2.20 (1 H, s, NH), 3.10 (2 H, m), 3.85 (1 H, q, J = 5 Hz), 3.90 (3 H, s), 4.18 (1 H, broad singlet to triplet), 7.00-7.65 (4 H, m), 8.20 (1 H, s, NH). Mass spectrum: m/e (relative intensity) 258 (M^+, 72%), 257 (11), 254 (35), 243 (10), 199 (28), 197 (59), 182 (29), 169 (70).

Trans **12a**: mp 152.5-153.0 °C (CH_3OH): R_f = 0.65; IR (KBr) 3310, 3150, 2950, 1725, 1440, 1420, 1200, 730 cm^{-1}; NMR ($CDCl_3$) δ 0.98 (3 H, t, J = 6.0 Hz), 1.68 (2 H, q, J = 6 Hz), 2.28 (1 H, s, NH), 3.07 (2 H, m, C_4H), 3.73 (3 H, s, OCH_3), 4.00-4.10 (2 H, m, C_1H, C_3H), 7.20-7.50 (4 H, m), 8.00 (1 H, s, indole NH). Mass spectrum: m/e (relative intensity) 258 (M^+, 80%), 257 (20), 254 (10), 243 (34), 243 (34), 229 (100), 199 (50), 197 (54), 182 (39), 170 (56), 169 (80).

Preparation of *trans*-(3-(Methoxycarbonyl)-9-methyl-1,2,3,4-tetrahydro-9*H*-pyrido[3,4-*b*]indol-1-yl)(1-ethane) (12d). Propionaldehyde (1.25 g, 0.021 mol) and N_a-methyl tryptophan methyl ester **11c** (hydrochloride, 5.0 g, 0.019 mol) were heated to reflux in a methanol/water solution (150 mL, 75/25% v/v) in a manner analogous to the previous experiment. The solution was refluxed for 52 h and then worked up similarly to the procedure described immediately above to provide the *trans*-N_a-methyl-1-ethyl-tetrahydro-β-carboline (**12d**, 6 g). This material was purified by column chromatography (silica gel, benzene/methylene chloride, gradient elution) to give **12d** (4.40 g) in 87% yield; mp 77-78 °C (benzene). IR (KBr): 3360, 1745, 760 cm^{-1}. NMR ($CDCl_3$): δ 1.10 (3 H, t, J = 7 Hz), 1.70 (2 H, m), 2.20 (1 H, s), 2.95 (2 H, m), 3.50 (3 H, s), 3.85 (3 H, s), 3.60-3.80 (1 H, buried under singlets), 3.90 (1 H, s, braod singlet to triplet, C_1H), 6.80-7.50 (4 H, m). Mass spectrum: m/e (relative intensity) 272 (M^+).

***trans*-(3-(Methoxycarbonyl)-1,2,3,4-tetrahydro-9*H*-pyrido[3,4-*b*]indol-1-yl)formyl Diethyl Acetal (15b).** 2-Benzyl-(3-(methoxycarbonyl)-1,2,3,4-tetrahydro-9*H*-pyrido[3,4-*b*]indol-1-yl)formyl diethyl acetal (10 g, 0.024 mol) was dissolved in a solution of absolute ethanol (150 mL) and acetic acid (45 mL). The mixture was subjected to catalytic hydrogenation (52.3 psi) for 24 h over 10% Pd/C (2.0 g). The catalyst was filtered from the mixture, and the solvent was removed under reduced pressure. The residue was treated with ammonium hydroxide (14%) and extracted with chloroform. The chloroform layer was dried with Na_2SO_4 and evaporated under reduced pressure to provide a crystalline solid (8.2 g, 0.024 mol), mp 124-125 °C (TLC on silica with benzene, R_f = 0.69). This material was shown to be *trans*-(3-(methoxycarbonyl)-1,2,3,4-tetrahydro-9*H*-pyrido[3,4-*b*]-indol-1-yl)formyl diethyl acetal (**15b**). All spectral data were identical with the spectra obtained for the trans isomer previously isolated from the Pictet-Spengler reaction of tryptophan methyl ester and glyoxal diethyl acetal (lit.[12] mp 125 °C). In ref 12, a typing error led to the reversal of the cis and trans assignments which was corrected in the Erata for *J. Org. Chem.*, 1979; however, we mention it here for the sake of completeness. The base of mp 98 °C (R_f = 0.75) was the cis diastereomer while the β-carboline of mp 125 °C (R_f = 0.69) was the trans isomer.

