

Influence of Solvent Properties on Cation-Macrocycle Complexation: Cesium Cryptates[#]

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Abstract. The chemical shift of the ¹³³Cs resonance has been measured as a function of the mole ratio of cryptands C222, C222B, C221, and C211 to the Cs⁺ ion in *N*-methylformamide and dimethylacetamide solutions. The overall formation constants of the cesium cryptates were calculated from the NMR titration curves. From these and previously reported data it is clear that solvent properties such as dipole moment, donicity, dielectric constant and hydrogen bonding ability affect macrocyclic ligand-cation complexation equilibria through specific solvation of the cation, the ligand and the complex. A model of M⁺ · L bonding in solution, involving a rather intimate electrostatic attraction between the cation and the local electron distribution of the macrocycle accompanied by little perturbation of the charge distributions of the separated partners, is presented. In addition to the specific interactions previously noted, the presence of the solvent mitigates the ion-multipole forces which would otherwise govern the long-range attraction.

Key words. Cesium cryptate stabilities, high dielectric solvents, ¹³³Cs NMR, electrostatic nature of complexation.

1. Introduction

Among the many factors which influence the formation of macrocyclic complexes of metal ions in solution, certainly not the least important is the ability of solvent molecules to solvate ions and thus to compete with the ligands for the coordination positions around a cation. Equally important, but often much less appreciated, is the interaction of some solvents with the macrocyclic ligands [1]. Thus both the cation and the ligand must be at least partially desolvated before the adduct can be formed. The two solvation mechanisms are usually different. Solvation of an alkali cation involves primarily ion-dipole forces (with some contribution from donor-acceptor interaction). On the other hand, solvation of macrocyclic ligands proceeds very largely through hydrogen bonding between the —OH, —NH₂, or even —CH₃ group of the solvent and the ether oxygens of crown ethers [1–3] and with oxygen and nitrogen atoms of cryptands [4].

In one of his early classical papers Pedersen suggested [5] that the formation of crown ether complexes of alkali ions results primarily from ion-dipole interactions between the cation and the local [—CH₂—O—CH₂—] dipoles of the macrocyclic ligands. A later study showed that the ligand-cation vibration observed for a given M⁺, L pair in the low frequency region of the infrared spectrum could not be

[#] This paper is dedicated to the memory of the late Dr C. J. Pedersen.

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observed in the Raman spectrum [6]. The weakness of the Raman scattering indicates that this vibration is accompanied by little change in the polarizability, and thus supports Pedersen's assumption about the electrostatic nature of the cation–ligand bonds. However, it has also been observed that, in the absence of 'hard-soft' interactions, the stabilities of macrocyclic complexes often vary inversely with the donor abilities of the solvents employed [7] (as expressed by the Gutmann donicity values [8]), i.e. with their ability to solvate alkali cations and therefore inhibit the metal–ligand complexation reaction. Thus both electrostatic and donor–acceptor interactions play a role in the formation of a macrocyclic complex. On this basis, relative stabilities of macrocyclic complexes in solvents which have very nearly the same donating capacity and similar dipole moments will be governed by electrostatic forces and should vary inversely with the dielectric constants of the media.

In this study we have extended our previous NMR investigations [9] related to the influence of solvent properties on macrocyclic complexation to the reactions of the cesium ion with diazapolyoxa macrobicyclic ligands (cryptands; we follow nomenclature proposed by J.-M. Lehn [10] whereby *cryptand* is the free ligand, and *cryptate* is the complex) in two amide solvents, *N*-methylformamide and dimethylacetamide, which have very similar donor properties and dipole moments, but differ in the values of the dielectric constant (Table I) and in the ability to form hydrogen bonds. The ^{133}Cs chemical shift provides a sensitive probe of the cationic environment. From the variation of the chemical shift with relative concentration of a selected macrocyclic complexant, a value of the formation constant of the cesium-macrocycle complex can be calculated. Previous studies on cesium cryptates in dimethylformamide solutions [11–13] are included in the discussion of our results.

Table I. Solvent properties and formation constants of the Cs^+ ion cryptates at 25°C.

