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Carbon-13 NMR Chemical Shifts and Relaxation Times as a Probe of Structural and Dynamic Properties in Alkali and Alkaline Earth Cryptate Complexes

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The C-13 NMR spectra of cryptands [2.1.1], [2.2.1], and [2.2.2] in the presence of Li^+, Na^+, K^+, Ca^{2+}, and Ba^{2+} in D_2O/MeOH or $CDCl_3$ have been analyzed. Generally, the carbons shifted to higher field upon complexation. Two exceptions to this were observed: the complexes $[2.1.1]\cdot Na^+$ and $[2.2.1]\cdot K^+$. The C-13 longitudinal relaxation time measurements show a surprising increase in magnitude for most alkali-metal, but not alkaline earth metal, complexes. This increase in relaxation times is interpreted in terms of ligand compression, desolvation, and solvent reorganization.

Introduction

Considerable effort[1] has been devoted to the study of macrobicyclic ligands and their metal complexes. Macrocyclic ligands, in general, have expanded coordination chemistry to the first two families of the periodic table and, due to the biological importance of some of their elements (Na^+, K^+, Ca^{2+}, etc.), research in this field has been very active over the last few years. Multinuclear NMR has emerged as a powerful technique to investigate the properties of these compounds, especially through the use of alkali-metal nuclei as NMR probes.[2] These nuclei offer several advantages. For example, because of their quadrupolar character, the nuclear relaxation properties depend upon the environment's electrical symmetry. Valuable structural information can therefore be obtained by interpreting the changes in these values.

The O-17 nucleus, although much less sensitive than the alkali-metal nuclei, is also a useful probe[3] since it is itself directly involved in the bonding interaction as donor counterpart to the M^+ acceptor. Likewise, the C-13 nucleus is a useful probe but has been used relatively little,[4–6] perhaps because it is not directly involved in the binding interaction. We have already demonstrated the utility of C-13 spin–lattice relaxation times to probe the microdynamics of complexation between alkali metals and lariat ethers[7] and with cryptands, in the preliminary report of this work.[8] We present here changes in C-13 NMR chemical shift and longitudinal relaxation time data upon complexation between cryptands [2.1.1], [2.2.1], and [2.2.2] with Li^+, Na^+, K^+, Ca^{2+}, and Ba^{2+} in D_2O/MeOH or $CDCl_3$ solutions.

Experimental Section

All cryptands (E. Merck, Darmstadt) were used as received. Alkali-metal perchlorates (Aldrich) were dried under vacuum at 110 °C for 48 h prior to use. Cryptand complexes (cryptates) of alkali metal ClO_4^- salts were prepared by adding 0.15 mmol of the salt to 0.50 mL of 99.8% $CDCl_3$ containing 0.15 mmol of the cryptand. For some of the systems under study, measurements were conducted in MeOH/D_2O, 90:10 by weight. MeOH and 99.7% D_2O were purchased from Aldrich and Merck Stable Isotopes, respectively, and vacuum transferred directly into the degassed sample tube. NMR samples, consisting of 0.50 mL of solution in 5-mm-o.d. tubes (Wilmad), were sealed under vacuum after careful degassing by at least three freeze–pump–thaw cycles. All glassware was rinsed with 0.02 M EDTA solution to remove paramagnetic impurities.

Natural-abundance ^{13}C NMR spectra were obtained on a JEOL FX90Q NMR spectrometer operating at 22.5 MHz. Data acquisition and Fourier transformation were performed with 8K data points. The spectra were obtained under H-1 noise-decoupling conditions and the chemical shifts of the ligand peaks were determined by using the center peak of the $CDCl_3$ triplet (77.0 ppm) as a secondary reference. Alternatively, the position of the MeOH C-13 resonance (48.0 ppm) was used as a reference.

Spin–lattice relaxation times (T_1s) were determined by using the inversion recovery technique (rather than the modified fast inversion recovery technique, which was used for some cases in the work reported previously[8]). A waiting time, t_w, of 30 s was utilized, which is much longer than the theoretically required minimum of $5(T_1)$ for all carbons under study. Thirteen different pulse intervals were utilized in each individual run, ranging between 0.05 and 3.00 s, to assure that a minimum of eight data points were used for each T_1 calculation. An average of 80–120 scans were needed for each value in order to obtain a reasonable signal-to-noise ratio, so that approximately 10 h of spectrometer time was required to complete each individual measurement. A minimum of three independent runs were accumulated for each sample from which we estimate a standard deviation of ±10%. Nuclear Overhauser enhancement (NOE) factors were measured for all samples by comparing relative intensities of all resonances under H-1 noise-decoupling conditions with their respective values under gated decoupling conditions. All NOE values fall between 2.80 and 2.98, indicating that relaxation occurs predominantly by the dipole–dipole mechanism. Neither the chemical shifts nor the relaxation times showed any concentration dependence in the range 0.08–0.80 M.

