Co^+ ion relative to the nitrogen donors, and thus the heterodimer complexes could be observed on the timescale of the trapping experiment. Third, the differences in the dimerization behavior may be caused by the differences in coordination symmetries of the metal ions. Transition metal cations have specific directional binding preferences and change hybridizations to minimize orbital repulsions [47,48]. Thus, the hybridization of the Co^+ ions may promote mixed dimer formation because of how the ligands approach and interact with the metal center. Some combination of the second and third reasons may cause the difference in complexation of the Co^+ versus Cu^+ and Ni^+ ions.

3.2.2. 2,2′-Bipyridine

The ligand exchange reactions involving 2,2′-bipyridine and the polyethers are summarized in Tables 4 to 6. The ligand exchange reactions involving 2,2′-bipyridine reveal a uniform trend. The (polyether + M^+) complexes react with 2,2′-bipyridine to form heterodimer (polyether + M^+ + 2,2′-bipyridine) complexes. Then these heterodimer complexes react with 2,2′-bipyridine to form more stable (2 × 2,2′-bipyridine + M^+) complexes, which typically do not undergo further reaction. These ligand exchange results indicate that the 2,2′-bipyridine ligand has a greater metal binding free energy than any of the polyethers within the two-ligand complexes. Stable heterodimers, (2,2′-bipyridine + M^+ + polyether), are formed for all of the various polyether ligands, but in every case the heterodimers undergo ligand exchange reactions with neutral 2,2′-bipyridine to ultimately form more stable (2 × 2,2′-bipyridine + M^+) complexes (Fig. 2).

Interestingly, the relative binding free energies of the ligands are reflected differently for the ligand exchange reactions of the single-ligand complexes relative to those of the dimer complexes. For example, first consider the reactions of the complexes involving 15-crown-5 and 2,2′-bipyridine. The (2,2′-bipyridine + Ni^+) complex undergoes ligand exchange reactions with 15-crown-5 to form both (15-crown-5 + Ni^+) and the heterodimer (15-crown-5 + Ni^+ + 2,2′-bipyridine), suggesting that 15-crown-5 has a *greater* binding free energy than 2,2′-bipyridine because it can completely displace 2,2′-bipyridine from the Ni^+ ion. Conversely, although the (15-crown-5 + Ni^+) complex reacts to form the heterodimer (15-crown-5 + Ni^+ + 2,2′-bipyridine) complex, simple ligand displacement of (15-crown-5 + Ni^+) by 2,2′-bipyridine to form (2,2′-bipyridine + Ni^+) complexes does not occur, thus indicating that the binding free energy of 2,2′-bipyridine is *lower* than that of 15-crown-5. Similar trends are observed for the reactions of the 12-crown-4, triglyme, tetraglyme, and 18-crown-6 ligands. In each case, the polyether can strip the metal ion from the (2,2′-bipyridine + M^+) complexes, but 2,2′-bipyridine cannot extract the metal ion from the (polyether + M^+) complexes. These results confirm that a single 2,2′-bipyridine ligand cannot successfully displace the larger polyether ligands when they are already bound to a metal ion, and thus 2,2′-bipyridine possesses a *lower* binding free energy.

In contrast to the results for the single-ligand complexes, if *two* 2,2′-bipyridine ligands are already bound to the metal ion, then a polyether cannot dislodge either ligand. For example, (2 × 2,2′-bipyridine + M^+) does not undergo any ligand displacement reactions when exposed to 18-crown-6, 15-crown-5, 12-crown-4, tetraglyme, or triglyme, even at extremely long reaction times (2000 ms). Likewise, when the two-ligand heterodimer com-