Solvent:		NMF	DMF	DMA
Donor number		25 ^a	26.6 ^b	27.8 ^b
Dielectric constant ^c (25°C)		182.4	36.71	37.8
Dipole moment ^c (Debye)		3.86	3.86	3.72
Ligand	Cavity size (Å) ^d	log <i>K</i>		
C211	1.6	$K \approx 0$	1.23 ± 0.07^e	0.74 ± 0.06
C221	2.2	2.4 ± 0.2	3.33 ± 0.04^e	3.07 ± 0.02
C222	2.8	2.35 ± 0.03	2.16 ± 0.03^f	1.82 ± 0.01
C222B	≈ 2.8	1.75 ± 0.08	1.70 ± 0.03^f	1.47 ± 0.01

^a H.-H. Chuang, L. Soong, G. E. Leroi, and A. I. Popov: *J. Solution Chem.* **18**, 759 (1989).

^b Ref. [8].

^c J. A. Riddick and W. B. Bunger: *Techniques of Chemistry, Vol II, Organic Solvents*, A. Weissberger, ed., Wiley-Interscience, New York, NY, 1970.

^d Ref. [10].

^e Ref. [13].

^f Ref. [12].

2. Experimental Part

2.1. CHEMICALS

N-methylformamide [NMF] and *N,N*-dimethylacetamide [DMA] (both Aldrich) were refluxed over granulated barium oxide and then fractionally distilled at reduced pressure either from barium oxide or from calcium hydride. The middle fraction was collected in both cases. The water content of the solvents was measured with a gas chromatograph and was found to be always below 70 ppm. The solvents were stored over freshly activated 3 Å molecular sieves, in a dry-box under dry nitrogen atmosphere.

Cesium iodide (Alfa) was used as received except for drying at 120°C for two days. Cesium tetraphenylborate was prepared by the metathetical reaction between cesium chloride and sodium tetraphenylborate in a tetrahydrofuran-water mixture. The solid product was filtered and dried for two days, under vacuum, at 70°C. Cryptands C211, C221, C222 and C222B (all from MCB) were used as received except for drying under vacuum at room temperature for two days. Deuterium oxide (KOR Isotopes) was used as received. All solutions were prepared and stored in a dry-box under a dry nitrogen atmosphere.

2.2. MEASUREMENTS

Cesium-133 chemical shifts were measured on a Bruker WH-180 NMR spectrometer with a field strength of 43.2 kG. At this field the ¹³³Cs nucleus resonates at 23.62 MHz. The solutions were placed in 10 mm o.d. NMR tubes with a coaxial 4 mm o.d. tube containing 0.5M CsBr in D₂O, which served as a chemical shift reference and the lock. Measurements were made on a series of thermostatted (25 ± 1°C) solutions containing a constant amount of cesium salt and a variable amount of the ligand. Chemical shifts reported in this work are given vs. an infinitely dilute aqueous solution of the cesium ion.

Carbon-13 NMR measurements were carried out on a Bruker WM-250 spectrometer operating at a field of 58.7 kG and a frequency of 62.9 MHz. Benzene-*d*₆ was used as the external reference and lock. Chemical shifts are given with respect to Me₄Si. Both in ¹³³Cs and ¹³C measurements, chemical shifts were corrected for the differences in the bulk diamagnetic susceptibility between the sample solvent and the reference solvent.

2.3. CALCULATIONS

Assuming that only a 1 : 1 complex is formed and that fast exchange conditions prevail, it can be readily shown [14] that in solutions containing both the free and the complexed cation, the observed chemical shift of the cesium ion is given by the equation:

$$\delta_{\text{obs}} = [(KC_M - KC_L - 1) + (K^2C_L^2 + K^2C_M^2 - 2K^2C_L C_M + 2KC_M + 2KC_L + 1)^{1/2}] \left[\frac{\delta_f - \delta_c}{2KC_M} \right] + \delta_c \quad (1)$$

where K is the concentration formation constant, C_L and C_M are the total concentrations of the ligand and of the cation respectively, δ_f is the chemical shift of the uncomplexed cesium ion, and δ_c is the chemical shift of the complexed cation.

