

Influence of pendant cyanoalkyl side-arms on the stabilities of metal ion complexes of monoaza- and diaza-18-crown-6 ethers in methanol

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Abstract

Pendant cyanomethyl and 2-cyanoethyl arms attached to the nitrogen atoms of aza-crown ligands can influence complex stabilities with metal ions in methanol in two distinct ways: by reducing the basicities of the ring nitrogen atoms, and by disrupting the solvation of the ligands and complexes. In Ag^+ complexes, and probably also in Zn^{2+} , Cd^{2+} and Pb^{2+} complexes, the dominant effect is the reduced nitrogen basicity, with a resulting net decrease in stability in the presence of the cyanoalkyl arms. The stability constants of the alkali metal ion complexes, however, are increased, with the main factor being the poorer solvation in methanol of the uncomplexed substituted macrocycles relative to the parent ligands, A18C6 and A₂18C6. For the alkaline-earth complexes, effects on free ligand solvation are overcompensated by a decreased solvation of the metal complexes; the side-arms prevent coordination of the complexed cations by methanol molecules, with a consequent reduction in complex stability. In no cases is there any evidence of direct interactions between the metal ions and the pendant cyanoalkyl arms.

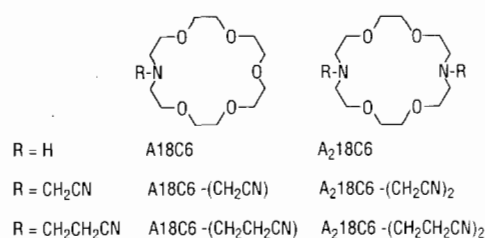
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Introduction

The ability of macrocyclic ligands, such as crown ethers, to form inclusion complexes with metal ions in solution is generally modified by the presence of pendant side-arms, whether or not they contain donor groups. Aza-crown ethers functionalized by the attachment of a coordinating side-arm at nitrogen show a stronger increase in the stability constants of their metal ion complexes than the corresponding C-functionalized crown ether complexes [1]. Several factors contribute to the change in the magnitude of the stability constant for a metal ion complex resulting from the presence of a pendant side-arm. The pendant arm may interact directly with the cation included within the ligand cavity, provided that the length and flexibility of the side-arm will allow this, or indirectly by changing the donor properties of the crown ether ring atoms. The latter

could result from an alteration of the conformational states of the macrocyclic ring either in the complexed or free (solvated) state, or from a polarization of the free electron pairs of the heteroatoms in the ring. Thus, for example, both the basicity and coordinating strength of ring nitrogen atoms are modified by electron-accepting or -donating substituents in pendant-arms attached to the nitrogen atoms [2]. In addition, intramolecular complexation of the side-arm by the macrocyclic ring of a ligand can influence the stabilities of metal ion complexes [3].

In this paper the effects of cyanoalkyl side-arms attached to the nitrogen atoms of monoaza- and diaza-crown ethers of the 18C6 type (Scheme 1) are discussed. The results of potentiometric, IR and ¹³C NMR studies show that the cyanoalkyl groups do not coordinate directly with the metal ions, but either act as electron-withdrawing substituents or change the interaction of



Scheme 1.

the parent crown ethers and their metal ion complexes with solvent molecules.

Experimental

Materials

Monoaza-18-crown-6 (A18C6; Aldrich) and 1,10-diaza-18-crown-6 (A₂18C6; Merck) were used as supplied without further purification. Alkali and alkaline-earth perchlorates, AgClO₄, TlClO₄, tetraethylammonium perchlorate (TEAP) were purified as previously described [4]. The alkali iodides were used as supplied for ¹³C NMR measurements. Methanol and propylene carbonate were of the highest purity available.

Potentiometric titrations

The stability constants, K (M⁻¹), for complexation of Ag⁺ with the various ligands were determined by pAg potentiometric titrations with two Ag/Ag⁺ electrodes, one in the reaction vessel and the other in the reference compartment. The stability constants of other metal ion complexes were determined by the disproportionation reaction of the metal with the Ag⁺ complex of the ligand under study. The detailed procedures have been described previously [4]. The concentrations of silver perchlorate and the ligand were around 10⁻⁴ and 10⁻³ M, respectively. The concentration of the metal salt was always higher than the ligand concentration, with the ratio of metal ion to ligand concentration increasing as the stability constant of the metal ion complex decreased.

In the organic solvents used, ion pair formation of the salts under study was negligible. This allowed titrations to be carried out in such a way that, at each step in the titration, the total salt concentrations in the reaction and reference vessels were identical. With this procedure, no activity coefficient corrections are necessary.

Determination of the composition of metal ion complexes

For the Ag⁺ complexes, the number of crown ether molecules per Ag⁺ was derived from the equivalence point of potentiometric titrations, and from the calculation of the stability constants using the mV readings

obtained. The composition of complexes of the other metal ions were determined from conductometric titrations at constant salt concentrations, and by ¹³C NMR titrations at constant total ligand concentration. Stability constants are required to be larger than 10³ M⁻¹ in order to utilize conductometric titrations. In the ¹³C NMR studies, the solubilities of the alkali metal iodides and alkaline-earth perchlorates in methanol were large enough such that sufficiently clear spectra could be obtained after about 3000 accumulations.

Determination of NMR spectra

¹H and ¹³C NMR spectra were run at 300 and 75.47 MHz, respectively, on a Bruker MSL 300 spectrometer. The ¹³C NMR spectra were obtained under ¹H-noise-decoupling conditions, and the chemical shifts of the ligand peaks were determined by using the central peak of the external C₆D₁₂ reference.

IR spectra of metal ion complex salts

Complexes were obtained as crystalline deposits from clear solutions of reactants. IR spectra were taken as nujol mulls on a Perkin-Elmer spectrometer.

Syntheses

The armed ligands 7-(cyanomethyl)-1,4,10,13,16-pentaoxa-7-azacyclooctadecane [A18C6-(CH₂CN)] and 7,16-bis(cyanomethyl)-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane [A₂18C6-(CH₂CN)₂] were prepared according to the procedure of Arnold *et al.* [5]. Changing the solvent from acetone to acetonitrile increases the yield slightly.

A18C6-CH₂CN: white crystals (85% yield); m.p. 46–47 °C. ¹H NMR (CDCl₃): δ (ppm) = 4.13 (s, 2H); 3.66–3.63 (m, 20H); 2.78 (t, 4H). ¹³C NMR (CDCl₃): δ (ppm) = 111.81 (s, 1C); 70.81 (s, 2C); 70.68 (s, 2C); 70.34 (s, 2C); 69.98 (s, 4C); 54.05 (s, 2C); 42.30 (s, 1C).