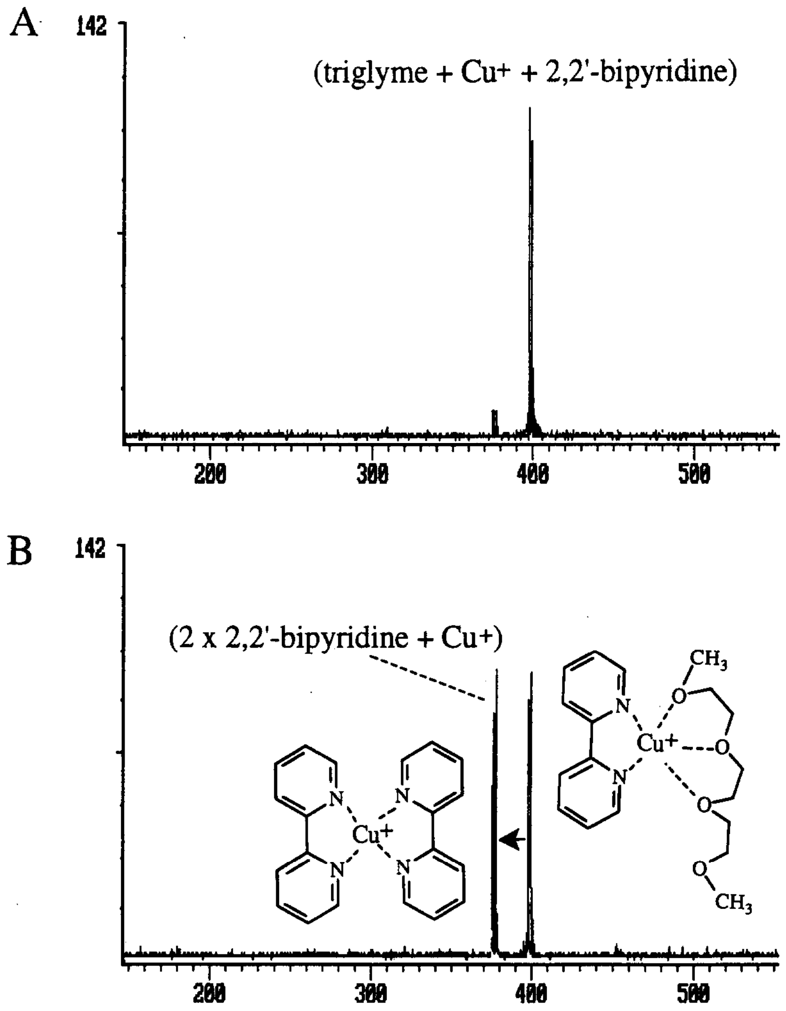

Fig. 2. Ligand exchange reactions for the (triglyme + Co^+ + 2,2′-bipyridine) complex with neutral 2,2′-bipyridine and triglyme. (A) Isolation of the (triglyme + Co^+ + 2,2′-bipyridine) complex. (B) Product distribution after 200 ms.

plexes (polyether + M^+ + 2,2′-bipyridine) are isolated, they react exclusively by replacement of the polyether ligand by a second 2,2′-bipyridine molecule. Thus, for the two-ligand complexes, 2,2′-bipyridine shows a *greater* metal binding free energy.

These observations suggest that the level of access to the metal ion (i.e. a steric effect) and entropic factors play significant roles in determining the success of ligand displacement reactions. A single 2,2′-bipyridine ligand cannot fully coordinate or shield the metal ion, so a polyether ligand can approach the unhindered metal ion, optimize its coordination interactions, and in many cases entirely displace the 2,2′-bipyridine ligand. A large activation barrier for the displacement reaction would not be expected. Moreover, a single crown ether is a relatively floppy ligand compared to 2,2′-bipyridine, possessing much greater flexibility for orienting its oxygen dipoles and having greater ability to partially encapsulate a lone metal ion and thus reducing the accessibility of the metal when approached by a 2,2-bipyridine ligand (i.e. steric hindrance). These noted effects must counteract the negative impact of entropy due to the extensive organization of the flexible polyether, with loss of numerous degrees of rotational and vibrational freedom upon complexation of the metal ion. By contrast, when two 2,2′-bipyridine ligands are bound to the metal ion, the metal ion is more fully coordinated and shielded, thus preventing the optimal approach of a polyether ligand because of steric hindrance, perhaps creating an activation barrier, and prohibiting displacement of either of the 2,2′-bipyridine ligands. In the heterodimer (polyether + M^+ + 2,2′-bipyridine) complexes, the positive charge of the metal ion is more delocalized than in the one-ligand complexes, resulting in overall weaker binding interactions and longer bonds between the metal ion and both the polyether and 2,2′-bipyridine ligands. In this situation, the favorable replacement of the polyether by a second 2,2′-bipyridine ligand probably stems from three effects. First, there may be some reduction in the degree of ligand–ligand repulsion when replacing the bulky polyether by a more compact 2,2′-bipyridine ligand. Second, in the heterodimer complexes, the ability of the polyether to optimize its oxygen dipoles and partially encapsulate the metal ion is restricted when the metal is already bound to the bidentate 2,2′-bipyridine molecule. Perhaps only two or three oxygen dipoles of the polyether, instead of four, five, or six, can interact with the metal ion in the heterodimer because the metal is also coordinated with two nitrogen dipoles. This restriction would substantially reduce the intrinsic binding free energy of the polyether and make it easier to dislodge from the metal ion. Third, there is a greater gain in entropy when the highly organized polyether bound to the metal ion is replaced by 2,2′-bipyridine. Ultimately, the most stable complex is the (2 × 2,2′-bipyridine + M^+) dimer.

Evidence to support the view that ligand–ligand repulsions play a dominant role in influencing the stabilities of the two-ligand complexes was sought by comparing some ligand exchange reactions of Ag^+ complexes and Au^+ complexes relative to the reactions of the smaller transition metal complexes. The Ag^+ cation is isoelectronic with Cu^+ but has a 25% greater ionic radius (1.26 Å for Ag^+, 0.96 Å for Cu^+). The size of the Au^+ ion is even greater (1.37 Å). The greater sizes of Ag^+ and Au^+ could conceivably reduce the severity of ligand–ligand repulsive interactions in the dimer complexes. The larger sizes of Au^+ and Ag^+ cations also lead to lower charge densities and naturally result in longer metal–ligand bonds and weaker interactions overall.

