

# Selective recognition of metal complexes by macrocyclic ethers: further observations on the macrocycle size dependence and the first-sphere ligand composition dependence of recognition thermodynamics <sup>☆</sup>

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## Abstract

Additional studies of solution phase recognition of  $\text{Ru}(\text{NH}_3)_x(\text{pyridine-}x)_y^{2+}$ ,  $\text{Ru}(\text{NH}_3)_x(2,2'\text{-bipyridine})_y^{2+}$  and  $\text{Ru}(\text{NH}_3)_4(1,10\text{-phenanthroline})^{2+}$  species by dibenzo crown ethers are reported. The factors most closely examined were crown size, ammine ligand content and ancillary ligand composition. The overall study confirms that recognition or association derives primarily from H-bond formation (ammine hydrogen/ether oxygen). Evidently opposing these interactions, however, are crown conformational rearrangements. Consequently, straightforward correlations between association strength and potential number of H-bond interactions are found only in selected cases. Based on comparisons of association constants for (bis)pyridine, bipyridine and phenanthroline ligand-containing species with dibenzo crowns, evidence is also found for favorable polypyridine/benzene interactions. NMR (NOE) measurements indicate that the preferred association geometries in solution are those that make each of the benzenes of the crown coplanar (or nearly coplanar) with the ligated polypyridine.

**Keywords:** Molecular recognition; Ruthenium complexes; Ammine complexes; Macrocyclic ether complexes

## 1. Introduction

We have been exploring the utility, or potential utility, of macrocyclic-ether-based molecular recognition effects for initiating or controlling intramolecular electron transfer reactions and for modulating the fundamental electronic structure of strongly coupled mixed-valence systems [1–6]. Targets for recognition are transition-metal am(m)ine complexes where recognition derives primarily from ammine-hydrogen/ether-oxygen H-bonding interactions [7,8]. Of obvious importance in these studies is control over recognition efficacy, i.e. macrocycle/metal complex association thermodynamics. In earlier studies we found that variations in solvent identity [9], ether macrocycle (crown) size [10], metal-complex oxidation state [2,10] and ancillary ligand composition [10] could be exploited in a reasonably systematic fashion to achieve variations in association constants ( $K$ ) over a range approaching  $10^9$ . We additionally found (as expected) that one or more ammonia ligands were always required in the first coordination sphere in order to induce detectable *second-sphere* (crown ether) association. Some-

what surprisingly, however, the strength of the association, as indicated by  $K$ , proved to be essentially independent of the *number* of ligated amines, at least for dibenzo-30-crown-10 as the macrocyclic host and ruthenium(II) as the guest metal center [10]. (In other words, this particular host was found to be selective in the sense that the guest needed to contain ligated  $\text{NH}_3$ , but unselective in the sense that all  $\text{NH}_3$ -containing guests (in a given oxidation state) tended to be recognized indiscriminately.)

In the current paper we report on a broader study of ligand compositional effects. We find that a significant sensitivity to ammine ligand number can be induced under some circumstances and that an enhanced sensitivity to ancillary ligand identity can also be induced. We also describe an expanded study of macrocycle size effects, with a particular emphasis on molecular guest association (or recognition) selectivity. Depending on the guest identity (and oxidation state), we observe for  $K$ : (a) 'normal' correlations with crown size (i.e. greater association strength with greater number of potential H-bond accepting sites); (b) inverse correlations; or (c) *non*-correlations. The variations seem to reflect primarily the interplay between energy-demanding host conformational changes and energy-releasing H-bond formation. We also find evidence for weak, but chemically significant, benzene

<sup>☆</sup> This paper is dedicated to Professor F. Basolo.

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(host)/bipyridyl ligand (guest) interactions. The specifics of these interactions have been mapped by one- and two-dimensional NOE methods.