A₂18C6-(CH₂CN)₂: white solid (70% yield); m.p. 106.5 °C. ¹H NMR (CDCl₃): δ (ppm) = 3.98 (s, 4H); 3.60 (b, 16H); 2.78 (b, 8H). ¹³C NMR (CDCl₃): δ (ppm) = 116.17 (s, 2C); 70.12 (s, 4C); 69.59 (s, 4C); 54.31 (s, 4C); 42.17 (s, 2C).

The 2-cyanoethyl substituted aza-18-crown-6 ligands 7-(2-cyanoethyl)-1,4,10,13,16-pentaoxa-7-azacyclooctadecane [A18C6-(CH₂CH₂CN)] and 7,16-bis(2-cyanoethyl)-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane [A₂18C6-(CH₂CH₂CN)₂] were prepared following procedures published in the literature [6].

A18C6-(CH₂CH₂CN): viscous oil (98% yield). ¹H NMR (CDCl₃): δ (ppm) = 3.65 (b, 20H); 3–2.95 (t, 2H); 2.56 (t, 2H); 2.82 (b, 4H). ¹³C NMR (CDCl₃): δ (ppm) = 119.58 (s, 1C); 70.74 (s, 6C); 70.39 (s, 2C); 70.17 (s, 2C); 54.32 (s, 1C); 51.35 (s, 2C); 16.53 (s, 1C).

$A_218C6-(CH_2CH_2CN)_2$: viscous oil (98% yield). 1H NMR ($CDCl_3$): δ (ppm) = 3.61 (s, 16H); 2.94 (t, 4H); 2.83 (b, 8H); 2.49 (t, b, 4H). ^{13}C NMR ($CDCl_3$): δ (ppm) = 119.20 (s, 2C); 70.78 (s, 4C); 70.13 (s, 4C); 54.07 (s, 4C); 51.25 (s, 2C); 16.64 (s, 2C).

Results

Stability constants of Ag^+ complexes

Complex formation of Ag^+ with cyanoalkyl-substituted aza-crown ethers was studied in methanol (MeOH) and propylene carbonate (PC) (Table 1). The equivalence points of potentiometric pAg titrations and conductometric titrations showed that only 1:1 complexes are formed. A comparison of the $\log K$ values in Table 1 shows clearly that the ratio of the stability constants for a silver(I) complex in the two solvents, K_{PC}/K_{MeOH} , is about $10^{3.9}$ for each of the four functionalized ligands. These values, when combined with the free energy of transfer of Ag^+ from MeOH to PC, $\Delta G_{tr} = 12.2 \text{ kJ mol}^{-1}$ [9], can be used via a Born-Haber cycle [10] to calculate the difference, eqn. (1)

$$\Delta G_{tr}(AgL^+) - \Delta G_{tr}(L) = -2.303RT \log K_{PC}/K_{MeOH} + \Delta G_{tr}(Ag^+) \quad (1)$$

The results are $\Delta G_{tr}(AgL^+) - \Delta G_{tr}(L) = -10.1 \text{ kJ mol}^{-1}$ (mean value) for the four functionalized crown ethers and -0.9 (18C6), -15.0 (A18C6) and -20.9 (A_218C6) kJ mol^{-1} for the parent aza-crown ethers.

It is likely that in the aza-crown ligands the dominant interaction is between Ag^+ and the ligand nitrogen atoms, but some involvement of the ethoxy groups might be expected. In order to investigate the extent of the contribution of the ethoxy groups to the complex stabilities, complex formation between Ag^+ and simple tertiary amines, $(CH_3CH_2)_2NR$ with $R = C_2H_5$, CH_2CN and C_2H_4CN , has been studied in PC, Table 2. It may be noted that the replacement of one ethylene group in triethylamine by a cyanomethyl or a 2-cyanoethyl group produces a substantial decrease in the stability constant of the triethylamine complex.

Stability constants of monovalent metal ion complexes

The stability constants for complex formation between the cations Na^+ , K^+ , Rb^+ and Tl^+ , and the various

monoaza- and diaza-18C6 ligands in methanol are collected in Table 3. The selectivities of the parent and *N*-cyanoalkyl-substituted ligands for K^+ over Na^+ and Rb^+ are almost the same. However, the cyanoalkyl groups produce an increase in the stability constants of the complexes. The increase in $\log K$ is approximately constant at around 0.8 for monoaza-18C6 in the presence of either the cyanomethyl or 2-cyanoethyl groups, while that for the corresponding diaza-crowns is larger but somewhat less uniform. The stability constants of the potassium complexes were also determined in PC (Table 4), in order to check whether these effects might be due to specific solvent effects in methanol. In contrast to the behaviour in methanol, it was found that the stability constants of the parent and substituted aza-crowns in PC are almost equal.

Stability constants of divalent metal ion complexes

The stability constants of the alkaline-earth cation complexes in methanol are presented in Table 5, and two features are immediately apparent. The first is that the complexes of Sr^{2+} and Ba^{2+} are of almost equal stability for each of the six ligands and are always much more stable than the corresponding Ca^{2+} complexes. The second is that stability constants with both A18C6 and A_218C6 are decreased by the presence of a cyanoalkyl arm, with the effect being almost twice as large for $A_218C6-R_2$ as for A18C6-R ($R = CH_2CN$, CH_2CH_2CN) (Table 5). Complexes of the heavy metal ions Zn^{2+} , Cd^{2+} and Pb^{2+} also generally experience a decrease in $\log K$ through the influence of the cyanoalkyl groups (Table 6).

^{13}C NMR shifts of the ligands and complexes

The chemical shifts of the ^{13}C NMR lines of the CN group and of the methylene carbon atoms in CH_2CN are effectively identical for monoaza- and diaza-crown ethers (Table 7). It is, therefore, unfortunately not possible to derive any information on the influence of the cyanoalkyl side-arms on the conformational states of the uncomplexed macrocycles from the ^{13}C NMR spectra of the ligands in CD_3OD . An analogous lack of variation is also observed for the methylene shifts of CH_2CH_2CN . The chemical shifts of the OCH_2 carbon atoms show only negligibly small changes for the three diaza-crowns, but the situation is a little more complex for the less symmetrical monoaza-crowns as the number

TABLE 1. Stability constants ($\log K$) of 1:1 silver(I)-ligand complexes in methanol and in propylene carbonate at 25.0 °C

	18C6	A18C6	A18C6-(CH_2CN)	A18C6-($CH_2CH_2CN_2$)	A_218C6	$A_218C6-(CH_2CN)_2$	$A_218C6-(CH_2CH_2CN)_2$
MeOH	4.05 ^a	6.03 ^b	5.12 ± 0.07	5.84 ± 0.02	9.99 ^a	6.64 ± 0.08	7.75 ± 0.04
PC	6.86 ^a	10.31 ^b	8.94 ± 0.15	9.50 ± 0.01	15.57 ^a	10.55 ± 0.01	11.90 ± 0.04

^aRef. 7. ^bRef. 8.