When the (2 × 2,2′-bipyridine + Ag^+) or (2 × 2,2′-bipyridine + Au^+) complexes are allowed to react with 18-crown-6, tetraglyme, 15-crown-5, triglyme, or 12-crown-4, displacement of the 2,2′-bipyridine ligands does not occur. For these cases, the results parallel the observations made earlier for the analogous Cu^+ complexes. The ligand exchange reactions with these larger metal ions indicate that the multidentate polyethers and 2,2′-bipyridine demonstrate nearly uniform behavior for the Ag^+, Au^+, and Cu^+ two-ligand complexes. The results suggest that the differences in the sizes of these three isoelectronic metal ions may be insufficient to cause a significant alleviation of ligand repulsion effects.

The general order of relative binding free energies of the ligands as determined by the reactions of the single-ligand complexes is 18-crown-6 > tetraglyme > 15-crown-5 ≃ triglyme > 2,2′-bipyridine > 12-crown-4 ≥ diglyme > monoglyme. Thus, the bidentate nitrogen-containing ligand has a lower binding free energy than that of the flexible hexadentate (18-crown-6) and pentadentate (tetraglyme, 15-crown-5) oxygen-containing ligands, but a greater binding free energy than the rigid tetradentate, tridentate, or bidentate oxygen donor atom ligands. This trend indicates that the nitrogen-donor atom ligands have remarkably high metal binding free energies relative to their isodentate oxygen-containing counterparts. By contrast, the apparent order of relative binding free energies of the ligands as determined from the reactions of the two-ligand complexes is 2,2′-bipyridine > 18-crown-6 > tetraglyme > 15-crown-5 ≃ triglyme > 12-crown-4 ≥ diglyme > monoglyme. The only difference lies in the placement of 2,2′-bipyridine in these scales, reflecting the ability of a polyether ligand to approach the metal ion and be able to orient its dipoles in an effective manner when the metal ion is surrounded by one versus two 2,2′-bipyridine ligands. The difference in the two trends underscores the potential pitfalls of predicting the net strength of binding interactions or binding sites of more complex polydentate ligands, such as biological molecules, on the basis of the behavior of smaller models, because the impact of ligand repulsions, steric effects, and charge delocalization may not be adequately reflected.

3.2.3. 4,4′-Bipyridine

The ligand exchange results involving 4,4′-bipyridine and the polyethers are summarized in Tables 7 to 9. The 4,4′-bipyridine ligand has a substantially lower metal binding free energy than 2,2′-bipyridine because its nitrogen atoms are situated at opposite ends of the aromatic skeleton such that they cannot chelate the metal ion. Isolation and reaction of the (4,4′-bipyridine + M^+) complexes result in rapid displacement of the 4,4′-bipyridine ligand by each of the polyether ligands, 18-crown-6, 15-crown-5, 12-crown-4, tetraglyme, triglyme, and diglyme. These ligand exchange results suggest that the 4,4′-bipyridine ligand has a lower binding free energy than any of the larger polydentate polyethers and thus can easily be dislodged from the metal ion. When reacting with 12-crown-4 or diglyme, the (4,4′-bipyridine + M^+) complexes also undergo attachment of the polyether ligand to the complex, resulting in formation of a stable heterodimer (polyether + M^+ + 4,4′-bipyridine), and indicating that the metal ion prefers to be more fully coordinated by binding to two ligands in these cases.

When the (polyether + M^+) complexes are isolated and allowed to react with 4,4′-bipyridine ligands, two types of behaviors are observed. For the larger polyethers, including 18-crown-6, 15-crown-5, tetraglyme, and triglyme, neither ligand displacement nor ligand attachment occurs, and thus the (polyether + M^+) complexes do not react at all with 4,4′-bipyridine. This result confirms that these polyethers have greater binding free energies than 4,4′-bipyridine. For the smaller polyethers, including 12-crown-4, diglyme, and monoglyme, attachment of a 4,4′-bipyridine molecule to the (polyether + M^+) complex occurs, resulting in stable heterodimer (polyether + M^+ + 4,4′-bipyridine) complexes. These latter reactions indicate not only that 4,4′-bipyridine has a similar binding free energy as the smaller polyethers but also that the smaller polyethers do not fully coordinate the metal ion on their own. The smaller polyethers have fewer coordination sites and are more rigid, meaning that their ability to reorient their oxygen dipoles for optimal coordination of the metal ions is limited.

Interestingly, stable heterodimers (4,4′-bipyridine + M^+ + polyether) are never observed for 15-crown-5, 18-crown-6, tetraglyme, or triglyme with any of the metal ions under any conditions. The absence of heterodimers for 15-crown-5, 18-crown-6, tetraglyme, and triglyme indicates that these polyethers have sufficiently greater binding free energies relative to 4,4′-bipyridine that they encapsulate the metal ion to prevent the competitive attachment of the weakly coordinating 4,4′-bipyridine ligand.