Results and Discussion

Chemical Shifts. The chemical shifts (in $CDCl_3$) obtained for Li^+, Na^+, and K^+ complexes of cryptands [2.1.1],

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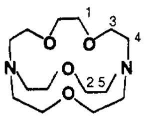
Table I. ^{13}C NMR Chemical Shifts and Relaxation Times (in seconds) for Cryptands and Their Alkali-Metal Complexes in Deuteriochloroform Solution

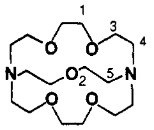
		chemical shift, δ				T_1, s			
cryptand	position	free	Li^+	Na^+	K^+	free	Li^+	Na^+	K^+
[2.1.1]	1	70.23	67.91	68.22	70.23[a]	1.01	0.90	0.58	1.05[a]
	2	69.76	65.06	68.75	69.76[a]	0.93	0.91	0.49	0.90[a]
	3	69.53	66.12	67.08	69.53[a]	0.96	0.91	0.52	0.98[a]
	4	57.06	51.06	57.56[b]	57.06[a]	0.91	0.92	0.51	0.92[a]
	5	55.24	49.74	54.20	55.24[a]	0.86	0.91	0.55	0.88[a]
[2.2.1]	1	70.17	68.05	68.14	68.78	0.76	1.25	1.01	0.52
	2	69.65	66.47	66.49	69.23	0.75	1.06	0.89	0.53
	3	69.42	66.83	65.97	67.31	0.77	1.19	1.00	0.47
	4	56.38	52.37	52.23	57.40[b]	0.72	1.19	1.06	0.49
	5	56.10	52.56	53.06	53.01	0.69	1.22	0.91	0.52
[2.2.2]	1	70.60	68.69	68.48	70.12	0.83	0.54	1.00	0.96
	2	69.58	68.22	67.55	67.19	0.80	0.51	0.98	0.90
	3	56.00	54.02	52.78	53.52	0.69	0.55	0.94	0.97

[a] These values correspond to those of the free ligand. Practically no salt dissolved in the cryptand/$CDCl_3$ solution.
[b] Lines shifted downfield.

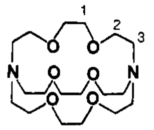
[2.2.1], and [2.2.2] and the corresponding free ligands appear in Table I. The spectrum of each ligand is dependent not only on complexation but also on the alkali-metal cation. As a general rule, inclusion of an alkali-metal ion in a cryptand cavity causes an upfield shift of the C-13 resonance lines. It is noteworthy that only two cryptate peaks oppose this trend (see Table I).



[2.1.1]



[2.2.1]



[2.2.2]

In this group, cryptand [2.2.2] shows the simplest spectrum, containing only three lines of equal intensity. The highest field resonance, corresponding to the $N-CH_2$ carbon atoms, is the most strongly affected by complexation. A related observation was recently reported by Cox et al.[9] on the solvent dependence of the H-1 chemical shifts of [2.2.2]. In this case, the α-methylene protons were the most solvent dependent. Our results are in good agreement with those reported by Popov et al.[10] for the complexation of K^+ with [2.2.2] in Me_2CO, DMF, and Me_2SO.

The spectra of cryptands [2.1.1] and [2.2.1] each exhibit five peaks as expected. The Li^+ complex of [2.1.1] shows the largest chemical-shift differences compared to the uncomplexed ligand. Thus, in $CDCl_3$, carbons 1–5 exhibit upfield shifts of 2.32, 4.70, 3.41, 6.00, and 5.50 ppm, respectively. When Li^+ is replaced by Na^+, the chemical-shift differences for these same carbon atoms are 2.01, 1.01, 2.45, –0.5, and 1.04 ppm, respectively. It is interesting that C-4 is shifted most upfield in the presence of Li^+ but downfield with Na^+. This behavior is paralleled in the case of Na^+ vs. K^+ complexes with the next higher homologue, [2.2.1]. When $K^+ClO_4^-$ is added to a solution of [2.1.1], no effect is observed. Potassium, the largest of these three cations, is known to be excluded from the macrobicyclic cavity because the latter is too small to accommodate it.[10]