TABLE 2. Stability constants ($\log K$)^a of Ag⁺ complexes with tertiary amines in PC at 25 °C

	Ligand		
	(C ₂ H ₅) ₃ N	(C ₂ H ₅) ₂ NCH ₂ CN	(C ₂ H ₅) ₂ NCH ₂ CH ₂ CN
$\log K_1$	7.83 ± 0.11	6.38 ± 0.01	4.38 ± 0.07
$\log K_2$	3.00 ± 0.05	5.97 ± 0.01	

^a K_1 refers to Ag⁺ + L = AgL⁺ and K_2 to AgL⁺ + L = AgL₂⁺.

of OCH₂ lines increases from three to five in the presence of the CH₂CN side-arm.

The ¹³C NMR lines exhibit both upfield and downfield shifts upon complexation. The induced chemical shift of the CN carbon atom depends upon the number of carbon atoms separating the ring nitrogen atom and the nitrile group. The CN carbon atom is shifted to higher fields in all complexes containing a cyanomethyl side-arm, but in complexes with a cyanoethyl substituent the CN carbon shifts are as likely to be positive as well as negative and they are generally of smaller magnitude than those of the cyanomethyl complexes. This is illustrated by the results in Table 8, which also show that there is no apparent simple relationship between the variations in shift and the charge, size, or chemical properties of the metal ion studied. The complexation induced chemical shift differences of the CH₂ carbon atoms in the cyanoalkyl side-arms are almost always negative and larger than the corresponding shifts of the CN carbon atom. These high-field shifts of the metal ion complexes generally show an irregular dependence upon ionic size, although there seems to be a tendency among the alkaline-earth complexes for a greater high-field shift for larger metal ions (Table 9). There are no obvious trends among the OCH₂ complexation shifts and any detailed discussion of the results is complicated by the large number of resonance lines.

Discussion

The ability of macro-monocyclic ligands to bind metal ions does not depend only on the effective cavity size

of the ligand and the number and species of donor atoms in the macromolecular ring; it is very sensitive also to the presence and mode of action of peripheral substituents. There are different mechanisms by which these pendant side-arms can alter the stabilities of complexes of the parent macrocycles. One obvious way is through the direct interaction of donor groups of the side-arms with a metal ion in the ring cavity. This has been observed frequently in the X-ray crystal structures of solid complex salts [15], and it is highly likely that in favourable cases similar interactions are responsible for changes in the stabilities of metal complexes in solution. It is equally clear that electron-donating or -accepting groups in a side-arm will modify the electron distribution of the ring atom bearing the pendant arm and thereby affect complex stabilities. In addition to the above, it will be shown that a side-arm strongly influences the interaction of crown ethers and their metal complexes with solvent molecules.

The present study was undertaken to investigate the influence of cyanoalkyl side-arms on the stability of metal ion complexes with the crown ethers monoaza-18-crown-6 (A18C6) and diaza-18-crown-6 (A₂18C6). The cyanoalkyl groups are attached to the ring nitrogen atoms and can only have an indirect influence on the stability of the parent crown ether complexes. In the case of the alkali metal cations, there is in any case little tendency for the cations to interact strongly with the nitrile group. This can be seen from a comparison of the solvation energies of metal ions in methanol and acetonitrile (AN), the latter being chosen as representative of the cyanoalkyl groups. Negative free energies of transfer of metal ions from methanol to acetonitrile are rare and even then generally small in magnitude [9]: K⁺, -1.5 kJ mol⁻¹; Rb⁺, -3.3 kJ mol⁻¹. An exception is the silver cation, which has a sufficiently negative free energy of transfer, estimated at -28 kJ mol⁻¹ [9], to indicate the possibility of strong interactions between the cyano group and Ag⁺. However, silver has a marked tendency to form strong, partly covalent, and centrosymmetrical bonds with two nitrogen atoms, and in A₂18C6 this is fully satisfied by bonding with the two amine nitrogens. Furthermore, in 2-cyanoethyl-substituted A18C6 an appropriate arrangement of amine and cyano nitrogen atoms is pre-

TABLE 3. Stability constants ($\log K$) of 1:1 metal ion (M⁺)-ligand complexes in methanol at 25 °C

	18C6	A18C6	A18C6-(CH ₂ CN)	A18C6-(CH ₂ CH ₂ CN)	A ₂ 18C6	A ₂ 18C6-(CH ₂ CN) ₂	A ₂ 18C6-(CH ₂ CH ₂ CN) ₂
Na ⁺	4.32 ^a	2.43 ^b	3.12 ± 0.10	3.36 ± 0.05	1.0 ^d	2.62 ± 0.15; 2.69 ^e	2.95 ± 0.09
K ⁺	6.29 ^a	4.18 ^b	4.76 ± 0.09	4.66 ± 0.07	1.8 ^e	3.98 ± 0.07; 3.91 ^e	3.68 ± 0.11
Rb ⁺	5.82 ^a	3.11 ^c	4.02 ± 0.06	4.07 ± 0.05	1.2 ^f	3.29 ± 0.10	3.03 ± 0.09
Tl ⁺	5.34 ^a	4.15 ^c	4.50 ± 0.07	4.74 ± 0.05	3.54 ^d	4.52 ± 0.05	4.09 ± 0.09

^aRef. 7. ^bRef. 11. ^cRef. 8. ^dRef. 12. ^eRef. 13. ^fRef. 14. ^gRef. 5.

