Journal of Inclusion Phenomena and Macrocyclic Chemistry **37:** 423–440, 2000.

Crown Ethers Analogues and their Complexes with NaSCN: Stoichiometry and Stability Constants Determined by ^{13}C NMR Spectroscopy

A. M. ALSTANEI[1], C. BENDIC[1], M. CARLES[2] and J. P. AYCARD[2]⋆
[1]*Department of Physical Chemistry, Faculty of Chemistry, University of Bucharest, 4–12 Elisabeta Blv., Bucharest, Romania;* [2]*Laboratory of Spectroscopy and Molecular Dynamics, UMR 6633, case 542, University of Provence, Aix-Marseille I, 13397 Marseille, Cedex 20, France*

(Received: 21 May 1999; in final form: 3 October 1999)

Abstract. ^{13}C NMR spectroscopy was used to study the complexation reaction between sodium ion and 12-crown-4, 15-crown-5, methylurazolyl-12-crown-4 and methylurazolyl-15-crown-5 in CD_3OD solutions. The type of complexes, the stability constants and the relative chemical shifts have been established by fitting experimental titration curves with theoretical functions of the observed chemical shifts. The single-crystal X-ray diffraction measurements for a new crystalline complex confirmed the stoichiometry of the complex.

Key words: crown ethers analogues, 12-crown-4, 15-crown-5, Na^+ ion, complex stability, ^{13}C NMR, X-ray diffraction

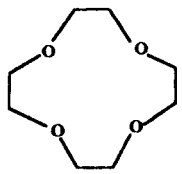
1. Introduction

A key area of coordination chemistry that has been developed over the last two decades is molecular recognition [1–3]. The main purpose is to design ligands that preferentially coordinate with specific metal ions [4]. To achieve this aim macrocyclic ligands have been used. The conformation of the coordinated macrocycle often differs from that observed for the free ligand. Such a feature is important in determining whether or not the required "recognition" is effective [5, 6].

Crown ethers are of general interest because of their widespread chemical and biological applications. The complexation of alkali metal cations to crown ethers and their conformations in solutions have been studied [7, 8] in order to understand the special ability of these compounds to host neutral and charged guest molecules.

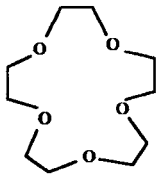
The NMR technique has found widespread application in the identification of changes at the molecular level, during molecule-molecule and ion-molecule interactions. The alkali metal ion NMR [9–11] spectra provide information about the solvation process and the stoichiometry of the crown ether complex. On the other hand structural data are better derived from the ^{1}H and ^{13}C NMR spectra of the ligand.

⋆ Author for correspondence.



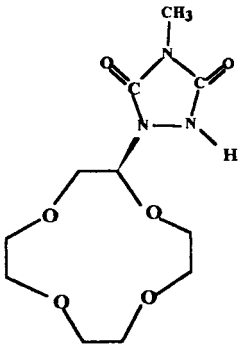
12C4

12-crown-4 **(I)**



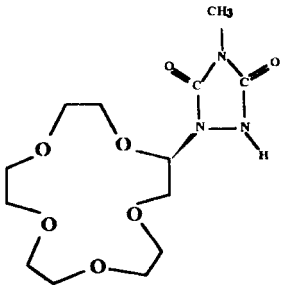
15C5

15-crown-5 **(II)**



mC4

α-methylurazolyl-12-C-4 **(III)**



mC5

α-methylurazolyl-15-C-5 **(IV)**

Figure 1. The studied crown ethers: 12-crown-4 (**I**), 15-crown-5 (**II**), α-methylurazolyl-12-C4 (**III**) and α-methylurazolyl-15-C-5 (**IV**).

After the photochemical reaction of 4-methyl-1,2,4-triazoline-3,5-dione (MTAD) with 12-crown-4 (**I**) and 15-crown-5 (**II**), described elsewhere [12] we have obtained the two new crown ether analogues (**III–IV**) (see Figure 1).

We must stress the unusual method used to synthesize the crown ethers, which are substituted at one carbon atom from the ring. This type of asymmetrical crown ether is only briefly found in the literature [13–15].

