Complexation Studies of Branched Acyclic and Macrocyclic Polyether Ligands Having Ether Oxygens Separated by Three Carbon Atoms

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Sixteen polyether ligands designed for selective complexation of small cations have been examined by ^{13}C NMR spectroscopy in acetonitrile or acetonitrile–methanol (95:5) solution for their ability to complex lithium, sodium or magnesium perchlorates. When ligand exchange was fast, titration curves could be recorded and analysed. When ligand exchange was slow, competition experiments provided more reliable information.

All ligands showed selectivity for the small Li^+ cation, not only against the larger Na^+ and Ca^{2+} cations, but also against the small Mg^{2+} cation. The only exception was the unsubstituted 12-crown-3 ligand, which forms a stable 2:1 sandwich complex with Na^+.

The acyclic branched ligands give much less stable complexes than the cyclic ligands having a 12-membered ring structure. Ligating side-arms increase the complex stability and the Li^+ selectivity of the cyclic ligands.

Twenty years ago the observation was made that lithium salts are complexed selectively, although weakly, by 1,5,9,13-tetraoxacyclohexadecanes.[1] Ten years later this complexation process was studied by dynamic NMR spectroscopy.[2] More recently, we have synthesized chemically related compounds of 12-ring and open-chain structure in the hope of finding ligands that give more stable complexes while retaining the selectivity for small cations (Li^+, Mg^{2+}) believed to be inherent in the 1,5-dioxa system. Some preliminary results have been reported[3,4] and more recently the synthetic work has been published.[5–8] Here we present a broad study of the complexation properties towards Li^+, Mg^{2+} and Na^+ cations.

The compounds studied are presented in Scheme 1. They comprise 1,5,9-trioxacyclododecane and derivatives without ligating side arms (**1**, **2**, **3**),[5,8] as well as derivatives carrying one, two or three ligating side arms (**4**, **5**, **6**, **7**),[8] the last two ligands having these side arms *cis* (**6**, **7**) or *trans* (**7**) to each other. For the investigation of *cis*-**7**, an inseparable mixture of *cis*- and *trans*-**7** had to be used, while pure *trans*-**7** was obtained in a separate synthesis. The study also includes acyclic ligands of singly branched structure (**8**, **9**, **10**)[6,7] and one of doubly branched structure (**11**).[6] For comparison, we have prepared and studied some mixed-structure ligands containing both 1,5- and 1,4-dioxa systems (**12**, **13**, **14**, **15**).[6]

Choice of solvent system and counter ion. Competing with complex formation with the present ligands is the strong solvation of both Li^+ and Mg^{2+} cations in water or methanol solution. On the other hand, the complexes formed in solvents like $CHCl_3$ are too stable to allow a gradation of complexation strength, and such solvents are not capable of dissolving the uncomplexed salt. Acetonitrile proved to be a good compromise, and had the further advantage of being a good solvent both for the complex and for any excess of the uncomplexed salt (Li-, Na- and Mg-perchlorates). Pure acetonitrile allowed a ranking of the acyclic ligands, which are generally weaker complexers, while the addition of 5% methanol was required to differentiate the 12-crown-3 ligands, which are generally stronger complexers. Both these solvents (when deuteriated) are also excellent solvents for NMR-titrations (see below). For solubility reasons, perchlorate was chosen as the counter ion.

Determination of complex stability. We have reported earlier that ^{13}C NMR spectroscopy is eminently suited to monitoring cation complexation by the familiar crown-ether ligands of 1,4-dioxa type when the dry salt is added portionwise directly to the NMR-tube.[9,10] The change of conformation on going from the free ligand to the complexed ligand is accompanied by the loss of downfield δ-interactions and the gain of upfield γ-interactions, resulting in net upfield shifts of as much as 5 ppm.[9–11] When the NMR spectrum shows fast exchange between free and com-