When comparing the reactions of Ni^+, Co^+, and Cu^+ ions, it is notable that the simple monomer complexes (4,4′-dipyridine + Ni^+) are rarely observed because of their low stabilities relative to the heterodimer (polyether + Ni^+ + 4,4′-dipyridine), (2 × 4,4′-dipyridine + Ni^+) dimer, and (polyether + Ni^+) complexes. That (4,4′-bipyridine + Ni^+) complexes are never observed when 18-crown-6, 15-crown-5, 12-crown-4, tetraglyme, or triglyme are present in the gas phase, whereas the analogous (4,4′-bipyridine + Co^+) and (4,4′-bipyridine + Cu^+) complexes are stable in the presence of those same polyethers points to another unusual metal-specific trend. We speculate that the reason for the differences in the stabilities of the (4,4′-dipyridine + M^+) complexes stems from the different number of d electrons of the metal center, which influences the optimum number of ligands that will coordinate. The Ni^+ ion has an odd number of d electrons (d^9), whereas both Co^+ (d^8), and Cu^+ (d^{10}) have an even number. This difference creates a different coordination symmetry, geometry, hybridization, and degree of unsaturation for each of the three metal ions. In our previous study of the chelation of monopositive metal ions with pyridyl ligands, it was found that Ni^+ favored coordination to three monodentate 4,4′-bipyridine ligands [42], whereas Co^+ and Cu^+ favored coordination to only two monodentate 4,4′-bipyridine ligands. Thus,

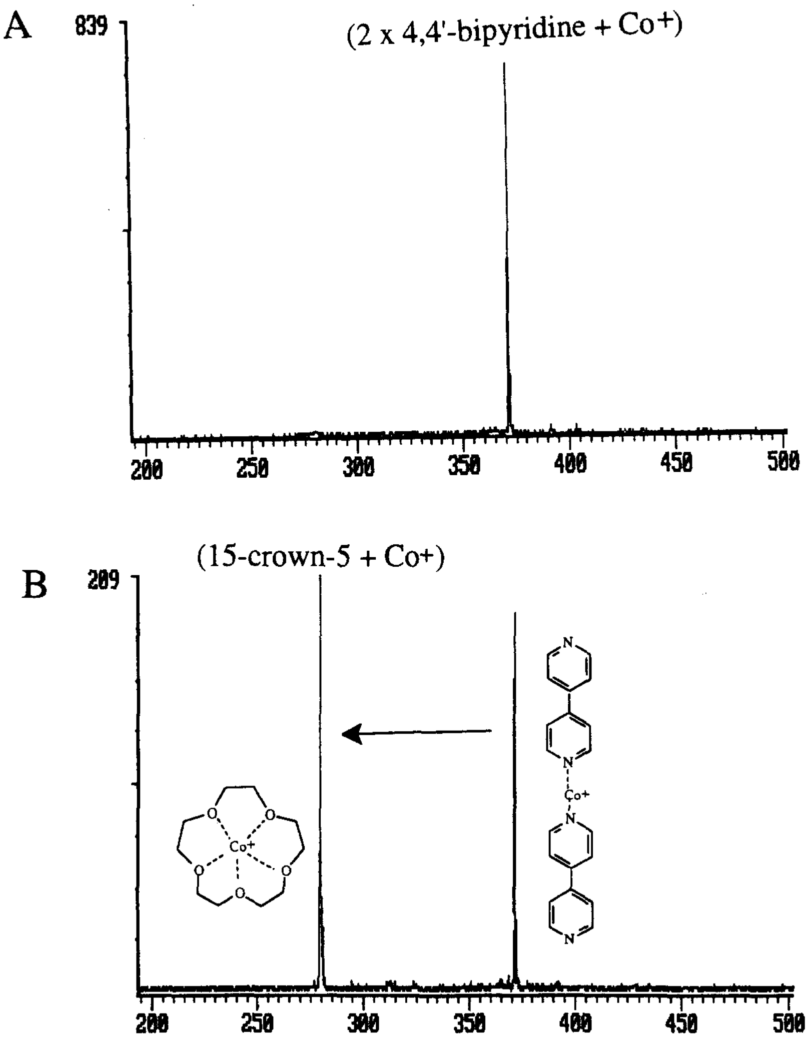

Fig. 3. Ligand exchange reactions for the (2 × 4,4′-bipyridine + Co^+) complex with neutral 4,4′-bipyridine and 15-crown-5. (A) Isolation of the (2 × 4,4′-bipyridine + Co^+) complex. (B) Product distribution after 200 ms.

the (4,4′-bipyridine + Ni^+) complexes may be intrinsically less stable than the analogous Co^+ and Cu^+ complexes, and indicate a preference for the Ni^+ ions to be coordinated to multiple ligands or at least one polydentate ligand.

The (2 × 4,4′-bipyridine + M^+) complexes undergo rapid ligand displacement when exposed to 15-crown-5, tetraglyme, triglyme, or 18-crown-6, thus preferentially forming (polyether + M^+) complexes. Interestingly, the heterodimers (4,4′-dipyridine + M^+ + polyether) are never observed as intermediates in these ligand exchange (Fig. 3). As shown in Fig. 3, the 15-crown-5 ligand is capable of displacing both 4,4′-bipyridine ligands so rapidly that the heterodimer complex is not observed. Similar behavior is noted for the reactions of 18-crown-6, tetraglyme, and triglyme. The absence of stable heterodimer intermediates underscores the weak metal binding free energy of 4,4′-dipyridine relative to the larger multidentate polyethers that can effectively surround the metal ion and rapidly displace both 4,4′-dipyridine ligands, virtually simultaneously. For 12-crown-4, diglyme, and monoglyme, the heterodimer complexes are observed as stable species, indicating that these polyethers have binding free energies similar to that of 4,4′-dipyridine, thus allowing formation of stable heterodimers. 4,4′-Bipyridine, a monodentate ligand, has a greater metal binding free energy than monoglyme, a bidentate ligand, demonstrating the greater intrinsic strength of M^+–N versus M^+–O bonds.