The simple structures of crown ethers such as 12C4 and 15C5 exhibit high symmetry in solution due to rapid tumbling and segmental motion and give a

single resonance signal in both ^{1}H and ^{13}C NMR spectra. Their α-methylurazolyl counterparts could also serve as host molecules for different cations.

In this work we attempted to elucidate:

(a) the influence of a new type of ligand (crown ether substituted with 4-methylurazolyl) upon the alkali ion complexation reaction, in comparison with 12C4 and 15C5.

(b) the stoichiometry of the complexes and calculation of the stability constants.

The complexation reaction was monitored by ^{13}C NMR spectroscopy.

2. Experimental

2.1. MATERIALS

Sodium thiocyanate (NaSCN, Aldrich) was used as received except for drying in vacuum at 150 °C for two days.

The macrocyclic ligands 12-crown-4 and 15-crown-5 (12C4, 15C5, Aldrich) were used without further purification, except for storage over freshly activated 3 Å molecular sieves.

Synthetic procedures for the crown ether analogues employed herein have been previously described [12] and they were used without further treatments.

2.2. NMR MEASUREMENTS

The ^{13}C NMR spectra were obtained using a Bruker AMX 400 MHz spectrometer operating at 100.63 MHz, at 25 $\pm$ 1°C, using CD_3OD as solvent.

The ^{13}C NMR spectra of the compounds were recorded (i) as free crown ethers and (ii) with increasing amounts of solid alkali metal salt (NaSCN) added to a known amount of crown ether in CD_3OD. The concentrations of the crown ether samples in CD_3OD were: [12C4] = 0.219 mol/l, [15C5] = 0.238 mol/l, [mC4] = 0.138 mol/l, [mC5] = 0.121 mol/l. The $[Na^+]$/[crown ether] molar ratio ([M]/[L]) was between 0 and 2.

2.3. X-RAY CRYSTALLOGRAPHIC MEASUREMENTS

A single crystal of the mC5-NaSCN complex (**V**) was obtained from an equimolar solution of mC5 and NaSCN in CD_3OD, by slow evaporation.

A summary of the crystallographic data is given in Table II. Diffraction intensities were collected on a Kappa CCD diffractometer using X-ray radiation at 25 °C. No absorption correction was made. The structure was solved by the maXus program.

3. Results and discussion

3.1. NMR RESULTS

Accordingly to their symmetry, compounds **I** and **II** give rise to a single resonance signal. For compounds **III** and **IV** we observed several groups of signals in different ranges:

- the signals assigned to the carbon atoms of the substituent are only little influenced by the complexation process (the induced chemical shift by complex formation ($\Delta\delta$) is about 0.35 ppm). They occur in the common range associated with the C=O and CH_3 groups, namely 156 ppm and 25 ppm.
- the signals of the macrocycle carbon atoms, are strongly influenced by the complexation and shifted to higher field.

According to the asymmetry of the molecules, mC4 and mC5 give rise to eight and ten signals respectively, associated with the carbon atoms from the macrocycle ring. Only the resonance of the substituted carbon atom could be definitely assigned as the most deshielded carbon from the macrocycle ring ($\delta \sim 86$ ppm). The signal of the other carbon atoms of the macrocycle appear together in the range 73–69 ppm (Figure 2).

Graphical representation of different variations of the induced chemical shifts as a function of salt concentration indicated the trendline of the chemical shift in the NMR spectra. The labeling of the signals in Figure 2 yields the common titration curves, which are specific to the complexation process. Thus we have obtained Figures 3–4, which represent the data basis for further calculations, namely the determination of the stability constants and the relative chemical shifts. Chemical shifts for the NMR titrations are available as supplementary material.

The complexation shifts, $\Delta\delta$, vs. molar ratio [M]/[L] display sharp inflexions at a molar ratio of 1 : 2 in the case of 12C4, and of 1 : 1 in the case of 15C5, as expected from previous NMR studies [16]. In the case of the crown ether analogues **III–IV** we were not able to make predictions about the type of the complex.