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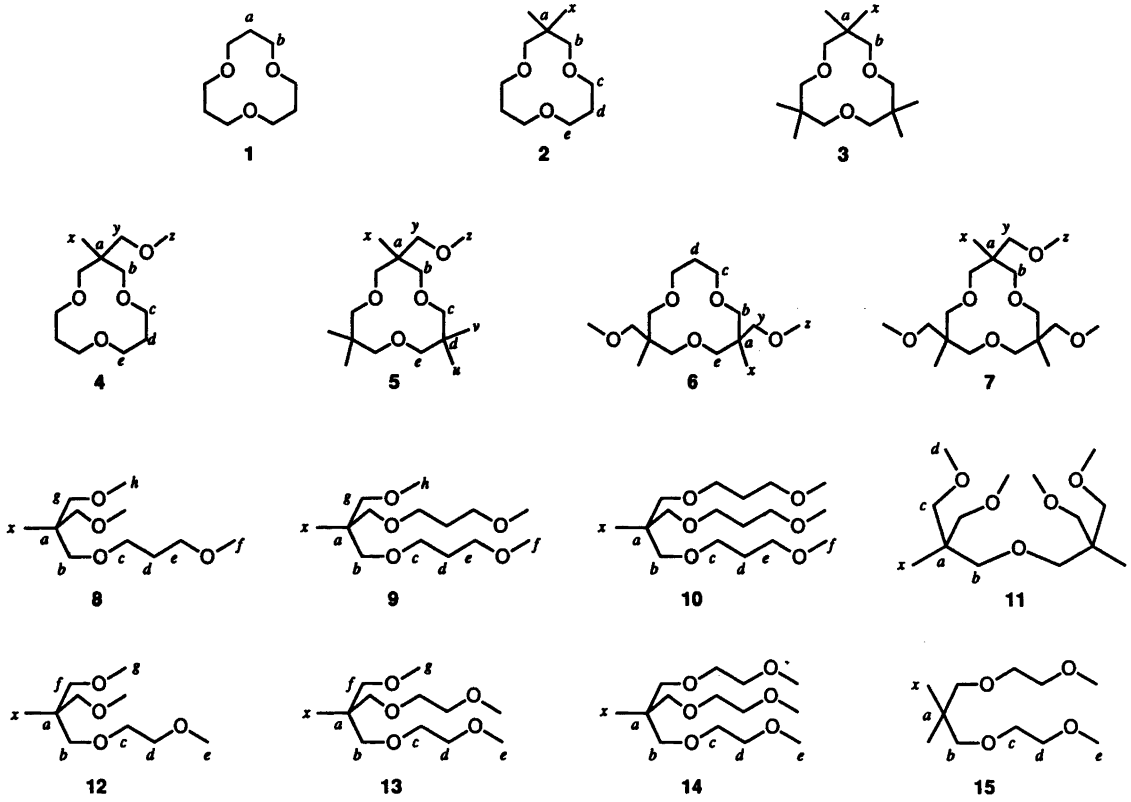

Scheme 1.

plexed ligand at room temperature, the 'titration curve' gives directly the stoichiometry and can be used to evaluate the complexation constant.

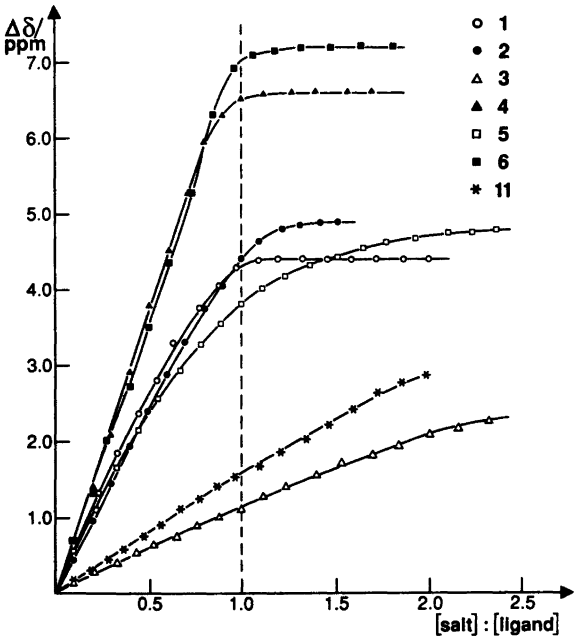

Fig. 1. ^{13}C NMR chemical shift displacement (Δδ) for the cyclic ligands **1–6** and for the acyclic ligand **11** in CD_3CN–CD_3OD (95:5) on portionwise addition of solid $LiClO_4$.

When macrocyclic ligands of 1,5-dioxa type are titrated with dry salts in the same way, large downfield ^{13}C shift changes occur for the α-carbons: for 16-crown-4 almost 6 ppm, for 12-crown-3 about 4.5 ppm.[3] Similar, but somewhat smaller, shift displacements occur with the acyclic ligands. The explanation is that upfield γ-interactions felt by the α-CH_2 carbons in the free ligand are lost upon