TABLE 4. Stability constants (log *K*) of K⁺ complexes in PC at 25 °C

	Ligand						
	18C6	Λ18C6	Λ18C6-(CH ₂ CN)	Λ18C6-(CH ₂ CH ₂ CN)	A ₂ 18C6	A ₂ 18C6-(CH ₂ CN) ₂	A ₂ 18C6-(CH ₂ CH ₂ CN) ₂
log <i>K</i>	6.14 ^a	5.39 ^b	5.33 ± 0.19	5.30 ± 0.07	4.43 ^a ; 4.32 ^b	4.60 ± 0.02	4.92 ± 0.01

^aRef. 7. ^bRef. 8.TABLE 5. Stability constants (log *K*) of 1:1 alkaline-earth metal complexes in methanol at 25 °C

	Ligand						
	18C6	Λ18C6	Λ18C6-(CH ₂ CN)	Λ18C6-(CH ₂ CH ₂ CN)	A ₂ 18C6	A ₂ 18C6-(CH ₂ CN) ₂	A ₂ 18C6-(CH ₂ CH ₂ CN) ₂
Ca ²⁺	3.87 ^a	3.81 ^b	2.87 ± 0.10	2.62 ± 0.09	3.87 ^a	2.78 ± 0.15	3.03 ± 0.16
Sr ²⁺	5.64 ^a	5.94 ^b	4.50 ± 0.06	4.95 ± 0.04	5.99 ^a	3.62 ± 0.09	3.86 ± 0.06
Ba ²⁺	7.31 ^a	5.90 ^b	4.91 ± 0.08	5.23 ± 0.06	6.12 ^a	3.53 ± 0.07	3.96 ± 0.03

^aRef. 7. ^bRef. 8.TABLE 6. Stability constants (log *K*) of 1:1 complexes of Zn²⁺, Cd²⁺ and Pb²⁺ in methanol at 25 °C

	Ligand					
	18C6	Λ18C6-(CH ₂ CN)	Λ18C6-(CH ₂ CH ₂ CN)	A ₂ 18C6	A ₂ 18C6-(CH ₂ CN) ₂	A ₂ 18C6-(CH ₂ CH ₂ CN) ₂
Zn ²⁺	2.22 ^a	2.22 ± 0.11	2.45 ± 0.10	4.84 ^a	2.53 ± 0.29	2.05 ± 0.13
Cd ²⁺	2 ^a			5.25 ^a	6.67 ± 0.09	6.74 ± 0.11
Pb ²⁺	7.7 ^a	6.12 ± 0.03	6.74 ± 0.07	9.48 ^a	6.00 ± 0.05	6.97 ± 0.07

^aRef. 7.TABLE 7. ¹³C NMR chemical shifts (ppm) of crown ether ligands in CD₃OD; external reference C₆D₁₂

	CN	OCH ₂	NCH ₂	CH ₂ (CH ₂)CN
A ₂ 18C6			44.06	23.38
A ₂ 18C6-(CH ₂ CN) ₂	90.66		44.04	28.28
A ₂ 18C6-(CH ₂ CH ₂ CN) ₂	94.16		44.57	28.51
Λ18C6		45.06	44.89	23.30
Λ18C6-(CH ₂ CN)	91.04	45.30	44.57	28.66
Λ18C6-(CH ₂ CH ₂ CN)	94.43		44.84	28.76
				25.65
				16.54
				-9.66
				16.55
				-9.79

TABLE 8. ¹³C NMR: changes in ¹³CN chemical shifts (ppm) caused by complex formation

Salt	Λ18C6-(CH ₂ CN)	Λ18C6-(CH ₂ CH ₂ CN)	A ₂ 18C6-(CH ₂ CN) ₂	A ₂ 18C6-(CH ₂ CH ₂ CN) ₂
NaI	-2.30	0.47	-1.46	0.91
KI	-2.72	0.48	-2.01	0.92
RbI	-2.65	0.21	-1.69	0.56
TiClO ₄	-2.77	0.24	-1.83	0.67
Ca(ClO ₄) ₂	-3.00	-0.49	-1.87	-0.05
Sr(ClO ₄) ₂	-3.38	-0.52	-2.73	-0.10
Ba(ClO ₄) ₂	+2.56	-0.28		-0.27

vented for steric reasons. Therefore, in the silver ion complexes also there is little chance of the cyano group coming into direct contact with the aza-crown complexed metal ion.

Prior to this study, only a small amount of information on aza-macrocycles with cyanomethyl and 2-cyanoethyl side-arms was available. The ligands have been synthesized sporadically [5, 6, 16], but stability constants

TABLE 9. Changes in $^{13}\text{CH}_2$ and $^{13}\text{CH}_2\text{CN}$ chemical shifts (ppm) caused by complex formation

Salt	A18C6-(CH_2CN)	A18C6-($\text{CH}_2\text{CH}_2\text{CN}$)	A ₂ 18C6-(CH_2CN) ₂	A ₂ 18C6-($\text{CH}_2\text{CH}_2\text{CN}$) ₂
NaI	-2.14		-1.66	-2.16
KI	-4.24	4.65	-3.14	-3.22
RbI	-3.48		-2.29	-2.37
AgNO ₃		-0.62	0.13	1.21
TiClO ₄	-4.38	-5.24	-3.85	
Ca(ClO ₄) ₂	0.07		-5.98	
Sr(ClO ₄) ₂	-1.06		-0.24	-2.64
Ba(ClO ₄) ₂	-4.11	-7.93	-7.09	-2.66

of metal ion complexes have been reported only once. Arnold *et al.* [5] showed that for Na^+ and K^+ complexes of A₂18C6, cyanomethyl side-arms alter the stability constants by one power of ten by comparison with the isosteric propargyl side-arms.

Ag⁺ complexes

The results in Table 1 show that the addition of a cyanomethyl group reduces the stability constants of the Ag⁺ complexes with A18C6 and A₂18C6 by 0.9 and 3.4 units in log *K*, respectively while the corresponding reductions for the 2-cyanoethyl group are noticeably smaller, at 0.2 and 2.2 units, respectively. The larger destabilizing effect of the cyanomethyl group compared with that of the 2-cyanoethyl group demonstrates convincingly that there is no direct interaction between the cyano group and the silver ion. Rather, the results point to an explanation in terms of the electron-withdrawing properties of the cyanoalkyl groups reducing the electron-pair donorities of the ring nitrogens to which the side-arms are attached. The resulting change in the basicities of these nitrogens has already been demonstrated experimentally for 2-cyanoethyl-substituted tetraazacyclotetradecane [17]. Thus, the $\text{p}K_{\text{a}}=9.34$ for the mono-protonated parent ligand is reduced to $\text{p}K_{\text{a}}=7.0$ for the tetracyanoethyl-cyclam.