Although 12-crown-4 and triglyme have the same number of oxygen atoms and thus are structural analogs, their different coordinating capabilities are clearly evident from their ligand exchange reactions with 4,4′-dipyridine. For instance, heterodimers (4,4′-dipyridine + M^+ + 12-crown-4) are observed, but (4,4′-dipyridine + M^+ + triglyme) complexes are not stable species because triglyme may rapidly dislodge the 4,4′-bipyridine ligands. These contrasting results are rationalized by the difference in flexibility of the two polyethers that influences their capabilities for optimal reorientation of the oxygen dipoles for interactions with the metal ion. Triglyme has a significantly more flexible skeleton relative to the rigid 12-crown-4 ligand, thus permitting enhanced dipole orientation and resulting in a greater binding free energy relative to that of 12-crown-4. In fact, the ligand exchange results for the reactions involving 15-crown-5 and triglyme with 4,4′-dipyridine are similar, suggesting that the cyclic ether with five oxygen binding sites has similar coordination capabilities as an acyclic ether with four oxygen binding sites. The greater flexibility of the acyclic ether maximizes the alignment of its dipoles for interactions with the metal ion and compensates for its fewer number of binding sites relative to 15-crown-5. A similar effect has been noted in a study of the bond dissociation energies of alkali metal/ether complexes [50]. In that study, the net binding energy of two glyme molecules bound to Na^+ was greater than the binding energy of 12-crown-4 bound to Na^+, a result attributed to the ability of the individual glyme molecules to align their dipoles more favorably than the rigid 12-crown-4 molecule [50].

On the basis of the ligand exchange reactions of 4,4′-dipyridine with the polyethers, the order of relative binding free energies of the ligands is 18-crown-6 > tetraglyme > 15-crown-5, triglyme > 12-crown-4 > diglyme ≥ 4,4′-dipyridine > monoglyme. Thus, these results indicate that a monodentate nitrogen-containing ligand has a relatively low metal binding free energy compared with the polydentate ligands with multiple oxygen donor atoms, but it still has a greater relative metal binding free energy than a bidentate oxygen-donor atom ligand.

3.2.4. Summary of ligand exchange results

The compilation of results from the ligand exchange experiments have shown that there are two dominant influences on the binding free energies. First, the number of coordination sites of each ligand and its flexibility or ability to participate in cooperative binding interactions are reflected in the relative binding free energies. Overall, the nitrogen-donor atom ligands have greater binding free energies than their isodentate oxygen-containing counterparts. Second, the ability of a ligand to approach the metal ion and successfully adopt a favorable binding conformation differs greatly when the metal is already bound to one versus two ligands. For example, when the metal is bound to two 2,2′-bipyridine ligands, the ability of a large flexible polyether with multiple oxygen binding sites to displace one of the 2,2′-bipyridine ligands is greatly reduced compared with when the metal is only bound to a single 2,2′-bipyridine ligand. In addition to these two trends, the electronic configuration of the metal ion also plays a more subtle role in terms of influencing the stabilities of certain monomer (pyridine ligand + M^+) and heterodimer (pyridine ligand + M^+ + polyether) complexes. However, the nature of the metal ion does not appear to change the trends in relative binding free energies of the various ligands; it simply influences the presence of certain types of complexes based on the optimum coordination number of the metal ion, its directional binding preferences, and its relative "softness."

3.3. CAD results for the monopositive heterodimer complexes

Collisionally activated dissociation was used to evaluate the fragmentation pathways of the (L_1 + M^+

Table 10
CAD product distributions for (bipyridine + M^+ + polyether) complexes: percentage of fragment ion distribution