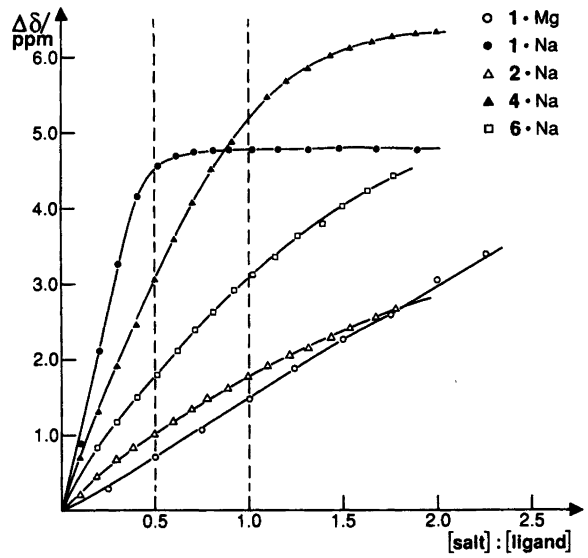

Fig. 2. ^{13}C NMR chemical shift displacement (Δδ) for selected cyclic ligands in CD_3CN–CD_3OD (95:5) on portionwise addition of solid $NaClO_4$ or $Mg(ClO_4)_2$.

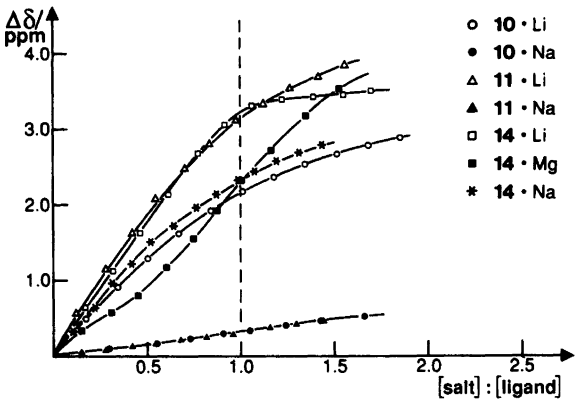

Fig. 3. ^{13}C NMR chemical shift displacement ($\Delta\delta$) for selected acyclic ligands in CD_3CN on portionwise addition of solid $LiClO_4$, $NaClO_4$ or $Mg(ClO_4)_2$.

adoption of the complex conformation.[2] For the β-CH_2 carbon the ^{13}C shift changes only slightly and upfield. Again, a fast-exchange spectrum is required to obtain a titration curve and to evaluate the complexation constant.

If ligand exchange is slow, an evaluation of the complexation constant must be based on ^{13}C intensity measurements of the separate signals for free and complexed ligand, and would therefore be less accurate for several reasons. Intensity measurements in ^{13}C spectra are inherently inaccurate, line widths may vary, and weak lines may not rise clearly above the noise level. The intermediate situation obtains if a titration is performed just above the coalescence temperature; the curve may become deformed into an S-shape.[12]

It must be emphasized that a comparison of kinetic barriers to ligand exchange, as determined by dynamic NMR spectroscopy, cannot be relied upon as a substitute for a comparison of thermodynamic equilibrium constants.[3] On the other hand, competition experiments between cations that are strongly complexed may give reliable information about the cation selectivity of a given ligand, provided the chemical shifts of the complexes are different and well resolved.

Results

Selected titration curves are shown in Figs, 1, 2 and 3. Titration curves for cyclic ligands with $LiClO_4$ are shown in Fig. 1; with $NaClO_4$ and $Mg(ClO_4)_2$ in Fig. 2. Titration curves for acyclic ligands are shown in Fig. 3. The doubly branched ligand **11**, titrated with $LiClO_4$, is included in Fig. 1 as well as in Fig. 3 to show the effect of adding 5% methanol to the acetonitrile solvent. Each curve represents the chemical shift for that α-CH_2 carbon which undergoes the strongest downfield displacement. Titrations were also planned with $Ca(ClO_4)_2$, but no significant shift displacement could be observed at a molar ratio of 1:1 for any of the ligands tried except the unsubstituted 12-crown-3 (**1**).[3]

The calculation of complexation constants was done graphically from the deviation of the observed curve from the horizontal line obtained by extrapolation of the limiting chemical shift to the vertical line representing the appropriate stoichiometry (1:1 or 2:1).

One main problem was to obtain the limiting chemical shift, corresponding to 100 % complexed ligand, when the complexation is very weak. In cases when $\Delta\delta_{lim}$ could not be established for a given weak complex, it could be assumed to be the same as in a strong complex of the same ligand with another cation. Alternatively, it could be estimated by counting the loss of γ-interactions when going from the likely conformation of the free ligand to the likely conformation of the complexed ligand.[1-3]

Another major problem occurred when complexation was so strong that the bend of the curve at 1:1 (or 2:1) stoichiometry became very sharp and hard to distinguish from the crossing of two straight lines.