## 2. Experimental

### 2.1. Materials

$[\text{Ru}(\text{NH}_3)_5(\text{py}-x)](\text{PF}_6)_2$  (py = pyridine;  $x = 4\text{-CH}_3$ , H, 3-Cl, and 3,5-Cl<sub>2</sub>),  $[\text{cis-Ru}(\text{NH}_3)_4(\text{py})_2](\text{PF}_6)_2$ ,  $[\text{Ru}(\text{NH}_3)_4(\text{bpy})](\text{PF}_6)_2$  (bpy = 2,2'-bipyridine),  $[\text{Ru}(\text{NH}_3)_4(\text{phen})](\text{PF}_6)_2$  (phen = 1,10-phenanthroline) and  $[\text{Ru}(\text{NH}_3)_2(\text{bpy})_2](\text{PF}_6)_2$  were prepared by literature methods [11].  $[\text{Ru}(\text{bpy})_3](\text{PF}_6)_2$  was obtained from  $[\text{Ru}(\text{bpy})_3](\text{Cl})_2$  (Aldrich) by metathesis in water with  $\text{NH}_4\text{PF}_6$ . Space-filled representations of the complexes (without counter ions) (HyperChem, version 4.0) are shown in Fig. 1. Dibenzo-30-crown-10 (DB-30-C-10) was purchased from Aldrich. Dibenzo-36-crown-12 (DB-36-C-12) and dibenzo-42-crown-14 (DB-42-C-14) were prepared by literature methods [10,12]. Space-filled representations of the macrocycles are shown in Fig. 2. Reagent grade nitromethane was purchased from Aldrich and distilled prior to use. (Nitromethane was employed as solvent because it is relatively uncompetitive with crown species for specific (H-bonding-based) solvation of the ammine sites [6], yet exhibits a substantial dielectric constant.)

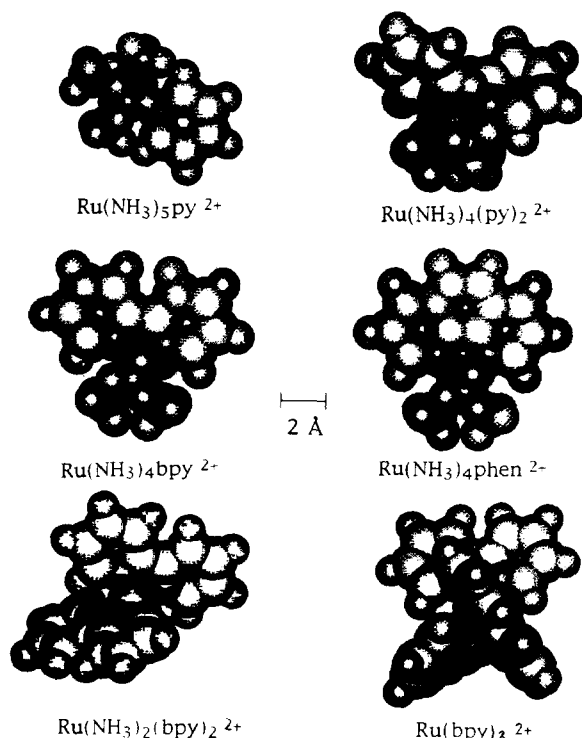


Fig. 1. Space-filled representations of complexes examined as guests.

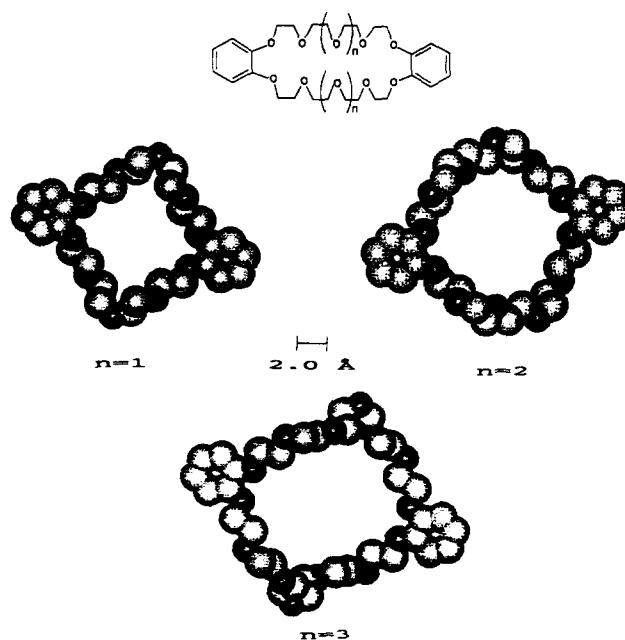
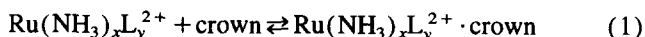


Fig. 2. Space-filled representations of macrocycles examined as hosts.