A series of solutions was prepared containing a fixed amount of the cesium ion and a variable amount of the ligand. The titration curve of the ^{133}Cs chemical shift vs. [ligand]/[cation] mole ratio thus obtained was fitted to Equation 1 by using a non-linear least squares program, KINFIT [15]. Since in our solutions the chemical shift of the 'free' cesium ion varies with the concentration of the salt and with the nature of the anion, and thus δ_f is a variable, the values employed in the equation were obtained from measurements of ^{133}Cs chemical shifts as a function of concentration of the cesium salt, as exemplified in a previous publication [16].

3. Results and Discussion

Titration curves obtained in *N*-methylformamide and in dimethylacetamide are shown in Figures 1 and 2. Formation constants of cesium cryptates calculated from these data are listed in Table I, together with the values previously obtained for dimethylformamide [DMF] solutions [11–13]. It is seen that in all three solvents the cryptates are rather unstable (K rarely larger than 1000), and the apparent stability order is $\text{C221} > \text{C222} > \text{C222B} > \text{C211}$, irrespective of the solvent. It should be noted that these are *relative* stability constants, which reflect the competition between the ligand and the solvent for the cesium cation. The table also shows that the three solvents have very nearly the same dipole moments and very similar

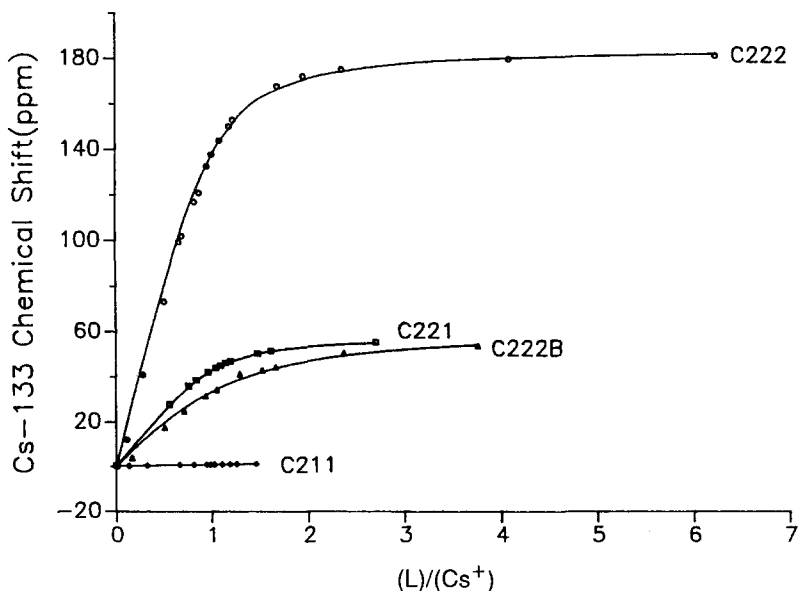


Fig. 1. Cesium-133 chemical shifts vs. cryptand/ Cs^+ mole ratio: 0.05M CsI in NMF.