In Tables 1 and 2 the ^{13}C chemical shifts of all carbon atoms and their structural assignments are listed for every ligand shown in Scheme 1, and for comparison also data for 16-crown-4.[3] All shift displacements ($\Delta\delta_{1:1}$) observed after the addition of one mole of the salt are also given. In addition, the limiting chemical shift ($\Delta\delta_{lim}$) for the α-carbon chosen for the curves in Figs. 1–3, and for calculating the log K values, is also given. Transferred or assumed values of $\Delta\delta_{lim}$ are given in parentheses.

In cases of slow exchange, most commonly observed with Mg^{2+}, the $\Delta\delta_{1:1}$ value given corresponds to that of the complex, hence $\Delta\delta_{lim}$, but complexation may of course be incomplete.

In the cases where the limiting chemical shift was reached very quickly, the stoichiometry was that of the expected 1:1-complex, except for the Na^+ complex of 12-crown-3 (ligand **1**), for which the curve shape reveals the clear 2:1 stoichiometry of a sandwich complex. The shapes of the curves for the titration of ligands **1** and **4** with $LiClO_4$ suggest a slight tendency towards 2:1 complex formation in the early phase, when there is still an excess of ligand present.

Discussion

Relative stabilities of Li^+ complexes. A comparison of the titration curves of Figs. 1 and 3, and of the log K values in Tables 1 and 2, allows the general conclusion that more stable complexes are formed with the cyclic than with the acyclic ligands, if due allowance is made for the competition from solvation when methanol is present in the acetonitrile solvent. The data for the doubly branched ligand **11**, measured in both solvent systems, demonstrate clearly such an effect, log K decreasing by at least 1.4 units when 5 % methanol is added.

It must be emphasized that the term 'cyclic' in the present context is restricted to the 12-membered ring systems (12-crown-3). The 16-membered rings (16-crown-4) give much weaker complexation, and the difference has been explained[3] in terms of conformational strain in the free 12-crown-3 ligand that becomes relieved in the complex,

Table 1. ^{13}C chemical shifts for free and complexed cyclic ligands in CD_3CN–CD_3OD (95:5). Complexation constants from analysis of ^{13}C NMR titration curves.

Compound	Carbon[a]	Free ligand	Li-complex				Na-complex				Mg-complex			
		δ	$\delta_{1:1}$[b]	$\Delta\delta_{1:1}$	$\Delta\delta_{lim}$	log *K*	$\delta_{1:1}$[b]	$\Delta\delta_{1:1}$	$\Delta\delta_{lim}$	log *K*	$\delta_{1:1}$[b]	$\Delta\delta_{1:1}$	$\Delta\delta_{lim}$	log *K*
16-Crown-4	α	67.2	71.3	4.1	5.9	1.3		Negl.				–		
	β	31.4	30.3	1.1										
1	*b*	68.4	72.7	4.3	4.4	3.5	72.9[c]	4.5[c]	4.8	3.2	70.0	1.5	(4.8)	0.01
	a	30.1	29.3	0.8			29.3	−0.8			29.7	−0.4		
2	*b*	77.0	81.4	4.4	4.9	2.2	78.8	1.8	(4.9)	0.3		–		
	c	70.0	73.2	3.2			71.4	1.4						
	e	68.4	72.3	3.9			69.9	1.5						
	a	36.7	36.2	−0.5			36.8	0.1						
	d	29.4	29.2	−0.2			29.4	0						
	x	23.2	22.5	−0.7			23.1	−0.1						
3	*b*	79.3	80.5	1.2	(3.0)	0.3		Negl.				Negl.		
	a	37.1	37.0	−0.1										
	x	23.1	22.9	−0.2										
4	*y*	77.7	82.0	4.3			81.3	3.6			82.3		4.6	
	b	74.3	80.8	6.5	6.6	3.9	79.5	5.2	6.6	1.6	81.6	Sl. ex.	7.3	
	c	70.1	73.6	3.5			73.2	3.1			75.1		5.0	
	e	68.3	72.8	4.5			72.0	3.7			74.2		5.9	
	z	59.7	60.1	0.4			59.8	0.1			61.2		1.5	
	a	41.6	39.7	−1.9			40.7	−0.9			39.3		−2.3	
	d	29.6	29.4	−0.2			29.3	−0.3			27.1		−2.5	
	x	18.6	18.1	−0.5			19.5	0.9			17.3		−1.3	
5	*c, e*	79.3	81.6	2.3										
	y	77.7	81.3	3.6										
	b	76.5	80.3	3.8	5.0	1.6		Negl.				Negl.		
	z	59.8	60.2	0.4	Br.									
	a	41.9	40.6	−1.3										
	d	37.1	37.2	0.1										
	u or *v*	23.1	23.0	−0.1										
	v or *u*	22.9	22.4	−0.5										
	x	18.5	18.1	−0.4										
cis-**6**	*y*	77.7	82.1	4.4			79.8	2.1			83.3		5.6	
	b or *e*	75.5	80.9	5.4			78.2	2.7			81.8		6.3	
	e or *b*	73.8	80.9	7.1	7.2	4.4	76.9	3.1	7.2	0.9	81.2	Sl. ex.	7.4	
	c	70.4	73.8	3.4	Br.		72.0	1.6			75.4		5.0	
	z	59.7	60.4	0.7			59.8	0.1			62.2		2.5	
	a	41.6	39.6	−2.0			41.1	−0.5			39.2		−2.4	
	d	28.5	28.7	0.2			28.9	0.4			27.5		−1.0	
	x	18.4	18.3	−0.1			19.0	0.6			16.9		−1.5	
trans-**7**[d]	*y*	77.4	82.2	4.8	5.1			Negl.			84.0	Sl. ex.		
	b	76.1	81.5	5.4	5.6	3.3					83.7			
			80.7		Br.						81.7			
		75.9	78.1								78.6			
	z, z'		76.4								74.1			
		59.7	60.4	0.7							62.6		2.9	
	a, a'		59.4	−0.3										
		41.7	42.6	0.9							42.6		0.9	
	x, x'		39.9	−1.8							39.9		−1.8	
		18.3	18.1	−0.2							17.1		−1.2	
			17.3	−1.0							16.7		−1.6	
cis-**7**	*y*	77.6	83.1	Sl. ex.	5.5			–			82.1	Sl. ex.	4.5	
	b	76.1	81.1		5.0						81.8		5.7	
	z	59.7	61.0		1.3						62.1		2.4	
	a	41.8	39.4		−2.4						40.8		−1.0	
	x	18.4	18.1		−0.3						17.3		−1.1	
11	*c*	76.4	77.8	1.4										
	b	74.7	76.3	1.6	(4.5)	0.3		–				–		
	d	59.6	59.9	0.3										
	a	41.9	41.3	−0.6										
	x	18.0	18.1	0.1										