Acknowledgment. This work was generously supported by a grant (No. HL 17897) from the National Heart, Lung and Blood Institute and facilities provided by a Biomedical Sciences Award to the University of Wisconsin—Milwaukee. We also wish to thank the Research Corp. for support of this work in its initial stages. A special thanks to Mr. Sandrin and Mr. S. Milosevich for the carbon spectra are in order.

Supplementary Material Available: Details of the X-ray crystal structure of *trans*-1-ethyl-3-(methoxycarbonyl)-1,2,3,4-tetrahydro-β-carboline (**12a**), tables of crystal and refinement data, atomic parameters, and structure factor amplitudes, and figures of the bond and torsion angles for **12a** and the crystal packing of the molecules of **12a** (20 pages). Ordering information is given on any current masthead page.

Natural-Abundance ^{15}N Nuclear Magnetic Resonance Spectroscopy of Coronands, Cryptands, and Some of Their Complexes with Diamagnetic Metal Ions[1]

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Abstract: Natural-abundance ^{15}N nuclear magnetic resonance spectra of nitrogen-containing crown ethers, cryptand ligands, and other ligands with pyridine-type nitrogens and their complexes with alkali, alkaline-earth, silver(I), and thallium(I) ions are reported. The complexation shifts tend to go downfield with increasing charge and increasing ionic character of the nitrogen-to-metal-ion bond but upfield with increasing polarizability of the ion. The downfield shifts are generally more pronounced if the ions fit tightly into the cyclic ligand. For those metal ions expected to form essentially covalent bonds to nitrogen, the complexation shifts are not easily predicted. Some of the thallium- and silver-cryptate complexes display sizable one-bond ^{15}N-metal couplings.

Introduction

Because complexation of metal ions with organic ligands is known to affect many of the NMR properties of the ligands such as chemical shifts, coupling constants, and relaxation times, many studies have been made of the thermodynamics, kinetics, and structural effects of complexation, using NMR techniques. The recent heightened interest in complexes of alkali and alkaline-earth metal ions with ethylenediaminetetracetic acid (EDTA) and its analogues,[3] naturally occurring complexones,[4] and especially crown ethers[5] and cryptands,[6] is the result of the demonstrated importance of alklai ion complexation in membrane-carrier processes.[4,6c] Proton and carbon-13 NMR studies have been made of complexing antibiotics,[4,7] chelate ligands,[8,9] crown ethers,[10] and

(1) Supported by the National Science Foundation and by the Public Health Service, Grant No. GM-11072 from the Division of General Medical Sciences.

(2) NATO Postdoctoral Fellow, 1976-1977.

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Table I. ^{15}N Chemical Shifts and Coupling Constants for Ligands and Their Dihydrochlorides

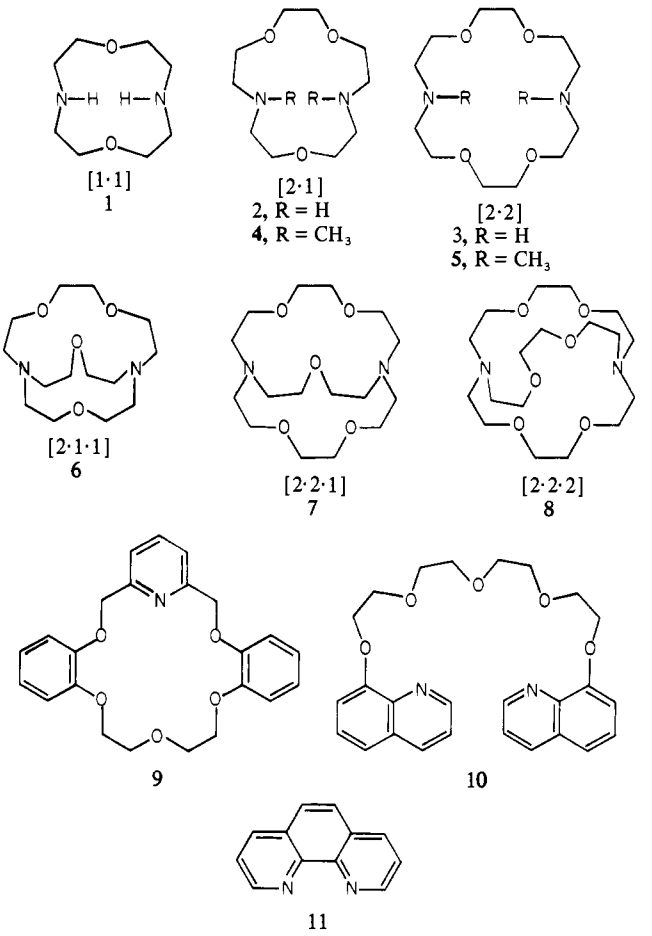
ligand	concn,[a] ^{15}N shift[b] CH_3OH	$CHCl_3$	coupling const,[c] Hz
1 [1·1]		0.7, 354.6	
2 [2·1]		0.8, 346.7	
dihydrochloride	0.9, 338.3	0.2, 344.7	
		0.5, 345.2	$^3J_{^{15}NH} = 3.3$[d]
3 [2·2]	0.4, 346.2		
4 N,N'-$(CH_3)_2$ [2·1]	0.6, 346.1	0.6, 346.8	
dihydrochloride	0.6, 336.1		
5 N,N'-$(CH_3)_2$ [2·2]	0.4, 345.2	0.4, 346.4	
dihydrochloride	0.4, 333.4		
6 [2·1·1]	0.2, 346.4	0.4, 347.9	
		1.5, 348.3	$^3J_{^{15}NH} = 3.6$
dihydrochloride	0.5, 338.6		$^1J_{^{15}NH} = 81.1$
7 [2·2·1]	0.2, 345.9	0.2, 346.8	
		0.7, 347.0	$^3J_{^{15}NH} = 3.3$
dihydrochloride	0.4, 337.4	0.2, 345.1	$^1J_{^{15}NH} = 83.5$
8 [2·2·2]	0.6, 345.4	0.3, 345.3	$^3J_{^{15}NH} = 3.1$[e]
dihydrochloride	0.3, 336.6		$^1J_{^{15}NH} = 80$