	Co^+		Ni^+		Cu^+	
	(Aromatic + Co^+)	(Polyether + Co^+)	(Aromatic + Ni^+)	(Polyether + Ni^+)	(Aromatic + Cu^+)	(Polyether + Cu^+)
(4,4-Bipyridine + M^+ + polyether)						
(4,4-Bipyridine + M^+ + 18-crown-6)	NA[a]		NA[a]		NA[a]	
(4,4-Bipyridine + M^+ + 15-crown-5)	NA[a]		NA[a]		NA[a]	
(4,4-Bipyridine + M^+ + 12-crown-4)	0%	100%	0%	100%	0%	100%
(4,4-Bipyridine + M^+ + tetraglyme)	NA[a]		NA[a]		NA[a]	
(4,4-Bipyridine + M^+ + triglyme)	NA[a]		NA[a]		NA[a]	
(4,4-Bipyridine + M^+ + diglyme)	0%	100%	0%	100%	0%	100%
(4,4-Bipyridine + M^+ + monoglyme)	0%	0% 100% Other[b]	0%	100%	20%	65% 15% Other[c]
(2,2-Bipyridine + M^+ + polyether)						
(2,2-Bipyridine + M^+ + 18-crown-6)	0%	70% 30% Other[d]	0%	100%	0%	100%
(2,2-Bipyridine + M^+ + 15-crown-5)	0%	100%	0%	100%	0%	100%
(2,2-Bipyridine + M^+ + 12-crown-4)	0%	30% 70% Other[e]	85%	0% 15% Other[f]	70%	30%
(2,2-Bipyridine + M^+ + tetraglyme)	0%	100%	0%	100%	0%	100%
(2,2-Bipyridine + M^+ + triglyme)	0%	50% 50% Other[g]	0%	100%	0%	100%
(2,2-Bipyridine + M^+ + diglyme)	30%	0% 70% Other[h]	100%	0%	100%	0%
(2,2-Bipyridine + M^+ + monoglyme)	85%	0% 15% Other[i]	100%	0%	100%	0%

[a] NA = mixed complex did not form, so CAD could not be undertaken.
[b] -$CH_3\cdot$ (55%), -($CH_3\cdot + C_2H_4O$) (5%), -46 (20%), other (20%).
[c] -($C_2H_4 + C_2H_4O$) (15%).
[d] -(18-C-6 + C_2H_3O) (30%).
[e] -$C_2H_3O\cdot$ (30%), -($C_2H_3\cdot + C_2H_4O$) (40%).
[f] -$C_2H_3O\cdot$ (10%), -($C_2H_3O\cdot + C_2H_4O$) (5%).
[g] -$CH_3\cdot$ (5%), -($CH_3\cdot + C_2H_4O$) (25%), -($CH_3\cdot + 2C_2H_4O$) (20%).
[h] -$CH_3\cdot$ (5%), -($CH_3\cdot + C_2H_4O$) (60%), -($CH_3\cdot + 2C_2H_4O$) (5%).
[i] -$CH_3\cdot$ (10%), -($CH_3\cdot + C_2H_4O$) (5%).

+ L_2) heterodimer complexes, as summarized in Table 10. The CAD spectra reflect the kinetically favored pathways for disassembly of the complexes and do not necessarily correspond to the thermodynamically favored pathways for assembly of the complexes or the overall thermodynamically favored products. CAD of the heterodimer complexes leads predominantly to loss of one of the ligands. Thus, it is of great interest to determine whether the heterodimer complexes disassemble to form the thermodynamically favored products, as determined by the previous ligand exchange experiments.

3.3.1. 2,2′:6′,2″-Terpyridine complexes

For the Ni^+ and Cu^+ reactions, heterodimer complexes involving 2,2′:6′,2″-terpyridine and any polyether ligand were not stable (as explained earlier), so the dissociation pathways of these complexes could not be evaluated. For the Co^+ reactions, the (2,2′:6′,2″-terpyridine + Co^+ + polyether) complexes dissociated exclusively by loss of the polyether ligand, resulting in (2,2′:6′,2″-terpyridine + Co^+) products. Thus, the CAD results indicate that the polyether ligand is always most easily displaced upon energization of the complex. This result agrees with the general trend noted from the ligand exchange results, in which 2,2′:6′,2″-terpyridine had the greatest binding free energy of all the various ligands. Therefore, the kinetically favored dissociation pathway (loss of the polyether) leads to the thermodynamically favored product (2,2′:6′,2″-terpyridine + M^+) for these systems.

3.3.2. 2,2′-Bipyridine complexes

For the heterodimer complexes involving 2,2′-bipyridine and 18-crown-6, 15-crown-5, tetraglyme, or triglyme, the complexes dissociate predominantly or exclusively by loss of the 2,2′-bipyridine ligand (Fig. 4(A)). That these complexes dissociate by loss of the 2,2′-bipyridine ligand, rather than by loss of the polyether ligand, agrees with the results predicted from the ligand exchange results for the one-ligand complexes. The ligand exchange results for the one-ligand complexes indicated that the 2,2′-bipyridine ligand had a lower metal binding free energy than 18-crown-6, tetraglyme, 15-crown-5, and triglyme. Likewise, the CAD results show that the loss of neutral 2,2′-bipyridine from each heterodimer complex is the kinetically favored process.

For most of the heterodimer complexes between 2,2′-bipyridine and 12-crown-4, diglyme, or monoglyme, the predominant loss on CAD is elimination of the polyether ligand, rather than the 2,2′-bipyridine ligand (Fig. 4(B)). This dissociation behavior also leads to formation of the thermodynamically favored product, (2,2′-bipyridine + M^+).