[a]Numbering as in Scheme 1. [b]Molar ratio salt : ligand = 1 : 1. [c]Molar ratio salt : ligand = 0.5 : 1. [d]Some of the signals for the free ligand and the complexes could not be assigned with certainty. Abbreviations: – = not examined, Sl. ex. = slow exchange at room temperature, Br. = broadening of the lines during titration, Negl. = negligible shift displacement (≤ 0.5 ppm).

Table 2. ^{13}C chemical shifts for free and complexed acyclic ligands in CD_3CN. Complexation constants from analysis of ^{13}C NMR titration curves.

Compound	Carbon[a]	Free ligand	Li-complex				Na-complex				Mg-complex			
		δ	$\delta_{1:1}$[b]	$\Delta\delta_{1:1}$	$\Delta\delta_{lim}$	log *K*	$\delta_{1:1}$[b]	$\Delta\delta_{1:1}$	$\Delta\delta_{lim}$	log *K*	$\delta_{1:1}$[b]	$\Delta\delta_{1:1}$	$\Delta\delta_{lim}$	log *K*
8	*g*	76.2	77.9	1.7				–				–		
	b	74.0	76.0	2.0	(3.2)	1.3								
	c or *e*	70.2	71.3	1.1										
	e or *c*	68.9	70.2	1.3										
	h	59.4	59.7	0.3										
	f	58.7	59.0	0.3										
	a	41.5	40.5	−1.0										
	d	30.8	29.9	−0.9										
	x	17.9	17.8	−0.1										
9	*g*	76.3	78.2	1.9				–				–		
	b	74.0	76.4	2.4	(3.2)	1.8								
	c or *e*	70.2	71.6	1.4										
	e or *c*	68.9	70.6	1.7										
	h	59.5	59.9	0.4										
	f	58.7	59.0	0.3										
	a	41.6	40.9	−0.7										
	d	30.7	30.1	−0.6										
	x	17.9	17.9	0										
10	*b*	74.0	76.2	2.2	(3.2)	1.7	74.3	0.3	(3.2)	−0.6		Br.		
	c or *e*	70.3	71.4	1.1			70.4	0.1						
	e or *c*	68.9	70.7	1.8			69.1	0.2						
	f	58.7	59.0	0.3			58.7	0						
	a	41.7	41.1	−0.6			41.6	−0.1						
	d	30.8	30.3	−0.5			30.6	−0.2						
	x	17.9	18.0	0.1			18.0	0.1						
11	*c*	76.3	78.8	2.5			76.6	0.3				Br.		
	b	74.6	77.8	3.2	(4.5)	1.7	74.9	0.3	(4.5)	−0.9				
	d	59.5	60	0.5			59.5	0						
	a	41.7	40.7	−1.0			41.6	−0.1						
	x	17.9	18.0	0.1			17.9	0						
12	*f*	76.2	78.7	2.5				–				–		
	b	74.5	77.6	3.1	(4.0)	1.9								
	c or *d*	72.5	71.4	−1.1										
	d or *c*	71.7	71.0	−0.7										
	g	59.5	59.9	0.4										
	e	59.0	59.2	0.2										
	a	41.5	40.6	−0.9										
	x	17.8	17.8	0										
13	*f*	76.2	77.1	0.9				–			79.9	3.7		
	b	74.4	77.8	3.4	(4.0)	2.3					77.2	2.8	(5.0)	0.7
	c or *d*	72.5	71.3	−1.2							70.9	−1.6		
	d or *c*	71.7	70.4	−1.3							71.9	−0.2		
	g	59.5	59.7	0.2							60.6	1.1		
	e	59.0	59.3	0.3							59.4	0.4		
	a	41.6	40.6	−1.0							40.3	−1.3		
	x	17.8	17.8	0							17.4	−0.4		
14	*b*	74.4	77.7	3.3	(4.0)	2.2	76.7	2.3	(4.0)	0.5	76.7	2.3	(5.0)	0.5
	c or *d*	72.6	71.5	−1.1			72.2	−0.4			71.3	−1.3		
	d or *c*	71.7	70.5	−1.2			71.4	−0.3			71.3	−0.4		
	e	59.0	59.3	0.3			59.1	0.1			59.3	0.3		
	a	41.7	40.3	−1.4			41.1	−0.6			40.7	−1.0		
	x	17.8	17.7	−0.1			18.3	0.5			17.5	−0.3		
15	*b*	77.9	81.4	3.5	(4.0)	2.4		–				–		
	c or *d*	72.6	71.1	−1.5										
	d or *c*	71.7	70.0	−1.7										
	e	59.0	59.4	0.4										
	a	37.0	36.1	−0.9										
	x	22.4	22.2	−0.2										