Supporting evidence for a reduced binding strength of the ring nitrogen atoms towards Ag⁺, arising from a negative induction effect of the cyano group, was sought from the stability constants of Ag⁺ complexes with related simple amine complexes in PC (Table 2). The Ag⁺ complex of triethylamine (TEA) is somewhat less stable than that of A18C6, despite the stronger basicity of TEA, $\text{p}K_{\text{a}}=10.75$ [18] compared with $\text{p}K_{\text{a}}=9.25$ [19] for A18C6. The replacement of an ethyl group in TEA by a cyanomethyl and a 2-cyanoethyl group does indeed lead to a reduction in complex stability; the decrease is, however, larger for the 2-cyanoethyl substituent. The influence of the cyanoalkyl groups cannot, therefore, be ascribed to a simple distance-dependent inductive effect. The differing responses of the complexes of the aza-crowns and simple

amine ligands to cyanoalkyl substituents suggests that a combination of an inductive effect and an interplay of the substituent and the crown ether ring are required to explain the reduced stabilities of the cyanoalkyl aza-crown complexes with the silver ion.

An additional factor to be considered is specific solvation interactions between methanol and the ligands and complexes, and in order to gauge their importance, the stability constants of the silver ion complexes in question were also determined in PC (Table 4). A graphical representation of the log *K* values in PC and MeOH for the cyanoalkyl-substituted aza-crown ethers (Fig. 1) shows a linear correlation with a slope of one. This effectively excludes any strong, specific hydrogen-bonding interaction of the cyanoalkyl aza-crown or their complexes in methanol. This argument is supported by

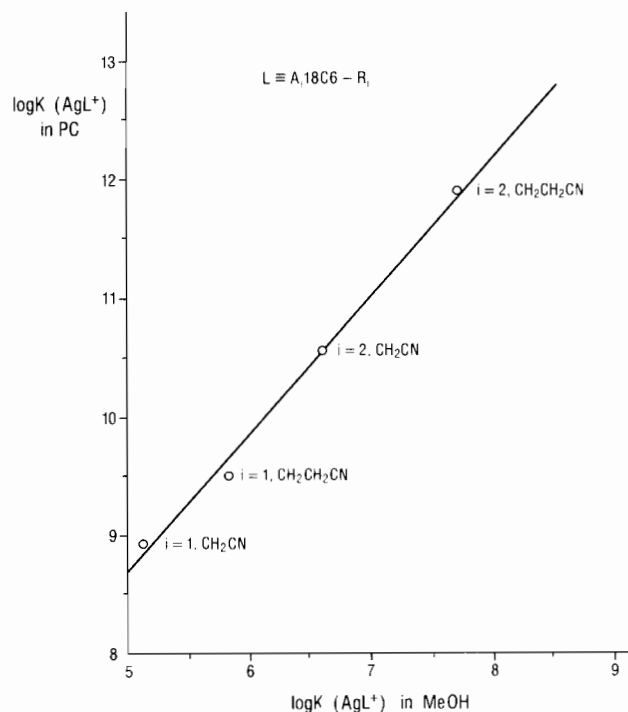


Fig. 1. Stability constants (log *K*) of silver ion complexes in methanol (MeOH) and in propylene carbonate (PC) plotted against each other.

the differences in free energies of transfer of the free and silver ion-complexed ligands (eqn. (1)), $\Delta G_{tr}(\text{AgL}^+; \text{MeOH} \rightarrow \text{PC}) - \Delta G_{tr}(\text{L}; \text{MeOH} \rightarrow \text{PC})$, which are almost constant at around -9.8 kJ mol^{-1} , Table 10. The parent macrocycles, A18C6 and A₂18C6, however, behave quite differently: their corresponding differences in free energies of transfer (eqn. (1)) are more negative by $\approx 8 \text{ kJ mol}^{-1}$ per nitrogen atom, and their $\log K$ values in MeOH and PC fall substantially above the line connecting the cyanoalkyl aza-crown results in Fig. 1. These shifts point to a stronger solvation of A18C6 and A₂18C6 in MeOH than in PC, presumably due to hydrogen bonding between methanol molecules and the secondary nitrogen atoms of the aza-macrocycles. The result is a reduction of the stability constants of the silver macrocycles in methanol.

Similar effects of specific interactions between methanol and the amine nitrogen atoms of A18C6 and A₂18C6 are to be expected for the complexes of K⁺, the alkali ion most similar in ionic size to Ag⁺. The $\log K$ values are illustrated in Fig. 2, and a notable feature is the increase in methanol of $\log K$ by one to two units on attachment of the cyanoalkyl side-arms to nitrogen, independent of the chain length (Fig. 2(a)). No such discrimination is observed in PC (Fig. 2(b)), where specific solute-solvent interactions are unlikely to be of importance. The results in Fig. 2 also highlight the much greater sensitivity of the Ag⁺ complexes to cyanoalkyl substitution, compared to K⁺, and emphasizes the difference in the coordination of Ag⁺ and K⁺. Although both sets of complexes are influenced by specific solvation in methanol, only the silver complexes show clear evidence of the inductive effect of the cyano group.

Alkali metal and thallium ion complexes

It has been shown above that the cyanoalkyl side-arms increase the stability constants of the potassium

complexes in methanol, and similar effects are also observed for the alkali metal cations Na⁺ and Rb⁺, and also for Tl⁺ (Table 3). Among the alkali metal cations, K⁺ forms the most stable complexes in all cases, as shown by the plots of $\log K$ values against ionic radii in Fig. 3. This demonstrates clearly that K⁺ fits optimally into the cavities of the ligands without inducing excessive strain, and the selectivity of K⁺ over Na⁺ and Rb⁺ is identical for 18C6, and the monoaza- and diaza-crown ethers, whether or not they contain cyanoalkyl side-arms.

It is apparent from the results in Table 3 and Fig. 3 that the replacement of a ring atom by a secondary nitrogen atom reduces the stability constants of the alkali metal complexes by two orders of magnitude – this is true for both the change from 18C6 to A18C6 and from A18C6 to A₂18C6. The exchange of the donor atoms leaves the tetrahedral arrangements of bonds and electron lone pairs unaffected [20], and while the difference in van der Waals volumes of ether oxygen and amine nitrogen [21] leads to a small reduction in ring size, this would have only a trivial effect on the stability constants for ions with the radii of the alkali metal cations. Therefore, the vertical displacement for complexes of the various ligands in Fig. 3, and the difference between the alkali metal and silver ion complexes, are probably best explained in terms of the HSAB principle [22]. The alkali metal cations, which are hard Lewis acids, prefer to interact with the ether oxygen atoms, which are hard Lewis bases, whereas the soft Lewis acid, Ag⁺, forms strong, partly covalent bonds with weak Lewis bases, such as amines.