### 2.2. Measurements

Hewlett-Packard 8452A diode array and OLIS-modified Cary 14 scanning spectrophotometers were used for electronic absorption spectral measurements. NMR spectra were recorded at room temperature on a Varian Unity Plus 400 spectrometer. All chemical shift data are reported in ppm relative to tetramethylsilane (TMS), based on the chemical shift of nitromethane (4.33 ppm, residual <sup>1</sup>H). Samples for 2D experiments were prepared by co-dissolving equimolar amounts of  $\text{Ru}(\text{NH}_3)_4(\text{bpy})^{2+}$  and DB-42-C-14 in degassed  $\text{CD}_3\text{NO}_2$ .

$\text{Ru}(\text{II})$  complex/crown association constants ( $K$ ) were obtained by evaluating shifts in metal-to-ligand charge-transfer absorption energies as



described previously [10]. In the spectral experiments, crown concentrations always exceeded metal complex concentrations by at least five fold. (Depending on the strength of binding, absolute metal complex concentrations ranged from about 0.05 to 0.2 mM.) Reported errors are standard deviations from multiple  $K$  determinations.

## 3. Results and discussion

Table 1 presents association data for each of the six underivatized (bi)pyridyl and phenanthroline metal complexes with each of the three available crowns. (Although dibenzo-24-crown-8 is also available, it was not examined here. Binding by this host generally is weak (and, therefore, difficult to quantify) [1,3]. Furthermore, there may be problems at high crown concentration with multiple crown bind-

Table 1  
Dibenzo crown ether/metal complex association constants ( $M^{-1}$ )

| Metal complex                        | DB-30-C-10      | DB-36-C-12     | DB-42-C-14     |
|--------------------------------------|-----------------|----------------|----------------|
| $Ru(NH_3)_5py^{2+}$                  | $650 \pm 50^a$  | $710 \pm 90$   | $1450 \pm 80$  |
| $Ru(NH_3)_4bpy^{2+}$                 | $800 \pm 100^a$ | $310 \pm 40$   | $6800 \pm 500$ |
| $Ru(NH_3)_2(bpy)_2^{2+}$             | $350 \pm 50^a$  | $180 \pm 30$   | $140 \pm 30$   |
| $Ru(bpy)_3^{2+}$                     | <sup>b</sup>    | <sup>b</sup>   | <sup>b</sup>   |
| <i>cis</i> - $Ru(NH_3)_4(py)_2^{2+}$ | $260 \pm 50$    | $130 \pm 30$   | $230 \pm 40$   |
| $Ru(NH_3)_4(phen)^{2+}$              | $2500 \pm 300$  | $1300 \pm 150$ | $15000^c$      |

<sup>a</sup> Taken from Ref. [10].

<sup>b</sup> Association not detected.

<sup>c</sup> Approximate value (association constant is almost too large to measure by MLCT energy shift method).

ing [9,13].) As expected, the tris bipyridyl complex, which lacks H-bond donating functionalities, displays no propensity for association with the macrocycles. The remaining entries in Table 1, however, comprise a matrix representing extensively varying numbers of potential H-bond donating and H-bond accepting functionalities per assembly. It follows that wide variability in association free energies and, therefore, association equilibrium constants, should be observed. Furthermore, the variations should be readily predictable on the basis of the total possible number of H bonds formed. Nevertheless, inspection of the table suggests that the predicted trends, at least in the broadest sense, are absent. Clearly, effects in addition to H bonding must be involved.