[a]Numbering as in Scheme 1. [b]Molar ratio salt : ligand = 1 : 1. Abbreviations: – = not examined. Br. = broadening of the lines during titration.

while there is no such driving force in the case of the 16-crown-4 ligand, or in the acyclic ligands.

Among the cyclic ligands, the series **1**, **4**, *cis*-**6** and *cis*- and *trans*-**7** deserves particular attention. Ligand **1**, which carries no ligating side-arm and no *gem*-dimethyl groups, gives already a very stable 1:1 complex, and the crystal structure reveals tetrahedral coordination due to anion contact with the Li^+ cation.[3] As expected, the presence of one ligating side-arm in ligand **4** increases the complex stability. The crystal structure[13] reveals pentacoordination, with either one perchlorate oxygen or one water molecule as the additional ligand. Ligand *cis*-**6**, which has two *cis*-related side-arms, offers built-in pentacoordination, and complex stability increases markedly. The observed broadening of lines during the titration also indicates a higher ligand-exchange barrier. A still further increase would be expected with ligand *cis*-**7**, having three *cis*-related side-arms, but titration was not possible because of the slow exchange spectrum at room temperature. We take, however, the increased ligand-exchange barrier as an indication of increased complex stability in this particular comparison, although we have already warned against the general validity of such conclusions.[3]

The effect of β-*gem*-dimethyl groups, as compared with unsubstituted β-positions, is to reduce complex stability dramatically, both for cyclic ligands without ligating side-arms (**2** and **3**) and for cyclic ligands with one side-arm (**5**). Steric hindrance to close anion-contact suggests itself as the reason, but the great similarity in ring conformation and other structural details between the $LiClO_4$ complexes of ligands **1** and **3**, as established by X-ray analysis,[3] does not support such an explanation. The effect of a methyl group is much less for *trans*-**7**, resulting in only a small decrease in complex stability compared with *cis*-**6**.

Among the acyclic ligands the complex stability (in pure acetonitrile) varies much less. In the series of ligands **8**, **9** and **10**, all with a single branching point, the weakest complexer is **8** with four ether oxygens. Ligand **9** with five ether oxygens is somewhat stronger. However, ligand **10** with six ether oxygens produces no further increase in complex stability, but a slight decrease. We interpret this in terms of a marginal need for Li^+ to attain hexacoordination that is outweighed by the steric problems involved in organizing all three elongated branches around the cation. The doubly branched ligand **11** with five ether oxygens gives an Li^+ complex whose stability is comparable to those of **9** and **10** and thus offers no added advantage.