The results in Fig. 3 also illustrate clearly the increase in stability of the alkali metal aza-crown complexes in the presence of the cyanoalkyl side-arms. The effect is essentially additive in $\log K$, as it is approximately twice as large for A₂18C6 as for A18C6. As discussed

TABLE 10. Free energies of transfer from methanol to propylenecarbonate

Ligand	Ag ⁺	Na ⁺	K ⁺	Rb ⁺	Tl ⁺
	$\Delta G_{tr}(\text{M}^+) \text{ (kJ mol}^{-1}\text{)}$				
	12.2	6.4	-4.3	-10.6	5.9
	$\{\Delta G_{tr}(\text{ML}^+) - \Delta G_{tr}(\text{L})\} \text{ (kJ mol}^{-1}\text{)}$				
18C6 ^a	-3.8	1.1	-3.4	-7.7	-4.3
A18C6	-12.2	-7.8	-11.2	-20.5	
		-9.7			
A ₂ 18C6	-19.6	-13.2	-19.3	-19.7	-14.1
A18C6-(CH ₂ CN)	-9.6		-7.6		
A18C6-(CH ₂ CH ₂ CN)	-8.7		-8.0		
A ₂ 18C6-(CH ₂ CN) ₂	-10.1		-7.8		
A ₂ 18C6-(CH ₂ CH ₂ CN) ₂	-11.5		-11.4		

^a $\log K^{\text{PC}} = 5.25 \text{ (Na}^+); 5.32 \text{ (Rb}^+); 7.13 \text{ (Tl}^+)$.

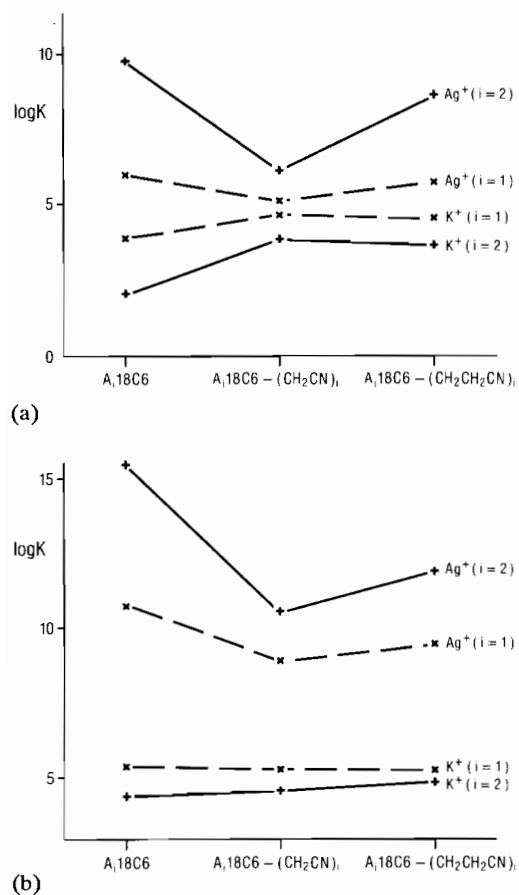


Fig. 2. Stability constants of Ag⁺ and K⁺ complexes in methanol (a) and in propylenecarbonate (b).

above, it is attributable primarily to the disruption by the cyanoalkyl side-arms of the solvation by methanol of the uncomplexed ligands. The increase of one unit in log *K* per cyanoalkyl substitution corresponds to a difference in ligand solvation of 5 kJ mol⁻¹, assuming that the interactions of the complexes with methanol are independent of cyanoalkyl substitution. This assumption that only A₁18C6 and A₂18C6 experience specific solvation in methanol is further strengthened by the observation (Table 10) that for the substituted aza-crowns the differences in free energies of transfer for the K⁺ complexes and the free ligands from MeOH to PC is constant at 8.7 ± 1.8 kJ mol⁻¹. An alternative explanation of this constant value in terms of an accidental compensation of changes in specific complex and ligand solvation is very unlikely. It may be noted also from the results in Table 10 that the transfer free energy differences for K⁺ and Ag⁺ complexes are very similar, despite the different types of coordination bonds formed by Ag⁺ and K⁺; the complexes, therefore, have strongly shielded metal cations and behave like organic cations.

The thallos ion, whose ionic radius is similar to that of Rb⁺, behaves like an alkali metal cation. The stability constant of its 18C6 complex is close to that of Rb⁺ (Table 3) and, like the alkali metal cations, forms weaker complexes in methanol with both 15C5 (log *K* = 3.31) [23] and 21C7 (log *K* = 4.55) [23]. The stability constants decrease in the sequence 18C6 > A₁18C6 > A₂18C6, and the cyanoalkyl side-arms shift log *K* to higher values. The increase, though, is somewhat less than for the alkali metal complexes.

Alkaline-earth ion complexes

The complex formation of alkaline-earth ions with 18C6, A₁18C6 and A₂18C6 in methanol is entirely different from that of the alkali metal cations. The stability constants of 18C6 complexes increase uniformly with increasing ionic radius (Fig. 4), consistent with Ba²⁺ being of optimum size for complexation with 18C6. The replacement of an ether oxygen by an amine nitrogen has quite different consequences for the three cations: the stability constants for Ca²⁺ is almost unaffected, that for Sr²⁺ increases a little, while that for Ba²⁺ decreases by one order of magnitude. The net result is a levelling off of the stability constants for the Sr²⁺ and Ba²⁺ complexes. Remarkably, there is virtually no further change on replacing a second oxygen to form the diaza-crown. It seems that, in contrast to the alkali metal cations, for which the changes are independent of cation size and additive for the nitrogens, the different van der Waals radii of oxygen (1.38 Å) and of nitrogen (1.5 Å) [21], and the smaller dipole moment of a secondary amine group compared with that of an ether-oxygen group [24], do influence strongly the stabilities of the alkaline-earth complexes. However, the ring size of 18C6 must also play a significant role, because the stability constants of the Ca²⁺, Sr²⁺ and Ba²⁺ complexes with 12C4, 15C5, 21C7 and related diaza-crown ethers [7], are all lower than those with 18C6, A₁18C6 and A₂18C6. Such behaviour is in accord with the relative sizes of the cations and ligand cavities for the Sr²⁺ and Ba²⁺ cations, but not for the smaller Ca²⁺.

A further distinction between the alkaline-earth and alkali metal complexes is to be found in their response to cyanoalkyl substitution in the aza-crown ligands. Namely, the stabilities of the alkaline-earth cyanoalkyl-substituted complexes are lower than those of the parent aza-crowns. On the basis of the earlier discussion, this implies that the presence of the cyanoalkyl side-arms reduces the solvation in methanol of the complexes relative to those of the parent aza-crown ethers.