[a] Moles/liter. [b] In ppm, upfield from external 1 M $H^{15}NO_3$, corrected for bulk susceptibility. [c] Precision estimated to be ±0.3 Hz. [d] KSCN complex in $CHCl_3$, $^3J_{^{15}NH} = 3.5$ Hz. [e] $Sr(NO_3)_2$ complex in $CHCl_3$, $^3J_{^{15}NH} = 2.6$ Hz.

cryptands,[11] which are informative of changes taking place in the ligand properties as the result of complexation. Corresponding studies have been reported for a few of those metal ions such as ^{133}Cs,[12] ^{205}Tl,[13] and ^{23}Na,[14] which have suitable properties for NMR investigation, of changes taking place at the metal ions themselves.

In most cases, the protons and carbons of the ligands do not become directly bonded to the metal through complex formation and, consequently, the changes at these atoms are expected to be essentially second-order effects. For this reason, there is special interest in the possibility of studying metal–ligand complexing by NMR spectroscopy of the oxygen and nitrogen directly involved in binding to metal. The only suitable isotopes for this purpose are ^{17}O, ^{14}N, and ^{15}N, and, of these, only ^{15}N has spin $^1/_2$ and is therefore expected to be most useful.[15] Nonetheless, because of the low natural abundance and low magnetic moment of ^{15}N, relatively few uses of ^{15}N NMR for this purpose have been reported. Examples include measurements of the ^{15}N chemical shifts of coordinated ammonia,[16] glycine,[17] and molecular nitrogen[18] as well as ^{195}Pt–^{15}N couplings in complexes of platinum with amines[19] and azo compounds.[20] An investigation of ^{15}N-enriched EDTA and its complexes with a variety of closed-shell metal ions[9a] showed that complexation resulted only in small ^{15}N chemical-shift changes, and these were rationalized by assuming a near cancellation of paramagnetic and diamagnetic contributions to the nitrogen shieldings.

Chart I



The large complexing constants and unusual solubility properties of crown ether and cryptand complexes might be expected to show more pronounced ^{15}N shift effects because the complexes are highly associated, especially in nonpolar solvents. Moreover, for the rigid cryptands, the structures of the complexes are known[6,21] to have the potential ligand-binding sites and the metal ions held in close proximity to one another. Within limits, ligands with different cavity sizes can bind metal ions with different radii without much loss of stability and without major structural reorientation of the ligand. In consequence of these expectations, we have investigated the ^{15}N NMR spectra of some diamagnetic metal-ion complexes of the crown-type nitrogen ligands **1**–**5**[6c] and cryptands **6**–**8**[6] as well as **9**, **10**, and **11** which have aza-aromatic nitrogens.

Results and Discussion

The ^{15}N chemical shifts of the uncomplexed ligands and their dihydrochlorides are given in Table I. The shifts show small solvent and concentration dependences so that, in making close comparisons, similar concentrations in the same solvents should be used.[22] The sensitivity to ring size for progressions **1** → **3**, **4** → **5**, and **6** → **8** is not large; decreases in ring size cause upfield ^{15}N shifts—the largest difference being about 8 ppm between **1** and **2**.