Closer examination of the table suggests that more limited trends or patterns do exist. For example, for  $Ru(NH_3)_2(bpy)_2^{2+}$  as the guest,  $K$  decreases as the host size increases. Prior work has indicated that the smallest of the available crowns (DB-30-C-10) is still sufficiently large to interact essentially completely with two ammonia ligands [9]. Increasing the size of the crown could conceivably result in increased steric demands (note the relative inaccessibility of ammine ligands in  $Ru(bpy)_2(NH_3)_2^{2+}$  in Fig. 1), but without yielding a corresponding increase in H-bonding interactions. Consequently,  $K$  would decrease. If the explanation were sufficient, the trend would be reversed for a guest such as  $Ru(NH_3)_5(py)^{2+}$  which is capable of engaging in progressively more interactions as the macrocycle size (and number of Lewis basic ether oxygens) is increased. The entries in the top row of Table 1 show that the trend apparently is reversed (within experimental error). Nevertheless, the dependence of  $K$  on crown size is so weak that a compensating factor must exist. (Note that no trend exists for the tetraammine species.) We suggest that the compensating factor may well be the (unfavorable) energy of crown conformational rearrangement, which presumably increases as the crown size increases. Energy minimization calculations (molecular mechanics (MM +, HyperChem), no solvent) provide modest support: In the absence of molecular guests, the preferred (calculated) conformations are the nearly planar forms shown in Fig. 1, rather than the folded or wrapped forms required for encapsulation of ammine metal complexes (see below).

If increasingly favorable H bonding to ammine ruthenium(II) guests is partially or completely compensated by increasingly unfavorable conformational considerations (as the size of the host increases), then systematic enhancement of the H-bonding *strength* should lead to increasing differentiation among the available crowns as hosts. Such effects would be detectable if, at the same time, the conformational requirements for each host were fixed (or approximately fixed) by fixing the shape, geometry and ammine content of the guest. Fig. 3 summarizes the results of an experiment designed to meet these requirements. In the experiment, the Lewis acidities of the ammine hydrogens (and presumably the strengths of individual ammonia ligand/ether oxygen H bonds) have been modulated by changing the identity of a remote pyridyl substituent for a structurally homologous series of pentaammine complexes. The electronic inductive effects of the substituents upon the ruthenium center and, ultimately, the ligated ammonias have been gauged (at least in a relative sense) by plotting association data against the Brønsted basicity of the free pyridine [14]. In any case, for the complex with the least basic (i.e., most strongly electron-withdrawing) pyridyl ligand (3,5-Cl<sub>2</sub>-py), association is enhanced (in comparison to the underivatized parent complex) and differentiation on the basis of macrocycle size is more clearly evident.

Viewing Fig. 3 in another way, the ability of the macrocyclic host to distinguish between guests featuring identical numbers of potential H-bonding sites, but differing H-bond formation propensities (i.e. Lewis acidities), is significantly dependent upon macrocycle size. In an earlier study of solvent effects upon association thermodynamics, we found that the extent of encapsulation of a related pentaammine guest increased slightly when DB-36-C-12 replaced DB-30-C-10 and more substantially when DB-42-C-14 replaced either [9]. An increase in the extent of encapsulation implies the formation of a larger number of H bonds. It follows then, that strengthening host/guest H bonds will have larger cumulative effects upon association free energies and induce larger

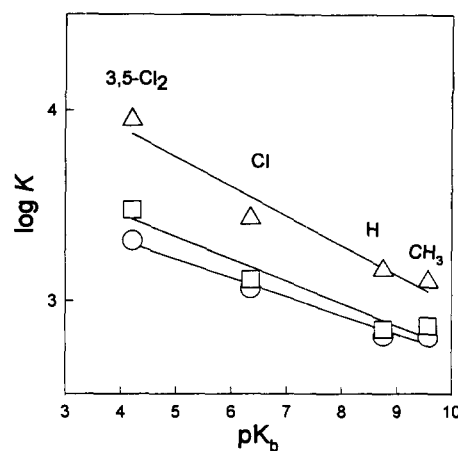


Fig. 3. Log of association constants (crown hosts with various  $Ru(NH_3)_5(py-x)^{2+}$  guests) vs. Brønsted basicity of free py-x ligand (see text). Key to hosts: (○) DB-30-C-10; (□) DB-36-C-12; (△) DB-42-C-14.