For comparison, the ligands **12**, **13** and **14** were also examined. These have the same 1,5-dioxa structure at the branching point, but the traditional 1,4-dioxa structure in the elongated branches. Their Li^+ complexes turned out to be somewhat more stable, and again, the elongation of the third branch (ligand **14**) also led not to an increase but to a slight decrease in complex stability. The same interpretation, steric difficulties in organizing three elongated branches around the cation, is proposed. To our surprise, the related and simpler ligand **15**, having only two elongated branches and a total of only four ether oxygens, proved to be at least as efficient at complexing Li^+.

Relative stabilities of Mg^{2+} complexes. Of particular interest was the observation of slow-exchange spectra for the cyclic ligands **4**, *cis*-**6** and *cis*- and *trans*-**7** carrying one, two and three ligating side-arms respectively in complexes with Mg^{2+}. The relative intensities of the signals of complexed and free ligand allowed only a qualitative comparison of the complexation strength. The $\log K$ values calculated therefrom were in fact so uncertain, and in such poor agreement with the conclusions from the competition experiments described below, that they were not included in Table 1.

In a 1:1 mixture of ligand **4** and $Mg(ClO_4)_2$ only the signals for the complexed ligand were seen. This was also the case for the 1:1 mixture of ligand *cis*-**6** and $Mg(ClO_4)_2$, hence, ligands **4** and *cis*-**6** both gave quite stable Mg^{2+} complexes. *trans*-**7** formed a less stable Mg^{2+} complex than *cis*-**6**; in the 1:1 mixture of ligand and salt, signals for free and complexed ligand were seen in the ratio ca. 1:3. Surprisingly, the Mg^{2+} complex of *cis*-**7** was also weaker than that of *cis*-**6**; in a 1:1 mixture of the ligand and $Mg(ClO_4)_2$ ca. 25 % uncomplexed ligand was still present.

The acyclic ligands generally formed weaker complexes than the cyclic ligands. The highest $\log K$ values that could be calculated from titration curves were obtained for the Mg^{2+} complexes of the acyclic ligands **13** and **14**. In two cases (**10**, **11**) only line broadening was observed, suggesting a relatively high decomplexation barrier, but very weak complexation.

Selectivity for Li^+ against Mg^{2+}. The Mg^{2+} complexes of the acyclic ligands are much less stable than the corresponding Li^+ complexes. Also, the cyclic ligands **1**, **3** and **5** responded very weakly to Mg^{2+}.

Sufficiently accurate $\log K$ values could not be calculated from the slow exchange spectra for the Mg^{2+} complexes of the cyclic ligands **4**, *cis*-**6** and *cis*- and *trans*-**7**. To evaluate selectivity, it therefore became necessary to carry out competition experiments between Li^+ and Mg^{2+} with these ligands.

The NMR spectrum of a 1:1:1 mixture of ligand **4**, $LiClO_4$ and $Mg(ClO_4)_2$ showed the presence of both the Li^+ and the Mg^{2+} complex, in a ratio of ca. 5:1.

A 1:1:1 mixture of ligand *cis*-**6**, $LiClO_4$ and $Mg(ClO_4)_2$ gave a spectrum almost identical with that obtained without $Mg(ClO_4)_2$. Only traces (<5 %) of the lines belonging to the Mg^{2+} complex were observed, hence a satisfactory Li^+ selectivity has been demonstrated.

The isolated *trans*-**7** ligand gave, in the competition experiment, Li^+ and Mg^{2+} complexes in a ratio of about 4:1, hence the Li^+ selectivity is inferior to that found for *cis*-**6**.

The clearest conclusion was obtained for *cis*-**7**, in similar competition experiments carried out with our unresolved mixture of *cis*- and *trans*-**7**. The line-rich spectra were carefully analysed. Slow-exchange spectra were obtained both

with Li^+ and Mg^{2+}, and in experiments with equimolar quantities of *cis*-**7**, $LiClO_4$ and $Mg(ClO_4)_2$, only the lines for the Li^+ complex were seen. This complete selectivity for Li^+ is noteworthy, considering that hexacoordination is normal for Mg^{2+}, but rare for Li^+.[14,15] Possibly, the higher charge of Mg^{2+} makes it more important in this solvent to retain anion contact, which becomes sterically impossible when the Mg^{2+} cation is hidden by three side-arms.