Because the rings in compounds **1**–**8** are at least somewhat conformationally flexible, one might expect that dipropylamine (δ 334.3), methyldipropylamine (δ 337.6), and tripropylamine (δ 329.8) in methanol solution[23] would be reasonable model sub-

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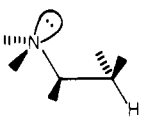
Table II. ^{15}N NMR Chemical Shifts of Metal-Salt Complexes

ligand/salt		log K_s[a]	concn,[a] ^{15}N shift[c] methanol	concn,[a] ^{15}N shift[c] chloroform
1 [1·1]	LiSCN			0.69, 355.3
2 [2·1]	LiSCN			0.86, 348.2
	NaSCN			0.72, 350.9
3 [2·2]	NaSCN			0.18, 347.5
	KSCN	2.0	0.31, 343.0	
	$Sr(NO_3)_2$		0.21, 340.8[d]	
	$Ba(SCN)_2$	6.7	0.22, 332.9[e]	
	$AgNO_3$	7.8[f]	0.34, 351.5	0.34, 349.7
	$TlNO_3$		0.22, 327.5[g]	
	$(CH_3)_3CNH_3Cl$			0.21, 342.0[h]
4 *N,N'*-$(CH_3)_2$ [2·1]	NaSCN			0.25, 353.7[i]
	$Ca(NO_3)_2$			0.55, 345.6[i]
5 *N,N'*-$(CH_3)_2$ [2·2]	NaSCN	3.26		0.20, 351.7[j]
	KSCN	4.38		0.20, 349.6[j]
	$Sr(NO_3)_2$		0.34, 346.1[k]	
	$Ba(SCN)_2$	6.67	0.32, 340.9	
	$AgNO_3$			0.41, 349.4
	$TlNO_3$		0.41, 335.0[g]	
6 [2·1·1]	LiCl	7.6		0.13, 353.7
	NaSCN	6.1		0.22, 353.2
	$Mg(SCN)_2$	4.0		0.22, 352.6
	$Ca(NO_3)_2$	4.34	0.76, 342.6	0.38, 342.2
7 [2·2·1]	NaSCN	8.8		0.66, 351.2
	KSCN	7.45	0.21, 346.2	0.21, 345.3
	$CaCl_2$	9.61		0.18, 342.5
	$Sr(NO_3)_2$	10.65		0.66, 341.2
	$Ba(SCN)_2$	6.3[f]		0.21, 336.1
	$AgNO_3$	10.6[f]		0.19, 347.1
8 [2·2·2]	NaSCN	7.21		0.16, 352.2
	KSCN	9.75		0.16, 345.0
	NH_4Cl			0.16, 340.4
	$Sr(NO_3)_2$	8.0[f]		0.44, 342.5
	$Ba(SCN)_2$	11.5	0.15, 336.1	0.15, 335.7
	$AgNO_3$	9.6[f]		0.16, 340.3
	$TlNO_3$	6.3[f]		0.16, 329.0

[a] Log of stability constant of complex in 96% methanol.[6c] [b] Moles/liter. [c] In ppm upfield from external 1 M nitric acid in D_2O corrected for bulk susceptibility. [d] 6% D_2O by volume. [e] 5% D_2O by volume. [f] Stability constant in water.[6c] [g] 30% D_2O by volume. [h] 5% CH_3OH by volume. [i] 6% CH_3OH by volume. [j] 25% CH_3OH by volume. [k] 25% D_2O by volume.

stances because δ-substituent effects are generally small.[23] However, substantial corrections are necessary for the effects of the oxygens in the ring. This follows from the ^{15}N shift of $CH_3OCH_2CH_2NH_2$, which is 9.4 ppm upfield from that of $CH_3CH_2CH_2CH_2NH_2$,[24] as well as the roughly 3-ppm upfield ^{13}C shift in hydrocarbons produced by replacement of a CH_2 by oxygen within a hydrocarbon chain[25] (which normally corresponds to about a 6-ppm ^{15}N shift[23,25]). On this basis, the upfield shifts of the ^{15}N nuclei of **3** (11.1 ppm), **5** (6.8 ppm), and **8** (14.8 ppm) in comparison with the models seem reasonable when one takes into account the higher strain in **8** and the possibility for forming N–H–O bridges in **5**. As with other saturated amines,[26] the differences in ^{15}N shifts between nonpolar solvents and methanol are small. It is well established that **8** complexes with metals through the in–in conformation of the nitrogens.[6,21] However, the conformation of the cryptand itself in solution is not known.[6,11] Proton NMR spectra of **8** at room temperature are in agreement with a time-averaged D_{3h} symmetry, but, at low temperature, a slowing of a conformational equilibrium has been observed with a $\Delta G^{\ddagger}$ of 4.4 kcal, which appears to involve interconversion of the conformations of the bridges without nitrogen inversion.[11]