An additional note of interest is that the (2,2′-bipyridine + Co^+ + triglyme), (2,2′-bipyridine + Co^+ + 12-crown-4), (2,2′-bipyridine + Co^+ + diglyme), and (2,2′-bipyridine + Co^+ + monoglyme) complexes not only undergo dissociation by loss of the 2,2′-bipyridine ligand but also undergo radical losses from the polyether portion of the complex. In these cases, the 2,2′-bipyridine unit remains intact and bound to the metal ion, and some smaller portion of the polyether molecules remain attached to the metal ion during the fragmentation process. The radical losses clearly occur from the polyether portion of the complex because similar losses have been observed previously for the dissociation of (2 × monoglyme + Co^+) and (2 × 12-crown-4 + Co^+) complexes [41]. As elucidated previously, the unusual radical losses are only observed when three conditions are met: 1) the metal ion is fully coordinated, 2) the two ligands have similar binding energies to the metal ion in order to prevent facile dissociation by elimination of a whole ligand from the complex during collisional activation, and 3) one of the ligands has sufficient flexibility to undergo the proper conformational changes needed to facilitate the radical losses [41]. Apparently, the (2,2′-bipyridine + Co^+ + polyether) complexes listed above are the only complexes that meet these three requirements. As determined earlier from the ligand exchange experiments for the single-ligand complexes, 2,2′-bipyridine showed a similar binding free energy as triglyme, 12-crown-4, and diglyme (i.e. requirement no. 2 above), so it is reasonable that the radical losses are observed for these heterodimer complexes. Although the exact structures of the resulting fragment ions are unknown, these radical losses conceivably may involve insertion of the metal ion into C–C or C–O bonds.

3.3.3. 4,4′-Bipyridine complexes

The dissociation patterns of the complexes involving 4,4′-bipyridine are quite different from those observed for the 2,2′-dipyridine complexes and show much less variation depending both on the metal ion and the polyether ligand. The heterodimer complexes involving 4,4′-bipyridine and 18-crown-6, 15-crown-5, tetraglyme, or triglyme are never observed because these four polyether ligands bind the metal ion so strongly that they effectively exclude the

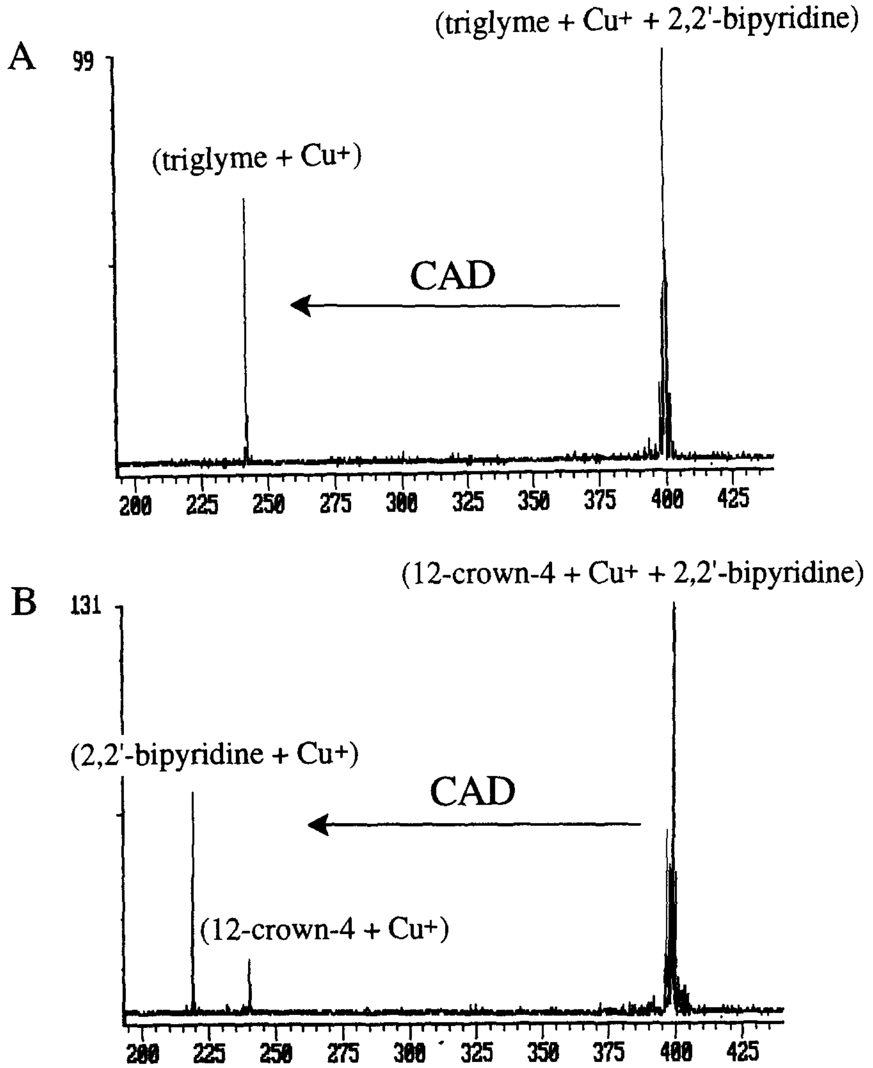

Fig. 4. CAD spectra for heterodimer complexes. (A) CAD of (triglyme + Cu^+ + 2,2′-bipyridine) complexes. (B) CAD of (12-crown-4 + Cu^+ + 2,2′-bipyridine) complex.