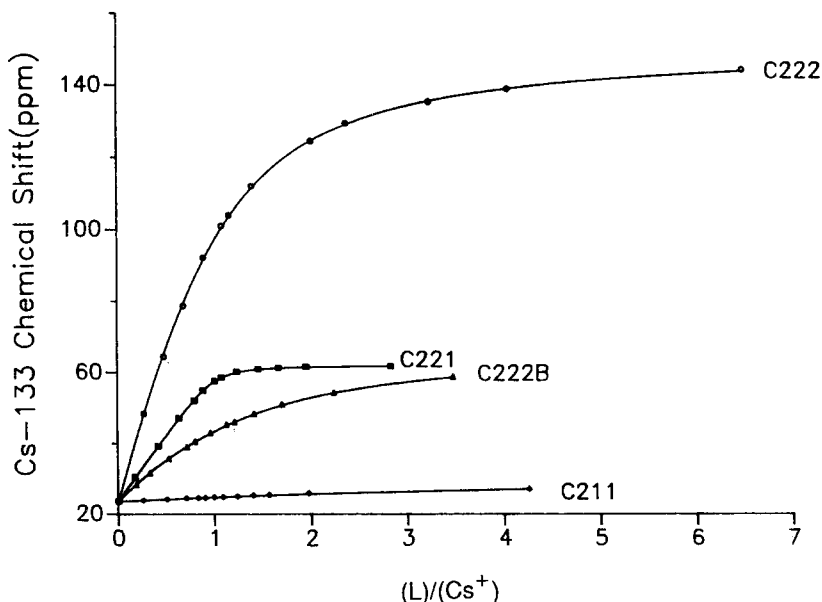
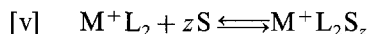
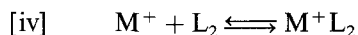
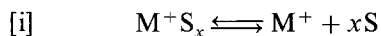
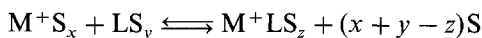


Fig. 2. Cesium-133 chemical shifts vs. cryptand/ Cs^+ mole ratio: 0.05M CsI in DMA.

solvating abilities. However, the dielectric constant of NMF is much higher than those of the other two solvents.

As shown in Figures 1 and 2, the addition of the selected cryptands to amide solutions of a cesium salt results in paramagnetic (downfield) shifts of the ^{133}Cs resonance. These shifts represent, of course, the *difference* in the environment of the solvated and complexed cesium cation. The magnitude of the shift is not related to the stability of the complex, but reflects rather the tightness of the ligand-cation juxtaposition, i.e. the overlap of the lone pair orbitals of the oxygen and nitrogen atoms of the ligand and the outer p -orbital of the cation. Constraints on the $\text{Cs}^+ \cdot \text{C222}$ geometry suggest that the overlap will be particularly strong for this complex (*vide infra*). Thus, although cryptand C322 forms a much more stable complex with the cesium cation than does C222 ($\log K = 7.0$ vs. $\log K = 3.5$ in water-methanol mixtures [17]), the chemical shifts of the complexed cation in methanol solution are 22 ppm and 220 ppm, respectively [18]. Figure 2 illustrates that addition of C222 results in a larger ^{133}Cs paramagnetic shift than that observed with C221; however, in the latter case the chemical shift levels off shortly after the 1:1 mole ratio, which indicates qualitatively that, as in other solvents [12], $K(\text{Cs}^+ \cdot \text{C221}) > K(\text{Cs}^+ \cdot \text{C222})$.

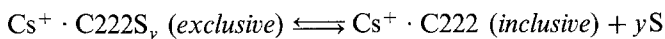
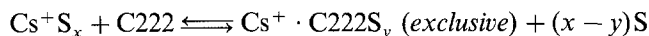
Formation constants (or free energies of formation) of macrocyclic ligand-cation complexes in solution, such as those reported in this paper *or elsewhere*, may be interpreted as representing the overall results of a series of reactions [19]. Of these, several elementary steps may have a strong effect on the quantity which is generally of primary interest: the *relative* stability of a given complex under a strictly defined set of conditions. Equations for the overall reaction and its component steps (which may occur in some concerted fashion) can be written:



These are: [i] desolvation (partial or complete) of the cation, [ii] desolvation (partial or complete) of the ligand, [iii] change in the conformation of the ligand (coincidental with [ii]?), [iv] the formation of the complex, and [v] solvation of the complex. It should be noted that in three of the five steps solvent molecules directly participate in the equilibria! Solvent properties such as the dielectric constant, dipole moment, donicity, and potentiality for hydrogen bonding will affect the reactions for each M^+ , L pair differently.