In an attempt to learn more about the conformations of the bridges, we have measured the three-bond $^{15}N-C-C-^{1}H$ couplings for several cryptates, and these are listed in Table I along with some $^{1}J_{^{15}NH}$ coupling constants for their salts. The two-bond $^{15}N-C-^{1}H$ splittings were in all cases too small to be detected under our experimental conditions. Unfortunately, few data are available to check the values against.[15,27,28] If we assume that the two-bond and three-bond couplings calculated for methyl- and ethylamines also apply to **8**, these suggest that if **8** has the in–in conformation **12**, average D_{3h} symmetry, and an average N–C–



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C–H dihedral angle of about 120°, the $^{3}J_{^{15}NH}$ couplings should be about 3.5 Hz, while $^{2}J_{^{15}NH}$ should be very small. The experimental values of 3.1–3.6 Hz for $^{3}J_{^{15}NH}$ and ~0 for $^{2}J_{^{15}NH}$ agree rather well with the predicted values and indicate dominance of the in–in conformation. The out–out conformation should have smaller values of $^{3}J_{^{15}NH}$ and larger values of $^{2}J_{^{15}NH}$. The couplings do not change very much on complexation of **2** with potassium thiocyanate in chloroform or of **8** with strontium nitrate in chloroform, which suggests that complexation may not involve major conformational changes.

The dihydrochlorides of **6**, **7**, and **8** in methanol solution have rather large $^{1}J_{^{15}NH}$ couplings (80–83.5 Hz) compared to the usual

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Table III. ^{15}N NMR Shift Changes on Complexation of Ligands with Metal Cations[a]

ligand (cavity size)[b]	δ values for cation, ionic radius[b]									
	2 H^+	Li^+, 1.56	Na^+, 1.96	K^+, 2.66	Mg^{2+}, 1.56	Ca^{2+}, 2.12	Sr^{2+}, 2.54	Ba^{2+}, 2.86	Ag^+, 2.26	Tl^+, 2.98
1 [1·1] (1.2–1.5)		0.7								
2 [2·1] (1.5–2.2)	−8.5	1.5	**4.2**							
3 [2·2] (2.6–3.2)	−9.8		2.8	−3.2[c] −3.2[d]			−4.0	−11.8	+5.0[c] +5.3[d]	−17.2
4 *N,N'*-$(CH_3)_2$ [2·1] (1.5–2.2)	−10.8		**6.9**			−1.2				
5 *N,N'*-$(CH_3)_2$ [2·2] (2.6–3.2)	−18.0		5.2	3.1			−0.3	**−5.5**	3.3	−11.4
6 [2·1·1] (1.6)	−9.3	**5.7**	5.2		4.6	−5.7[c] −3.8[d]				
7 [2·2·1] (2.2)	−9.2		**4.5**	−1.5[c] −0.3[d]		−4.1	**−5.8**	−10.7	0.4	
8 [2·2·2] (2.8)	−8.7		7.1	−0.1			−2.8	−9.6[c] −9.3[d]	−4.8	−16.3

[a] In ppm, $\Delta\delta = \delta$(complex) − δ(ligand). Boldface values correspond to complexes with especially large stability constants (see Table II). [b] In A.[6] [c] $CHCl_3$. [d] CH_3OH.

73 Hz for ammonium nitrogens.[15,29] Because the NH^+ protons are expected to be inside the cage,[30] it is not surprising that the values be somewhat unusual. The ^{15}N chemical shifts of a number of metal–salt complexes of ligands **1–8** are given in Table II, and the changes in shift resulting from complexation and of protonation in Table III. Chloroform was the solvent of preference, but methanol or methanol containing some D_2O was used when necessary to obtain sufficient solubility. The complexation shifts which correspond to formation of complexes of highest stability are printed in boldface in Table III.

It is clear that complexation of ligands **1–8** with metal ions results in both upfield and downfield shifts of the ^{15}N resonances, although the protonation shifts are uniformly downfield. Alkali metal ions mainly produce upfield shifts, while alkaline-earth metal ions mainly produce downfield shifts. One interesting feature of the results is that the induced shift for M^+ minus the induced shift for M^{2+} for a given ligand is quite constant (8.1–10.9 ppm), even though the induced shifts for a given metal change substantially. Inspection of the shift changes of Table III, along with the cavity diameters and ion sizes contained therein, shows some reasonably consistent trends. Thus the complexation shifts tend to go downfield with increased charge and ionic character of the nitrogen–metal ion bond, but upfield with increasing polarizability of the ion. The downfield shifts are more pronounced if the ions fit tightly into the cyclic ligand.