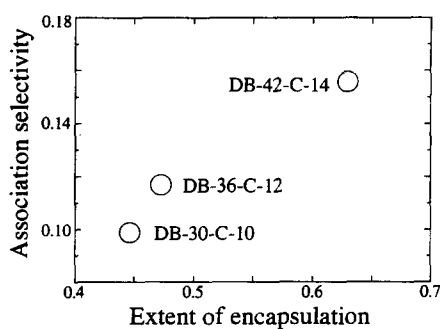


Fig. 4. Association selectivity (negative of slope in Fig. 3) vs. extent of encapsulation achieved by crown species with a pentaammine guest.

increases in association constants with larger hosts. Data consistent with this interpretation are presented in Fig. 4, where association selectivity for each crown (as measured by the negative of the slope of each plot in Fig. 3) is plotted against the independently measured [9] extent of encapsulation achieved by that crown for pentaammine guests.

Returning to Table 1, we initially expected that selectivity with the largest host could be achieved by varying the number of amines coordinated to the guest. For the guest series comprised of  $\text{Ru}(\text{bpy})_3^{2+}$ ,  $\text{Ru}(\text{NH}_3)_2(\text{bpy})_2^{2+}$ ,  $\text{Ru}(\text{NH}_3)_4(\text{bpy})_2^{2+}$  and  $\text{Ru}(\text{NH}_3)_5(\text{py})_2^{2+}$ , substantial variations in  $K$  were indeed seen—and with DB-36-C-12 the variations occur as expected. With the other hosts, however, the largest association constants observed were those for the tetraammine rather than pentaammine complex. Evidently, a factor in addition to H bonding must be involved in the association process. One possibility would be a benzene/bipyridine stacking interaction. Stoddart and co-workers [7,15,16] have shown crystallographically that this type of interaction is important in the encapsulation of square planar a(m)mine bipyridine complexes by dibenzo crowns (where typically both benzenes interact with the bpy ligand). To test the idea, we also examined  $\text{Ru}(\text{NH}_3)_4(\text{py})_2^{2+}$  as a guest (where the pyridine rings are no longer coplanar; Fig. 2). Table 1 shows that the association constant is decreased substantially, such that the  $\text{Ru}(\text{bpy})_3^{2+}/\text{Ru}(\text{NH}_3)_2(\text{bpy})_2^{2+}/\text{Ru}(\text{NH}_3)_4(\text{bpy})_2^{2+}/\text{Ru}(\text{NH}_3)_5(\text{py})_2^{2+}$  series exhibits (with DB-42-C-14) the expected 'normal' ordering of association strength with ammine ligand content. (Evidently the octahedral geometries of  $\text{Ru}(\text{bpy})_3^{2+}$  and  $\text{Ru}(\text{NH}_3)_2(\text{bpy})_2^{2+}$ , and resulting orthogonal orientations of adjacent bipyridines, sterically preclude similar interactions with the dibenzo species.)

As a further test of the stacking idea, we also examined  $\text{Ru}(\text{NH}_3)_2(\text{phen})^{2+}$  as a guest. As indicated by Table 1, substantial increases in association equilibrium constant accompany the replacement of either pyridine (one aromatic ring, taken twice) or bipyridine (two aromatic rings) by phenanthroline (three (fused) aromatic rings) in the Ru(II) coordination sphere. Literature discussions of related interactions tend to emphasize the ability of multiple, electron-deficient hydrogen atoms to interact electrostatically with electron-rich ring regions [17–19]. Alternatively (or additionally), they emphasize gains in solvent 'self-association

energy' following the displacement of solvent from faces of the aromatic host and guest [19–22]. According to this argument, the larger the area desolvated (by guest/host association) the larger is the gain in solvent self-association energy and the larger is the guest/host association constant. The trend for the tetraammine species in Table 1 is at least consistent with such discussions.