In most previous studies of macrocyclic complexation reactions the influence of solvent–ligand interactions has been ignored. In the few cases where such interactions have been investigated, however, it has been clearly demonstrated that they may profoundly affect the extent of such reactions [1]. Carbon-13 NMR spectra of C221 in a number of solvents have been measured previously in our laboratory [4]; the C-4 and C-5 signals, which overlap in the spectrum of the *free* ligand, are split when direct solvent–ligand interaction occurs. In this work we have observed such a splitting for C221 in NMF, but not in DMA or DMF. The ^{13}C NMR spectrum of C221 in NMF (in the absence of cesium salt) is reproduced in Figure 3, which also shows the carbon atom numbering scheme for the ligand. Most likely the splitting reflects hydrogen bonding interactions between C221 and NMF, which are not possible in DMF or DMA. There is little doubt that similar interactions occur between NMF and the other cryptands.

Studies of C222 complexation with the Cs^+ ion in four different solvents, including DMF, have shown that the reaction occurs in two steps [11, 18]. Initially, the cation binds to the heteroatoms of two strands, forming an *exclusive*, partially-solvated, crown-like complex. The second step involves the penetration of the completely desolvated cation into the ligand cavity to form the *inclusive* [20] complex:



Thermodynamic parameters measured for the two reactions are given in the cited references. The values of the $\log K$ reported in Table I for the $Cs^+ \cdot C222$ cryptate are thus composites, which include both equilibria; therefore, they cannot be compared directly to formation constants calculated for cases in which only exclusive complexes are formed.

The situation for C222B is less clear. While the cavity dimensions of the free ligand should be very nearly the same as those of C222, the substitution of a benzene ring on one chain will tend to make the ligand less flexible, and may

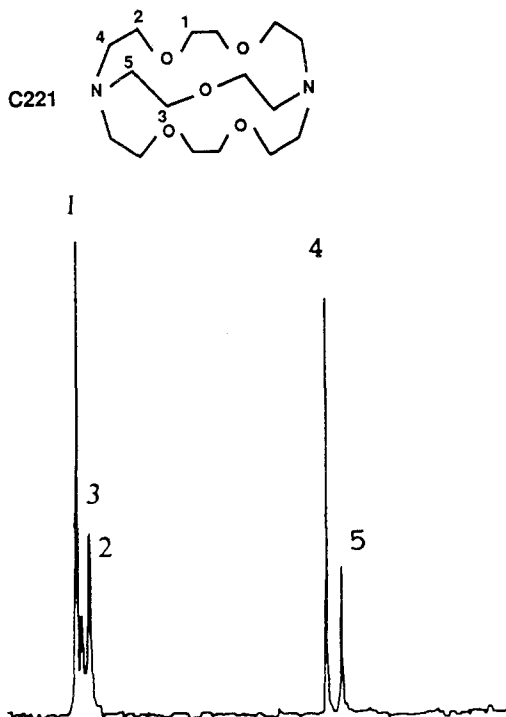


Fig. 3. Carbon-13 NMR spectrum of C221 in NMF at 25°C. The separation between the C4 and C5 signals is 0.81 ppm.

preclude or mitigate the formation of the inclusive complex with Cs^+ . For the other two ligands studied in this work, C211 and C221, the cavities are much too small to allow the formation of an inclusive cesium cryptate.

Since the dipole moments and the donicities of the three solvents are essentially the same, their solvating abilities, *vis-à-vis* the Cs^+ ion, should also be approximately the same. Presuming that their interactions with the ligand and the complex are relatively similar, one would expect the overall complexation constant to be smaller in the high dielectric constant solvent, NMF. From Table I, this solvent dependence of $\log K$ is observed in the two cases where only a single-step complexation reaction, to form the exclusive complex, can occur. The same inverse dependence of the complexation constant on the solvent dielectric constant has been observed for Cs^+ · crown ether complexes in amide solvents [9].