In general, the pattern of induced ^{15}N shifts for **1–8** is similar to that found for complexation of some of the same ions with EDTA, where both upfield and downfield shifts were also observed.[9a] We expect that ^{15}N shifts will be a composite of diamagnetic and paramagnetic contributions. For saturated nitrogens as in ligands **1–8**, the second-order paramagnetic effect, which can be rationalized by mixing into the usual ground-state wave functions one or more excited-state wave functions, corresponds in a general way to that of $n \rightarrow \sigma^*$ transitions. Complexation of metal ions with nitrogen lone pairs would be expected to increase $n \rightarrow \sigma^*$ transition energies[31] and, on this account, produce upfield shifts. Clearly, a second-order paramagnetic effect based on this very simple approach can hardly be evoked to account for the results. Further evidence regarding its importance, operating in this particular way, can be seen from the data in Table IV for the shift changes produced by metal-ion complexing with **9**, **10**, and **11**. These ligands have pyridine-like nitrogens which show large hydrogen bonding and protonation shifts toward higher fields, in general accord with predictions of the simple second-order paramagnetic effect. Although the data are hardly extensive, the trends indicate that metal complexation with alkali metal ions

Table IV. ^{15}N Chemical Shifts of Pyridine-like Nitrogens on Complexation with Some Alkali-Metal Ions

ligand	metal salt	concn[a]	solvent	^{15}N shift[b]	Δδ[c]
9		0.19	$CHCl_3$	64.3	
9	KSCN	0.23	$(CH_3)_2SO$	67.2	2.8[d]
10		0.56	CH_3OH	84.6	
10	NaSCN	0.28	CH_3OH	88.3	3.7
10	$Ba(SCN)_2$	0.28	CH_3OH	89.1	4.5
10		0.27	$(CH_3)_2SO$	71.1	
11		0.86	$(CH_3)_2SO$	64.9	
11	LiSCN	0.86	$(CH_3)_2SO$	78.9	14.0
11	$HClO_4$	0.55	$(CH_3)_2SO$	130.1	65.2[e]

[a] Moles/liter. [b] In ppm upfield from 1 M $H^{15}NO_3$ in D_2O solution. [c] Shift of complex − shift of ligand. [d] The value of Δδ would be almost certainly larger if the ligand shift were taken in $(CH_3)_2SO$, in which it was insufficiently soluble. [e] Protonation shift.

produces at least as large, and often potentially larger, upfield shifts of pyridine-like nitrogens as does hydrogen bonding with methanol. These upfield shifts are, however, substantially smaller than 65–100-ppm changes associated with protonation of this type of nitrogen[32] and not much larger than the shift changes that alkali metal ions produce on complexation with saturated nitrogens (Table III).

The right-hand columns of Table III show the ^{15}N-shift changes caused by Ag^+ and Tl^+, metal ions expected to have a higher degree of covalent bonding to nitrogen than the alkali or alkaline-earth ions. The Tl^+-induced shifts are all downfield, with the secondary nitrogens of **3** being shifted the most and the tertiary nitrogens of **5** being shifted the least. The situation with Ag^+ is quite different, both diamagnetic and paramagnetic shift changes being found (Table III). One possible explanation has to do with the degree of bonding between silver ion and amines, secondary amines usually giving more stable complexes than tertiary amines.[33] The bicyclic Ag^+ and Tl^+ complexes dissociate sufficiently slowly to show ^{15}N–$^{107,109}Ag$ and ^{15}N–$^{203,205}Tl$ couplings (Table II). This is expected for the Tl^+ complex with **8** from proton NMR studies.[6,34,35] The reduced couplings $K = ({}^1J_{^{15}N\text{-}M})/(\gamma_{^{15}N}\gamma_M)$ in s rad^{-2} T^{-2} for Tl^+·**8**, Ag^+·**8**, and Ag^+·**7** are 850, 1300, and 950, respectively. These values are reasonably comparable to the corresponding values calculated for nitrogen–^{195}Pt couplings of 1420 for saturated nitrogens[13] and 2230 for double-bonded nitrogens[13] as well as with 515 for the nitrogen–