3.2. DETERMINATION OF STABILITY CONSTANTS

The measurements of equilibria between the ligand, the cation and the complexes are based on the observation of an apparent spectroscopic property x, which in our case refers to a time averaged NMR shift, δ_{obs}.

The experimental titration curves can be treated in terms of the formation of either a 1 : 1 or 1 : 2 metal – ligand complex. In special cases, where a qualitative appreciation of the complex type from the shape of the experimental curve is not possible, the assumption of the existence of both 1 : 1 and 1 : 2 complex formation can be taken into account. The determination of the stability constants has been treated in the literature and there are several methods for their determination [16, 17]. We report here a general method to treat the determination of the stability

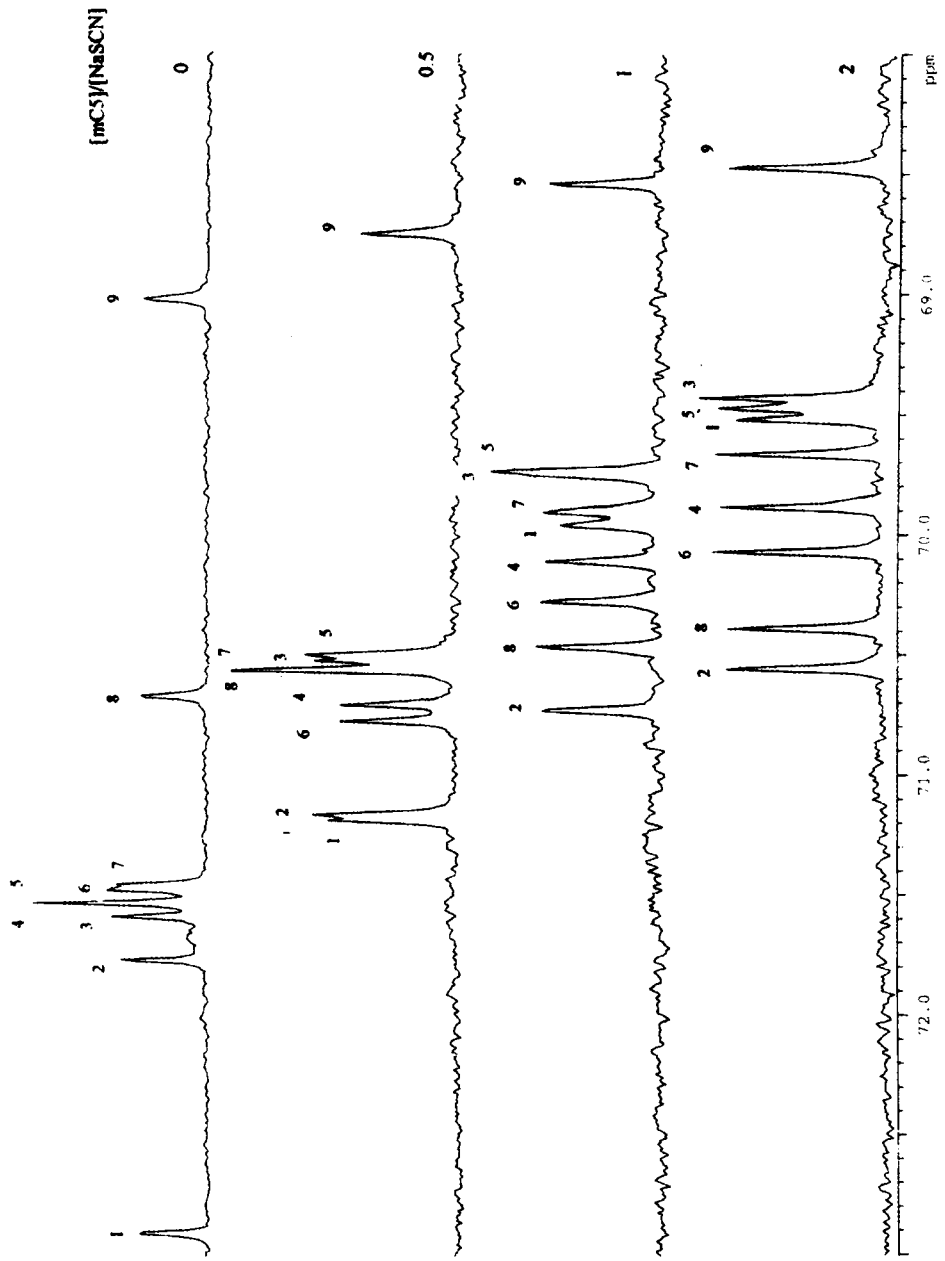


Figure 2. ^{13}C signals upfield shifts of the unsubstituted macrocyclic carbon atoms of mC5 at different NaSCN concentration.