4. Conclusions

The general subject of cation/macrocyclic ligand/solvent interactions has not been thoroughly discussed in the literature, especially with regard to the role of the solvent. It seems particularly appropriate in this volume to present an overview of the topic from a broader perspective than the new results reported in this paper. In particular, the nature of the interaction between an alkali metal cation and the

macrocyclic ligand (step [iv], above) deserves deeper scrutiny than has been given in the literature heretofore. As mentioned above, in an early notable paper Pedersen suggested that the $M^+—L$ bond is electrostatic [5], and the weakness of the scattering from this vibration in the experimental Raman spectra [6] is consistent with the small polarizability change to be expected under such circumstance. In our view, the important features of $M^+ \cdots L$ bonding *in solution* involve a rather intimate attraction between the positively-charged spherical ion and the local electron distribution of the macrocyclic complexant, the latter being dominated by the presence of non-bonding electron pairs. (The classical, long-range, ion-multipole forces which govern electrostatic interactions in the gas phase are mitigated by the charge distributions of intervening solvent molecules; the electrostatics specific to $M^+ \cdots L$ binding govern the interaction only when the partners are rather proximate.) In this 'close-binding' model, very little perturbation of the charge distributions of the separated partners accompanies the rather strong electrostatic interactions of the cation with the lone pairs of electrons on the macrocycle, which in many cases can adjust its conformation to partially envelop the cation and maximize the number of interacting electron pairs. The oxygen atoms in a strand of a macrocyclic ligand have two lone pairs of electrons, and thus high 'local dipole and polarizability'; a nitrogen atom with its single lone pair will be less electronegative, and will be a poorer partner for 'hard' acids, such as the alkali cations. Thus one would expect the aza-complexes to have smaller complexation constants than their oxygen counterparts with a particular alkali cation in a given solvent, as is indeed observed experimentally [21, 22].

Such a picture of electrostatic bonding has been recently propounded to account for the bonding between monopositive transition metal cations and neutral molecules in the gas phase [23–26]. For example, theoretical calculations reveal that the bonding between Sc^+ , Ti^+ , V^+ , Cr^+ , Ni^+ and Cu^+ ions with CO is essentially electrostatic, with very little charge transfer [23, 25, 26], unlike the covalent Dewar–Chatt scheme which has been accepted for the neutral species [27]. The attractive portion of the *ab initio* potential surfaces for the $M^+—CO$ ground states is well represented by a classical electrostatic interaction potential, as is that for $Sc^+—OC$ [23]. The metal–ligand binding in $LiCO^+$ and $ScNH_3^+$ ions [28, 29] is also clearly electrostatic, and rather strong.

In an alkali cation–macrocyclic ligand complex one expects the electrostatic attraction to be maximized, within geometrical limitations, until it balances the Pauli repulsion between the electrons on the metal and the ligand. The increased electron density thus predicted in the neighborhood of the metal ion is consistent with the large paramagnetic shifts observed in the alkali cation NMR spectra, relative to the corresponding gaseous atom, when $M^+ \cdot L$ complexes are formed [30]. For a given ligand, then, one might expect the interaction to be stronger for Li^+ than for Cs^+ because of the closer proximity of the cation to the negative charge distribution on the ligand; however, geometrical constraints related to the cation/cavity fit may well be dominant.

Although solvent molecules do not appear explicitly in reaction [iv], to the extent that the electrostatic interaction between M^+ and L occurs over long range, the bulk properties of the solvent will affect the equilibrium constant for this step via the conventional inverse dependence on the dielectric constant. If *specific* interac-

tions of the solvent with the cation, the ligand and the complex (steps [i], [ii] and [v]) vary little from one solvent to another, for instance when solvents of similar donicity and functionality are intercompared, then the complexation constant measured for the overall reaction may reflect the influence of the dielectric properties of the solvent on the complexation equilibrium, [iv]. Indeed, some such correlations of cation/ligand stability constants with solvent dielectric constant have been suggested [9, 17, 19, 31] and the log K values we measure for $\text{Cs}^+ \cdot \text{C211}$ and $\text{Cs}^+ \cdot \text{C221}$ are inversely related to this property. However, we cannot reiterate too strenuously the danger of drawing such correlations for other systems without extreme caution. The dependence of the overall complexation constant on the properties of the solvent will usually be governed by differences in the interactions in steps [i], [ii] and/or [v], determined by differences in the solvent donicity, dipole moment, and/or its propensity for hydrogen bonding.

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