(29) T. Axenrod, "NMR of Nuclei Other Than Protons", T. Axenrod and G. A. Webb, Eds., Wiley, New York, 1974, p 81.
(30) This is most likely the case because the dihydrochloride of 1,7-diaza-4,10,15-trioxabicyclo[5.5.5]heptadecane ("[1.1.1]") also has both protons inside the cavity; J. Cheyney and J. M. Lehn, *J. Chem. Soc., Chem. Commun.*, 487–489 (1972).
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(33) "Gmelin Handbuch der Anorganischen Chemie", 8th ed., 61, Vol. 6, Springer-Verlag, Berlin, 1975, p 37.
(34) J. M. Lehn, J. P. Sauvage, and B. Dietrich, *J. Am. Chem. Soc.*, **92**, 2916–2918 (1970).
(35) For kinetics of complex formation, see also B. Tümmler, G. Maass, E. Weber, W. Wehner, and F. Vögtle, *J. Am. Chem. Soc.*, **99**, 4683–4690 (1977).

$^{111,113}Cd$ couplings in the cadmium ethylenediaminetetraacetic complex.[9a] It is interesting to note that in $Ag^+ \cdot 7$, the reduced coupling is smaller than that in $Ag^+ \cdot 8$, even though the nitrogens are much closer to Ag^+. This accords with the expected preferred linear sp complexation of Ag^+.

The complex between **8** and $TlNO_3$ showed a sharp doublet for its ^{15}N resonance at the boiling point in chloroform solution, which indicates that the rate of dissociation ($J = 356$ Hz) is much less than 10^3 s^{-1} under these conditions. In contrast, $Ag^+ \cdot 8$ in chloroform gives a 35–45 Hz broad line at 25 °C, which changes to a broad doublet at 10 °C. With the assumption that coalescence is at about 25 °C, $\Delta G^{\ddagger}$ of dissociation of this complex is on the order of 15 kcal.

Crown ethers and cryptands form complexes with ammonium ions,[36] and these offer the opportunity to investigate both the change in ^{15}N shift of the ligand and of the ammonium ion as the result of complexation. Interestingly, in each of the cases studied, both kinds of ^{15}N resonances move downfield. Thus, with **8** complexed with NH_4Cl in chloroform, the ligand–nitrogen resonance moves 4.7 ppm downfield relative to the ligand in chloroform, and the ammonium nitrogen resonances move downfield by 4.7 ppm relative to the ammonium nitrate in water. With **3** complexed with $(CH_3)_3CNH_3Cl$ in chloroform containing 5% methanol, the ligand resonances move 2.7 ppm downfield relative to the ligand in chloroform, and the $(CH_3)_3CNH_3$ nitrogen resonance is 5.7 ppm downfield of $(CH_3)_3CNH_3Cl$ in methanol. Downfield ^{15}N shifts of ammonium cations on transfer from a polar solvent such as methanol to a nonpolar solvent such as chloroform are well documented.[23] The downfield shift of the ligand, when complexed with ammonium ions, may be the result of an equilibrium transfer of a proton from ammonium ion to ligand.

The state of the anion in solutions of metal salt complexes in nonpolar solvents such as we have used is important with respect to understanding the chemistry of the complexes. Thiocyanates are useful in the preparation of the solutions of the complexes because "soft" anions with their smaller solvation energies generally enhance the solubility of the complexes in nonpolar solvents. The thiocyanate nitrogen provides a further ^{15}N probe which may have considerable utility in more detailed studies of metal salt complexes. Thiocyanate in water has a nitrogen resonance of about 171 ppm (^{14}N shift = 168 ppm[15]) which changes to 163.2 ppm in dry dimethyl sulfoxide. Addition of small amounts of water to the dry dimethyl sulfoxide solution causes a small upfield shift to 163.9 ppm. In chloroform, with metal thiocyanates complexed with **8**, the ^{15}N resonance of the thiocyanate is 161.7 ppm. However, with sodium thiocyanate complexed with **2** in chloroform, the thiocyanate nitrogen comes at 168 ppm, a value indicating a sizable interaction between the thiocyanate ion and complexed cation.