In discussing the above complexation behaviour of the alkaline-earth ions, it is necessary to take into account the greater solvation requirement of the cations. The coordination number of Ca²⁺, Sr²⁺ and Ba²⁺ with

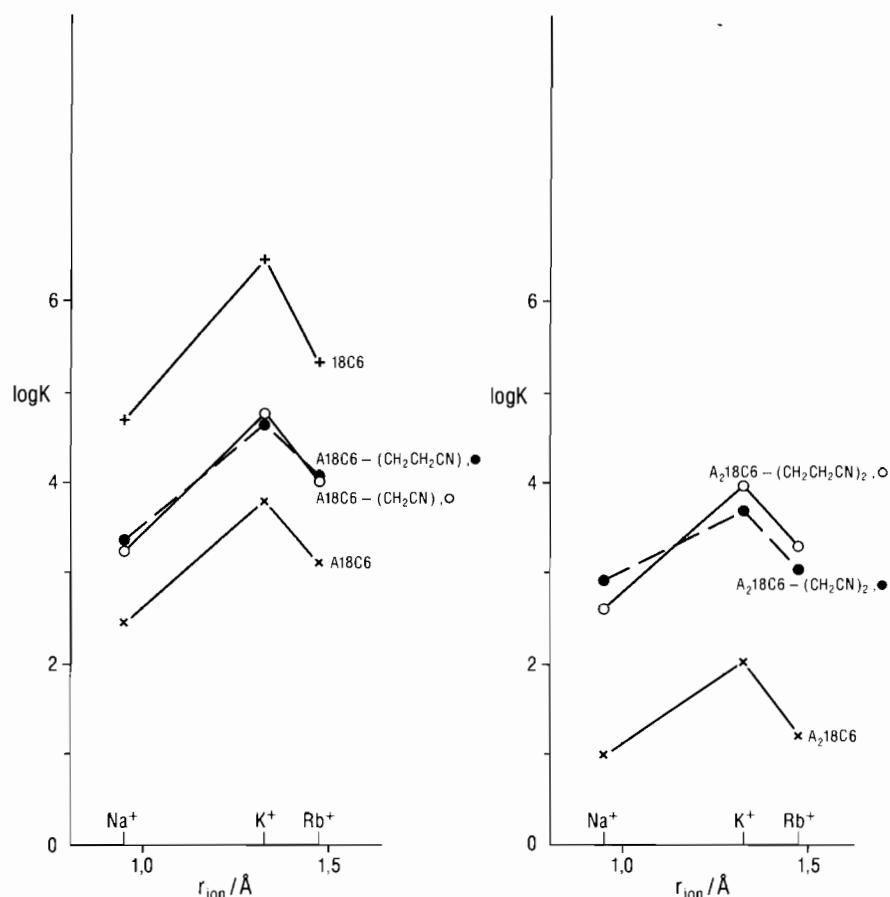


Fig. 3. Stability constants ($\log K$) of alkali metal ions in methanol plotted vs. the ionic radii.

water molecules is eight [25], and the crystal structures of Ca^{2+} and Ba^{2+} complexes with the macrobicyclic ligand (2,2,2), show that, in addition to six oxygen bonds and two nitrogen bonds with the ligand, the complexed metal ions form bonds with crystal water molecules and anions [26]. In solution, therefore, methanol molecules will coordinate the complexed cations, utilizing that part of the metal ion's surface which is not shielded by the crown ether. The decreased stability of the complexes containing the cyanoalkyl side-arms could then be accounted for by a disruption of bonding between the complexed cation and methanol molecules, providing that the resulting loss of solvation energy is greater than the corresponding loss for the parent aza-crowns, discussed earlier.

Heavy metal ion complexes

The stability constants of some heavy metal ion complexes with various 18C6 ligands in methanol are listed in Table 6. Strikingly, the stability constants of the Zn^{2+} complexes are almost completely independent of the ligand, with the exception of the somewhat higher stability of the $\text{A}_2\text{18C6}$ complex. The attachment of cyanoalkyl side-arms to $\text{A}_2\text{18C6}$ in the Pb^{2+} complex

leads to a reduction in stability constant, similar to the behaviour of the alkaline-earth complexes, and an increase in stability constant of the Cd^{2+} complex. The difference between the stability constant of the cyanoalkyl-substituted aza-crowns and 18C6, $\Delta \log K$, for the heavy metal cations is plotted as a function of ionic radii in Fig. 5. The most outstanding feature is the sharp maximum for Cd^{2+} , and it is tempting to relate this to an optimum fit of Cd^{2+} within the ligand cavity. However, the cavity size of the various 18C6 ligands, at around 2.5–3.0 Å [27], is much larger than the ionic radius of Cd^{2+} , so that the roof-shape relationship observed must reflect different types of bonding interactions for Zn^{2+} , Cd^{2+} and Pb^{2+} with the macrocycles. The corresponding $\Delta \log K$ values for the alkali metal and alkaline earth cations, which are also included in Fig. 5, are linearly dependent upon the ionic radii of the cations.

Spectroscopic measurements

The ^{13}C NMR spectra in CD_3OD of the cyanoalkyl and the ring- NCH_2 carbon atoms (Table 7) indicate that the effect of the cyanomethyl and 2-cyanoethyl substituents on the structure of the aza-crowns is very