When $Na^+ClO_4^-$ is added to a $CDCl_3$ solution of [2.2.1], the chemical-shift changes for carbons 1–5 are 2.03, 3.16, 3.45, 4.15, and 3.04 ppm, respectively. These are similar to those for the $Li^+ClO_4^-\cdot$[2.2.1] complex, 2.12, 3.18, 2.59, 4.01, and 3.54 ppm, and are also all upfield. Chemical shifts for the K^+ complex are 1.39, 0.42, 2.11, −1.02, and 3.09 ppm. In both the $Na^+\cdot$[2.1.1] and $K^+\cdot$[2.2.1] complexes, C-4 is shifted downfield, whereas all other carbons are shifted upfield. In the free ligands, C-4 is the most upfield resonance and corresponds to the methylene α to nitrogen in the longest chain in each ligand. Both of these exceptional cases correspond to the complexes that Popov and co-workers[10] have identified as "exclusive", i.e., those complexes in which the cation is too large to be accommodated within the macrobicyclic cavity, but still interact with the ligand structure.

Table II. ^{13}C NMR Relaxation Times (in seconds) for the Cryptand [2.2.1] and Its Alkali-Metal Complexes in $MeOH/D_2O$ (90:10, v/v) at 36.0 ± 1.0 °C

cryptand position	free	Li^+	Na^+	K^+
1	0.77	2.22	1.15	1.11
2	0.82	2.01	1.11	1.00
3	0.76	1.96	0.99	1.02
4	0.74	2.06	1.17	1.07
5	0.71	1.94	1.17	n.a.[a]

[a] Not applicable.

Relaxation Time Studies. The C-13 relaxation times determined in $CDCl_3$ for [2.1.1], [2.2.1], and [2.2.2] with Li^+, Na^+, and K^+ perchlorates are summarized in Table I.

Upon complexation with lithium, the T_1 values of [2.1.1] remain essentially unchanged. On the other hand, formation of the $Li^+\cdot$[2.1.1] complex leads to a substantial increase in the individual T_1 values. Prior to our preliminary report of this work,[8] only Popov[3] and Lehn[11] and their co-workers had observed such relaxation time increases upon complexation. All previous work in this area reported substantial T_1 decreases upon complexation.[12] In contrast to the Li^+ complexes with [2.1.1] and [2.2.1], addition of Li^+ substantially diminishes [2.2.2]'s relaxation times.

Complexation of Na^+ by [2.1.1], [2.2.1], and [2.2.2] leads to a decrease, an increase, and an increase in relaxation times, respectively, all relative to the corresponding free ligands. The changes with K^+ are as follows: [2.2.1], relaxation times decrease and with [2.2.2], a slight increase is observed. No complex is formed between K^+ and [2.1.1] (no salt dissolves), and no spectral changes are observed. Similar results are observed in $MeOH/D_2O$, although the changes are often more pronounced, and these are summarized in Table II.

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Table III. ^{13}C NMR Relaxation Times (in sec) for Cryptands and Their Alkaline Earth Metal Complexes in $MeOH/D_2O$ (90:10, v/v) at 36.0 ± 1.0 °C

ligand	ion	relaxation time for position				
		1	2	3	4	5
[2.2.1]	none	0.77	0.82	0.76	0.74	0.71
[2.2.1]	Ca^{2+}	0.42	0.37	0.40	0.39	0.41
[2.2.2]	none	0.85	0.85	0.75	n.a.[a]	n.a.
[2.2.2]	Ca^{2+}	0.50	0.46	0.50	n.a.	n.a.
[2.2.2]	Ba^{2+}	0.40	0.40	0.41	n.a.	n.a.

[a] Not applicable.

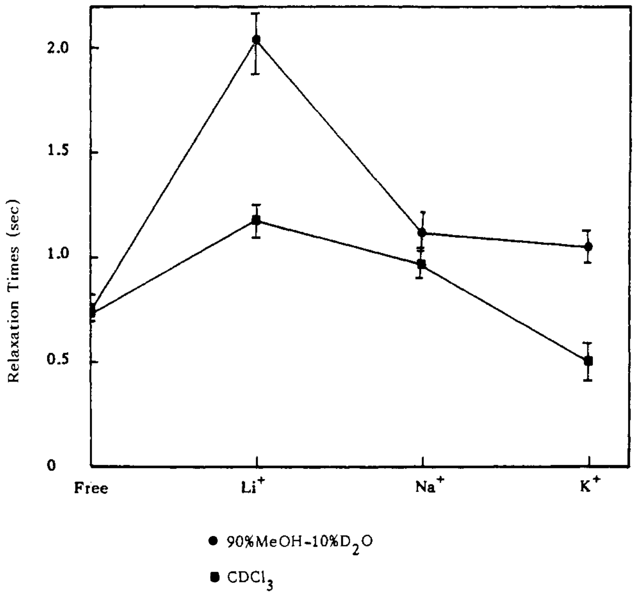

Figure 1. Solvent and cation dependence of ^{13}C NMR relaxation times in [2.2.1] cryptand.