Experimental Section

Nitrogen-15 NMR spectra were taken with a Bruker WH-180 wide-bore spectrometer operating at 18.25 MHz, with the use of 15-mm tubes or 16–17-mL samples in 25-mm tubes. The reference was 95% ^{15}N-enriched nitric acid (1 M in D_2O or H_2O) contained in a concentric 5-mm capillary. Upfield shifts from the reference were given positive values. Bulk-susceptibility corrections[32] were calculated with a bulk-susceptibility constant of 0.715×10^{-6}, and the corrections for the samples were assumed to be the same as for the solvent. Solutions of three different complexes at 0.2 M in chloroform gave the same value for the bulk-susceptibility correction as chloroform itself when determined in coaxial cells by the NMR method.[32] For mixed solvents, corrections were calculated on the basis of the appropriate volume fractions. The corrections were −0.1 ppm for chloroform and +0.8 ppm for methanol. With respect to other commonly used ^{15}N resonance standards, 1 M nitric acid absorbs 6.2 ppm upfield from neat nitromethane and 298.7, 332.8, and 355.0 ppm downfield, respectively, from urea (2 M in H_2O), tetramethylammonium chloride (2 M in H_2O), and the ammonium resonance of ammonium nitrate (2 M in H_2O), without suceptibility corrections.

In taking the spectra, 20 μs (25 °C) pulses were usually used. The repetition rates were 1 s for secondary amines and amine hydrochlorides and 6 s for tertiary amines, with estimated T_1 values of 50–60 s. With 0.2 M solutions, satisfactory signal-to-noise ratios could be obtained with 1000–2000 scans. Because continuous broadband decoupling (usually 3–5 W) caused undesired heating of the complex and their hydrochloride samples, nitrogen gas cooled at 0 °C was run through the probe to keep the sample temperatures at 10–35 °C. The sweep widths were 7000–10 000 for shift determinations and 1000 for determination of coupling constants. The accuracy of the chemical shifts is estimated to be better than 0.2 ppm and that of the coupling constants about 0.3 Hz.

The cryptand ligands **1,10-diaza-4,7,13,16,21,24-hexaoxabicyclo[8.8.8]hexacosane (8)**, **1,10-diaza-4,7,13,16,21-pentaoxabicyclo[8.8.5]tricosane** (7), and **1,10-diaza-4,7,13,19-tetraoxabicyclo[8.5.5]eicosane (6)** were commercial samples (Merck, PCR) and were used without further purification. **7,16-Diaza-1,4,10,13-tetraoxacyclooctane (3)**, **7,13-diaza-1,4,10-trioxacyclopentadecane (2)**, and **4,10-diaza-1,7-dioxacyclodecane (1)** were prepared by cyclizing the sodium salts[37,38] of the corresponding ditosylamine[39] and ditosyl esters[40] in dry *N,N*-dimethylformamide[37,38] and reducing the resulting *N,N'*-ditosyldiaza crown ethers with lithium aluminum hydride in tetrahydrofuran.[41] The yields were 30–40% overall. The N,N'-dimethylated monocyclic ligands **7,16-dimethyl-7,16-diaza-1,4,10,13-tetraoxacyclooctadecane (5)** and **7,13-dimethyl-7,13-diaza-1,4,10-trioxacyclopentadecane (4)** were prepared from **3** and **2** in 90% yield with the aid of the Eschweiler–Clark methylation procedure for secondary amines.[42] The resulting dihydrochlorides were treated with a slight excess of tetramethylammonium hydroxide (25% aqueous solution), and the mixture was adsorbed on a short column of alumina (Woelm neutral, activity grade I) and eluted with chloroform. Solutions of the metal thiocyanate–ligand complexes were prepared by boiling the stoichometric amount of thiocyanate with chloroform solutions of the ligand and removal of the excess salt by filtration or, alternatively, by mixing solutions of the individual components in methanol followed by removal of the solvent, dissolution in chloroform, and removal of any insoluble material by filtration. Some of the complexes of the monocyclic ligands were not soluble in pure chloroform or pure methanol, and, for these, stoichometric amounts of salt and ligand were dissolved in solvents or solvent mixtures, as given in Tables II and IV. The dihydrochlorides of the ligands were prepared either by addition of a stoichometric amount of hydrogen chloride in methanol to the free amine, evaporation to dryness, and dissolution in methanol or by passing of dry hydrogen chloride into solutions of the complexes in methanol and filtration of the precipitated chloride salts, followed by successive dissolutions in methanol, filtration, and evaporation to dryness until the residual material was completely soluble in absolute methanol. The ligands could be recovered from these dihydrochlorides with tetramethylammonium hydroxide, by passing them through an alumina column and eluting with chloroform.

Pyridinodibenzo-18-crown[6][39] **(9)** and **1,13-bis(8-chinolyl)-1,4,7,10,13-pentaoxatridecane**[43] **(10)** were kindly supplied by Professor F. Vögtle. **1,10-Phenanthroline (11)** was a commercial product (Aldrich).

Acknowledgment. We thank Professor Dr. F. Vögtle and coworkers for samples of ligands and also Professor S. I. Chan for helpful discussions.

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