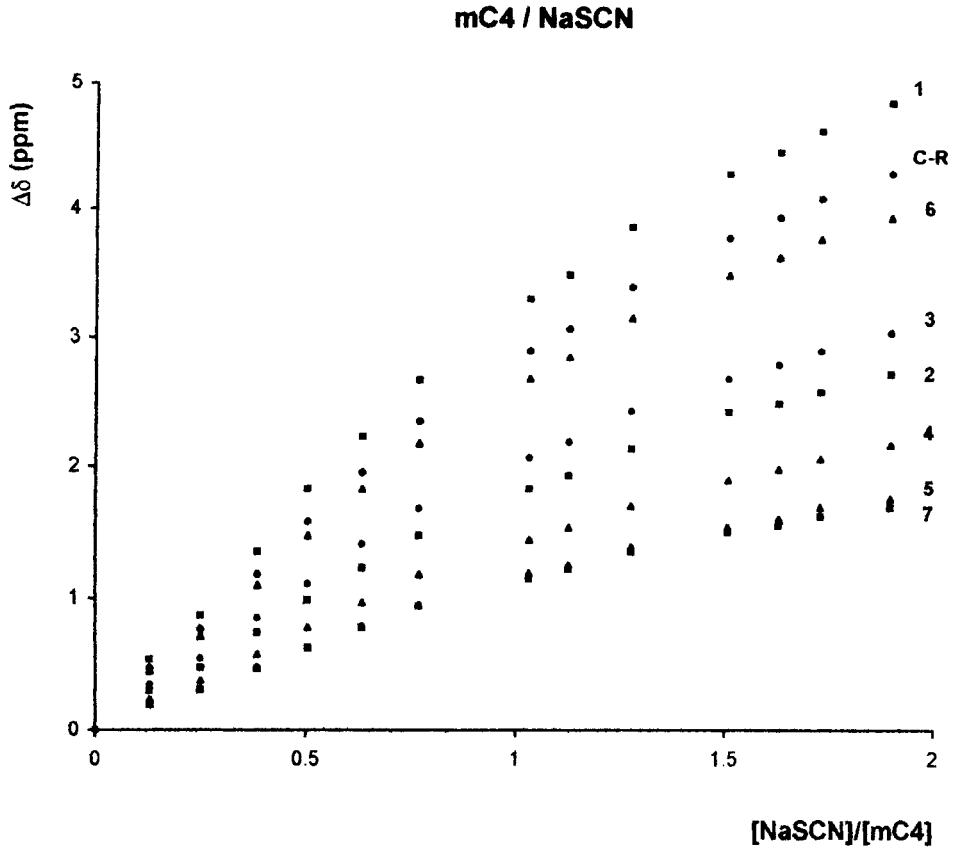


Figure 3. ^{13}C complexation shifts ($\Delta\delta$) of the macrocyclic ring carbons of mC4 at different NaSCN concentration – experimental curves.

constants, regardless of the kind of complex formed. A detailed description of this method is given in the Appendix.

The stability constants, the relative chemical shifts and the type of complex were established by fitting experimental titration curves using theoretical functions (see Appendix), to the observed chemical shifts (Figures 5–8). The statistical parameters of the fitting procedure, namely r^2, F factor and standard error, have allowed the complex type implied in every case to be decided without ambiguity. The results of such theoretical treatment for the crown ethers studied are presented in Table I.

The ^{13}C-NMR spectra exhibited different signals for all carbon atoms in the case of crown ether analogues (**III**, **IV**) which allowed the evaluations of K independently. For these two compounds the presented values of the stability constants (Table I) are the results of the average for all independent K.