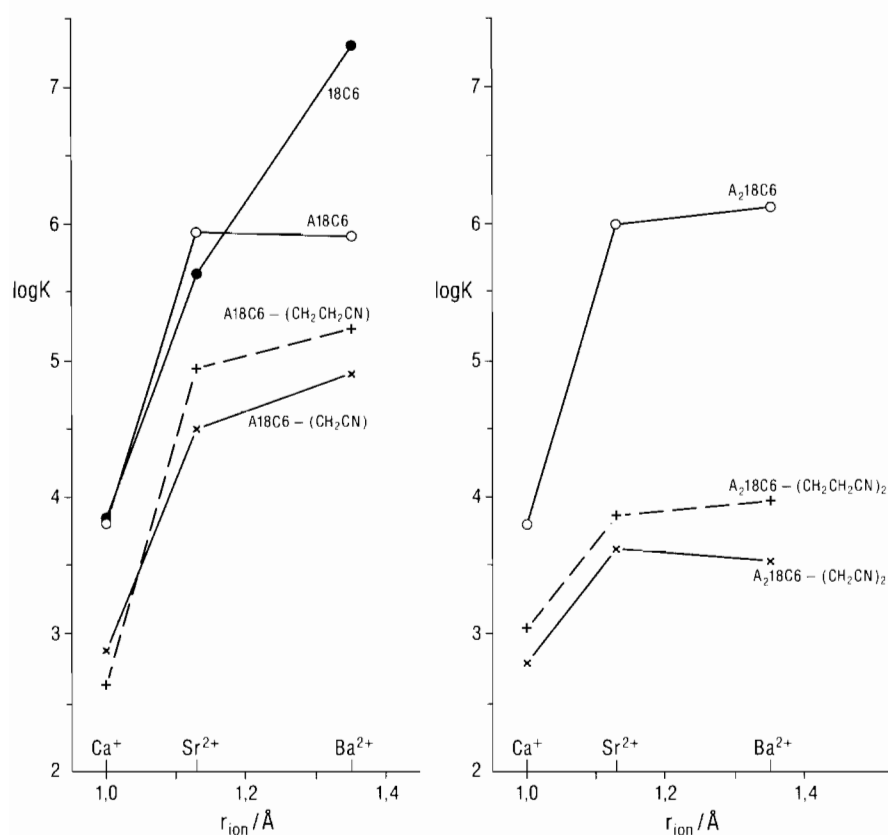


Fig. 4. Stability constants ($\log K$) of alkaline-earth metal ions in methanol plotted vs. the ionic radii.

TABLE 11. $\text{C}\equiv\text{N}$ stretching frequencies of cyanoalkyl-substituted diaza-18-crown-6 ligands and their metal ion complex salts of 1:1 composition

	$\text{L} = \text{A}_218\text{C}6-(\text{CH}_2\text{CN})_2$		$\text{L} = \text{A}_218\text{C}6-(\text{CH}_2\text{CH}_2\text{CN})_2$	
	ν (cm^{-1})	$\Delta\nu = (\nu_{\text{ML}} - \nu_{\text{L}})$ (cm^{-1})	ν (cm^{-1})	$\Delta\nu = (\nu_{\text{ML}} - \nu_{\text{L}})$ (cm^{-1})
L	2225			
$\text{LiClO}_4\text{-L}$	2238	13	2248	
$\text{NaClO}_4\text{-L}$	2248, 2234	23.9	2252	4
KSCN-L	2246	21	2251	3
$\text{RbClO}_4\text{-L}$	2237, 2228	12.3	2252	4
$\text{CsClO}_4\text{-L}$	2226	1	n	
$\text{AgClO}_4\text{-L}$	2166	-59	n	
$\text{TiClO}_4\text{-L}$	2238	13		
$\text{Ca}(\text{ClO}_4)_2\text{-L}$	2243	18	2249	1
$\text{Sr}(\text{ClO}_4)_2\text{-L}$	2228, 2240	15.3	2249	1
$\text{Ba}(\text{ClO}_4)_2\text{-L}$	2244	11	2249	1

n: impossible to obtain a spectrum of sufficient resolution.

similar. The chemical shifts of the cyanoalkyl carbon atoms are identical for monoaza- and diaza-crown ethers, as are those for the ring- NCH_2 groups.

The ^{13}C NMR chemical shifts of all of the diaza-crowns in CD_3OD are changed on complexation with metal cations, but there is no simple relationship between the size of the shift, or indeed the sign, and the charge and size of the metal ion or the nature of the

ligand (Tables 8 and 9). This is true even of the carbon atoms in the cyanoalkyl side-arms. A similar conclusion holds for the IR stretching frequencies of the cyano group (Table 11), with the exception of the Ag^+ complexes. The shifts of the $\text{C}\equiv\text{N}$ stretching frequencies of the cyanoalkyl-substituted $\text{A}_218\text{C}6$ ligands to lower frequency in the case of the Ag^+ complex of $\text{A}_218\text{C}6-(\text{CH}_2\text{CN})_2$ and to higher frequency, when Ag^+ is com-

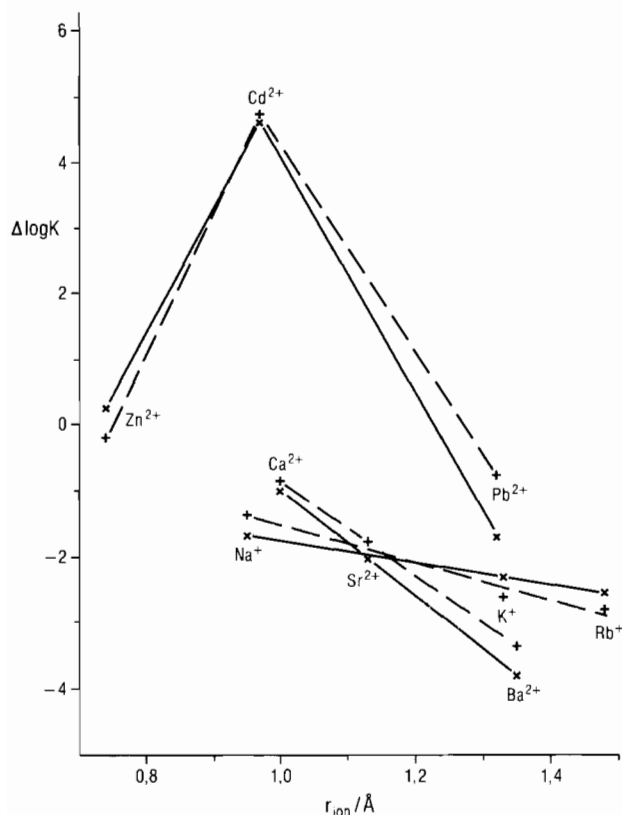


Fig. 5. Stability constants of metal ion complexes in methanol with cyanoalkyl-substituted diaza-18-crown-6 referred to the stability constants of the related 18-crown-6-complexes: $\Delta \log K$. The pendant side-arms are cyanomethyl (\times) and cyanoethyl ($+$).

plexed with $A_218C6-(CH_2CH_2CN)_2$, may indicate that the strong bonding between Ag^+ and the aliphatic nitrogen atoms of these ligands interferes in different ways with the negative induction effect of the cyano group [28, 29]. Unfortunately, the solubilities of the silver ion complexes with cyanoalkyl-substituted azacrowns are too low such that only the $^{13}CH_2$ signals, amplified by proton decoupling, could be determined.

Overall, the spectroscopic findings confirm the conclusions from the potentiometric titrations that the cyanoalkyl side-arms have a negligibly small interaction with metal ions encircled within a macrocyclic ring.

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