Complexation of Ca^{2+} or Ba^{2+} by these three ligands differed from the results observed for the alkali metals. In all cases where dissolution of $M^{2+}(ClO_4^-)_2$ occurred, relaxation times decreased. These results are recorded in Table III.

Although a full set of comparative data between $CDCl_3$ and $MeOH/D_2O$ was desirable, many of the complexes we attempted to form proved quite insoluble. Similar solubility problems plagued our study of divalent cations, the results of which study are shown in Table III (see above). Only $Ca^{2+}\cdot[2.2.1]$, $Ca^{2+}\cdot[2.2.2]$, and $Ba^{2+}\cdot[2.2.2]$ are sufficiently soluble in $CDCl_3$ for these studies.

Relaxation times for [2.2.1] in either $CDCl_3$ or $MeOH/D_2O$ are almost identical. When [2.2.1] is complexed by Li^+, Na^+, or K^+, the relaxation times increase, decrease, or decrease even more, respectively, in either solvent system. These changes are graphed in Figure 1. Note that even though the T_1 values are identical in either solvent, the relaxation times are quite different when a cation is present. The complexes have much higher relaxation times in $MeOH/D_2O$ than in $CDCl_3$.

Discussion

Within experimental error (±10%), all ligands and their corresponding complexes exhibit isotropic motion in solution, as judged by the invariability of T_1 values for all carbon atoms in each sample. Since NOE values in all cases are at or very near the theoretical maximum, the average T_1 values of each sample can be used as an inverse measure of the single rotational correlation time governing molecular reorientation in solution, as described by eq 1.[13]

$$(T_1)^{-1} = n_H \gamma_H^2 \gamma_C^2 \hbar^2 r_{CH}^{-6} \tau_C \qquad (1)$$

The inverse correlation observed (Figure 1) between relaxation time and cation diameter cannot be rationalized on the basis of anion solvation effects alone. Since perchlorate anion solvation in aqueous methanol solution must be similar regardless of which monovalent cation is cryptated, the difference in relaxation times must relate to the specific cation–cryptand interactions in the complex formed. The larger the charge-to-size ratio of the cryptated monovalent cation, the stronger the interactions and the larger the ligand structural distortions will be. As the ligand is distorted (compressed), the overall molecular rotational axis size decreases, leading to a decrease of the correlation time. This explanation is strongly supported by results from X-ray crystallographic studies.[13] For example, the M^+–N and M^+–O distances in [2.2.2] for M = Na are 2.75 and 2.57 Å, respectively,[13a] and for M = K, these values are 2.87 and 2.78 Å.[13b] These values correlate very well with the relaxation time changes observed for these systems. Clearly, the greatest ligand compression occurs with those monovalent cations having the smallest sizes and highest charge densities.

Further proof of ligand compression is found in the observed chemical-shift changes upon complexation. When a strong complex is formed, the endo–endo conformation is favored over the endo–exo and exo–exo ones about the nitrogen lone pairs,[1a] as evidenced by the upfield shifts of the α carbons. This conformational change in turn results in an average decrease of the molecular diameter and a decrease of the correlation time.

On the basis of the known ionic radii of Ca^{2+} and Ba^{2+}, the cryptates formed should be of the "inclusive"[10] type. Following the arguments above, we expected that the complexes would exhibit longer relaxation times than the free ligand and that the Ca^{2+} complex of [2.2.2] would have correspondingly longer relaxation times than the Ba^{2+} complex. Instead, relaxation times were decreased for all complexes (see Table III). The anticipated difference between Ca^{2+} and Ba^{2+} is still apparent, but the values are nearly the same when experimental error (±10%) is considered.

The Ca^{2+} and Ba^{2+} complexes differ from those of the alkali metals in that they contain two charges rather than one. Consequently, solvation about a Ca^{2+} complex must be higher than about a corresponding Na^+ complex. This higher degree of interaction between the complex and the solvent causes the increased correlation time and the corresponding decrease in T_1s.

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