Given the apparent thermodynamic evidence for favorable benzene/bipyridine interactions (and the more compelling evidence for favorable benzene/phenanthroline interactions), we sought confirmation via NMR (NOE) methods. We also sought to establish, at least partially, the structure of the host/guest assembly (specifically, the DB-42-C-14/ $\text{Ru}(\text{NH}_3)_4\text{bpy}^{2+}$  assembly) in solution. Table 2 summarizes the shifts that are induced in the aromatic region of the  $^1\text{H}$  spectrum by association. All hydrogens of the ligated bipyridine are shifted upfield, with the largest effects observed at the 3 (3') position. We attribute the shifts to interactions with the ring current of benzene. Complementary shifts are observed for both the  $\alpha$  ( $\alpha'$ ) and  $\beta$  ( $\beta'$ ) hydrogens of benzene. Despite the shifts, no alteration in the number of peaks is seen. We conclude, therefore, that the local symmetry of the assembly is maintained, at least in the aromatic region. For hydrogens on the ether chains (in the absence of the guest), we observe multiplets at 4.15, 3.85, 3.70 and 3.63 ppm and a singlet at 3.61 ppm. In the presence of the guest, these shift upfield and coalesce (four resolvable singlets between 3.57 and 3.77 ppm). Presumably the spectral changes are consequences of macrocycle conformational changes brought about by H-bond formation at neighboring ether oxygen sites.

Returning to the aromatic spectral region, we also observed significant NOE interactions (2D NOESY method) between the benzene hydrogens of the crown and the bipyridine hydrogens. Polarization transfer clearly occurs between the aromatic rings in the host/guest assembly. Although we encountered difficulties in quantitating the NOE interactions, we did find that the 3 (3'), 4 (4') and 6 (6') hydrogens contributed roughly equally to NOEs for both the  $\alpha$  and  $\beta$

Table 2  
Association-induced chemical shifts (ppm) in  $\text{Ru}(\text{NH}_3)_4\text{bpy}^{2+}$ /dibenzo-42-crown-14  $^1\text{H}$  NMR spectra

| Resonance              | Chemical shift      |                     | Assignment |
|------------------------|---------------------|---------------------|------------|
|                        | Isolated host/guest | Host/guest assembly |            |
| 3(3')                  | 8.34                | 7.82                |            |
| 4(4')                  | 7.90                | 7.56                |            |
| 5(5')                  | 7.52                | 7.20                |            |
| 6(6')                  | 9.07                | 8.95                |            |
| $\alpha$ ( $\alpha'$ ) | 7.00                | 6.92                |            |
| $\beta$ ( $\beta'$ )   | 6.92                | 6.72                |            |

hydrogens. (Somewhat smaller effects exist for the 5 (5') hydrogens.) These observations, together with the observations (above) on local symmetry, are suggestive of a coplanar (or nearly coplanar) configuration with benzene centered over the two pyridyl rings. (We assume that the second benzene occupies a similar position under the bipyridine, if the assembly is viewed normal to the interaction plane.) This type of geometry has been reported previously for  $\text{Pt}(\text{NH}_3)_2(\text{bpy})^{2+}$  with dibenzo crowns (crystallographic studies [15,16]). Finally, we were also able to observe a correlation between  $\alpha$  hydrogens and 5 (5') hydrogens via 2D COSY. The observation is perhaps suggestive of weak, but significant, bonding (dative) interactions between benzene and bipyridine.

#### 4. Conclusions

Within various subsets of metal ammine hosts and crown ether guests, correlations as well as inverse correlations exist between recognition efficacy (association strength) and either crown size or ammine ligand content. The correlations are due to the favorable enthalpic effects of multiple H-bond formation (ammine hydrogen/ether oxygen). As expected, the correlations are enhanced when guest modifications that enhance H-bond strength are introduced. The inverse correlations, on the other hand, appear to be due to systematic increases in conformational energy costs when crown sizes are enlarged. Finally, based on comparisons of association constants for (bis)pyridine, bipyridine and phenanthroline ligand-containing species with dibenzo crowns, evidence is found for favorable (poly)pyridine/benzene interactions. NMR(NOE) measurements indicate that the preferred geometries in solution are those that make each of the benzenes coplanar (or nearly coplanar) with the ligated polypyridine.

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