Selectivity for Li^+ against Na^+. In view of the generally weak complexation of Na^+ and the resulting very low accuracy of the calculated log *K* values, only brief comments are justified. Except for ligand **1**, the log *K* values for Na^+ complexation are lower by about 2–3 units, and the selectivity for Li^+ is therefore satisfactory, even for ligands **4** and **6**, which form moderately stable Na^+ complexes. Very high Li^+ selectivity is obtained with ligands *cis*- and *trans*-**7**, which both form extremely weak Na^+ complexes. The only exception is the simplest cyclic unsubstituted ligand **1** because of its ability to form a 2:1 sandwich with Na^+. The difference in log *K* is only 0.3 units, hence the selectivity for Li^+ against Na^+ is almost completely lost.

Conclusions

Our complexation studies show that the 1,5-dioxa based ligands display a clear selectivity for the small Li^+ cation against not only the larger Na^+ cation, but also against the equally small Mg^{2+} cation. This is true for both the cyclic (12-crown-3-based) and the acyclic structures The outstanding exception is the unsubstituted 12-crown-3 ligand which forms a 2:1 sandwich complex with Na^+ whose stability approaches that of its 1:1 complex with Li^+.

The studies further show that the level of complexation is unacceptably low for all acyclic ligands. The enhancing effect of increased branching or lengthening of the branches is, to a large extent, counterbalanced by steric hindrance to complex formation.

Only the 12-crown-3 based ligands give complexes of satisfactory stability. The formation of sandwich complex with Na^+ is suppressed, and the stability of the Li^+ complex is increased, even with the presence of only a single ligating side-arm. The Li^+ complex stability is further increased with the introduction of one and of two additional *cis*-related ligating side-arms. In addition, the selectivity for Li^+ against Na^+ and Mg^{2+} is highest for the 12-crown-3 ligand (*cis*-**7**) having three ligating side-arms on the same side of the ring.

The present study was limited to comparisons within one family of ligands, and the solvent systems were chosen to fit this purpose. Only a few members were investigated in methanol, and the complex stability found to be very much reduced. No comparison was made with other types of Li^+-selective ligands.

Experimental

The synthesis of the ligands has been described earlier.[5,6,8]

The ^{13}C NMR spectra were recorded at 50 MHz on a Bruker CPX-200 instrument or a Gemini 200 instrument, and at 75 MHz on a Varian XL 300 instrument. The temperature was held at 25 ± 1 °C.

Ligand solutions were 0.2–0.6 M in pure acetonitrile (acyclic ligands) or in acetonitrile containing 5 % methanol (cyclic ligands). The volumes were 2.5 ml (Bruker instr.) or 0.6 ml. The titration experiments were performed by adding portions of solid perchlorate salt directly to the ligand solution in the NMR tube, and measuring the ^{13}C NMR chemical shifts after each addition.

References

1. Dale, J. and Krane, J. *J. Chem. Soc., Chem. Commun.* (1972) 1012.
2. Aalmo, K. M. and Krane, J. *Acta Chem. Scand., Ser. A 36* (1982) 219.
3. Dale, J., Eggestad, J., Fredriksen, S. B. and Groth, P. *J. Chem. Soc., Chem. Commun.* (1987) 1391.
4. Dale, J. and Fredriksen, S. B. *Pure Appl. Chem. 61* (1989) 1587.
5. Dale, J. and Fredriksen, S. B. *Acta Chem. Scand. 45* (1991) 82.
6. Dale, J. and Fredriksen, S. B. *Acta Chem. Scand. 46* (1992) 271.
7. Dale, J. and Fredriksen, S. B. *Acta Chem. Scand. 46* (1992) 278.
8. Fredriksen, S. B. and Dale, J. *Acta Chem. Scand. 46* (1992) 574.
9. Krane, J., Amble, E., Dale, J. and Daasvatn, K. *Acta Chem. Scand., Ser. B 34* (1980) 255.
10. Dale, J. *Isr. J. Chem. 20* (1980) 3.
11. Borgen, G., Dale, J., Daasvatn, K. and Krane, J. *Acta Chem. Scand., Ser. B 34* (1980) 249.
12. Sudmeier, J. L., Evelhoch, J. L. and Jonsson, N. B. H. *J. Magn. Reson. 40* (1980) 377.
13. Tinant, B. and Declercq, J. P. (Louvain la Neuve). *Unpublished results.*
14. Shannon, R. D. *Acta Crystallogr., Sect. A 32* (1976) 751.
15. Olsher, U., Izatt, R. M., Bradshaw, J. S. and Dalley, N. K. *Chem. Rev. 91* (1991) 137.

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