4,4′-bipyridine ligand from attaching to the metal ion (as explained earlier). For the other polyether complexes, with the exception of the (4,4′-bipyridine + Co^+ + monoglyme) complex, the heterodimers dissociate exclusively by loss of the 4,4′-bipyridine ligand. For these CAD experiments, the results indicate that the 4,4′-bipyridine ligand is more easily displaced than 12-crown-4, diglyme, or monoglyme upon activation of the heterodimer complexes. This result agrees with the general trend noted for the ligand exchange results, in which 4,4′-dipyridine had a lower binding free energy than 12-crown-4 and diglyme. However, the ligand exchange results indicated that the binding free energy of 4,4′-bipyridine was greater than that of monoglyme. Thus, for the CAD of the (4,4′-bipyridine + Ni^+ + monoglyme) and (4,4′-bipyridine + Cu^+ + monoglyme) systems, the kinetically favored pathway (i.e. loss of 4,4′-bipyridine) does not lead to the thermodynamically favored product (i.e. formation of (4,4′-bipyridine +

M^+). This result may be because monoglyme is a bidentate ligand, whereas 4,4′-bipyridine is only a monodentate ligand. During activation of the heterodimer complex, elimination of the monoglyme portion requires that both coordinating interactions from the two oxygen atoms of monoglyme to the metal ion must be broken at the same time, otherwise the ligand can reattach to the metal ion. The monodentate 4,4′-bipyridine ligand cannot engage in this type of cooperative binding so it might be kinetically favored for elimination.

The (4,4′-bipyridine + Co^+ + monoglyme) complex represents an unusual situation in which the complex predominantly undergoes elimination of radical losses, such as $CH_3\cdot$ in conjunction with C_2H_4O units, from the monoglyme portion of the complex. The monoglyme ligand has coordinating capabilities that are most similar to 4,4′-bipyridine, so each of the two ligands have nearly equal binding free energies for the metal ion, as determined by the ligand exchange experiments. As described above, this latter feature may be key for facilitating the radical losses that require a stable, strongly bound complex [41].

4. Conclusions

In general, multidentate nitrogen-donor atom ligands have substantially greater metal binding free energies than the isodentate oxygen-containing polyethers. The overall order of relative binding free energies determined from the ligand exchange experiments involving the single ligand metal complexes is 2,2′,6′,2′-terpyridine > 18-crown-6 > tetraglyme > 15-crown-5 ≃ triglyme > 2,2′-bipyridine > 12-crown-4 ≥ diglyme > monoglyme. By contrast, the order of relative binding free energies of the ligands as determined from the reactions of the two ligand complexes is 2,2′,6′,2′-terpyridine > 2,2′-bipyridine > 18-crown-6 > tetraglyme > 15-crown-5, triglyme > 12-crown-4 ≥ diglyme > monoglyme. The difference between the two scales reflects the greater impact of steric effects in the two ligand complexes due to ligand–ligand repulsions and the degree of accessibility to the metal ion. Entropy effects play a more important role in the ligand exchange reactions of the two ligand complexes. The flexible polyethers incur a greater loss of entropy when they bind the metal ion relative to when the more rigid pyridyl ligands bind the metal ion. This factor, along with the reduction of the number and net enthalpy of the binding interactions between the metal ion and polyether, enhances the displacement of the polyether ligands by the pyridyl ligands in the two ligand complexes.

CAD also gives insight into the relative strength of the binding interactions of the ligands to the metal ions in the heterodimer complexes. For the heterodimers containing 2,2′,6′,2″-terpyridine as one of the ligands, the polyether ligand is always most easily displaced. For these complexes, there is no evidence that the metal ion inserts into the C–C or C–O bonds of the polyether because there are no fragment ions that involve bond cleavages of the polyether or pyridyl ligands. For the heterodimers containing 2,2′-bipyridine or 4,4′-bipyridine, the pyridyl ligand is typically eliminated during CAD. These losses lead to the thermodynamically favored polyether/metal complexes, as confirmed by the complementary ligand exchange experiments. Radical losses from the polyether portion of the heterodimer complexes are observed when the metal ion is fully coordinated, the two ligands are both strongly bound to the metal ion, and one of the ligands has enough flexibility to undergo the proper conformational changes needed to facilitate the radical losses. The radical losses indicate that the metal ion may undergo insertion into bonds of the polyether upon collisional activation of the complex.

In summary, the combination of systematic ligand exchange studies for one-ligand and two-ligand complexes along with collisionally activated dissociation experiments have allowed an evaluation of the nature of the binding interactions in mixed-ligand complexes. Direct analogies between the behavior of the one-ligand and two-ligand complexes are frequently not apparent, largely because of the greater degree of ligand–ligand repulsion and steric shielding of the metal ion in the two-ligand complexes. The change in behavior as the metal ion becomes more fully coordinated and its charge becomes more delocalized could be relevant when considering the complexation of large biological molecules that have numerous possible coordination sites. For example, the favored binding sites predicted on the basis of evaluation of the binding interactions of model compounds may not accurately reflect the binding sites in biological molecules. The type of strategy described in the present study could also be applied toward elucidation of the nature of binding interactions in many other self-assembled complexes in the gas phase.

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