For the 12C4 crown ether, we found only the 1 : 2 complex. This result agrees with previous studies in the solid state by X-ray diffraction method [18–20]. With different sodium salts, by conductometric and potentiometric measurements [21–

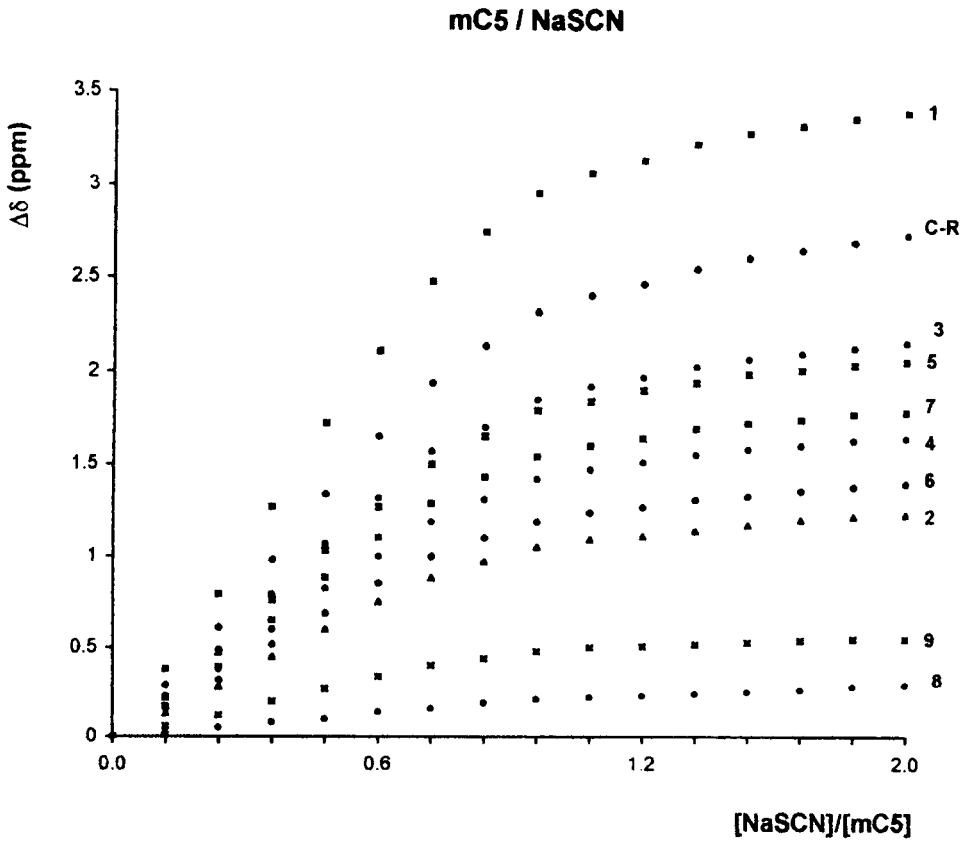


Figure 4. ^{13}C complexation shifts ($\Delta\delta$) of the macrocyclic ring carbons of mC5 at different NaSCN concentration – experimental curves.

Table I. Complex stability constants and calculated relative complexation shifts of Na^+-crown ether complexes

Crown ether	Type of complex M : L	log K	$\Delta\delta$ (ppm)	r^2/F
12-C-4 (I)	**1 : 2**	**4.01**	$\Delta\delta L_2M = 4.92$	0.99976/41263.6
15-C-5 (II)	**1 : 1**	**3.42**	$\Delta\delta LM = 1.94$	0.9817/644.50
mC4 (III)[*1]	**1 : 1**	**0.71**	$\Delta\delta LM = 8.66$	0.99919/14858.48
mC5 (IV)[*2]	**1 : 1**	**2.20**	$\Delta\delta LM = 2.85$	0.99911/15769.54

[*] The calculated log K is the result of the average for all independent K for all carbon atoms.
[1] $\Delta\delta$ calculated for the substituted carbon atom of the ring of the mC4.
[2] $\Delta\delta$ calculated for the substituted carbon atom of the ring of the mC5.

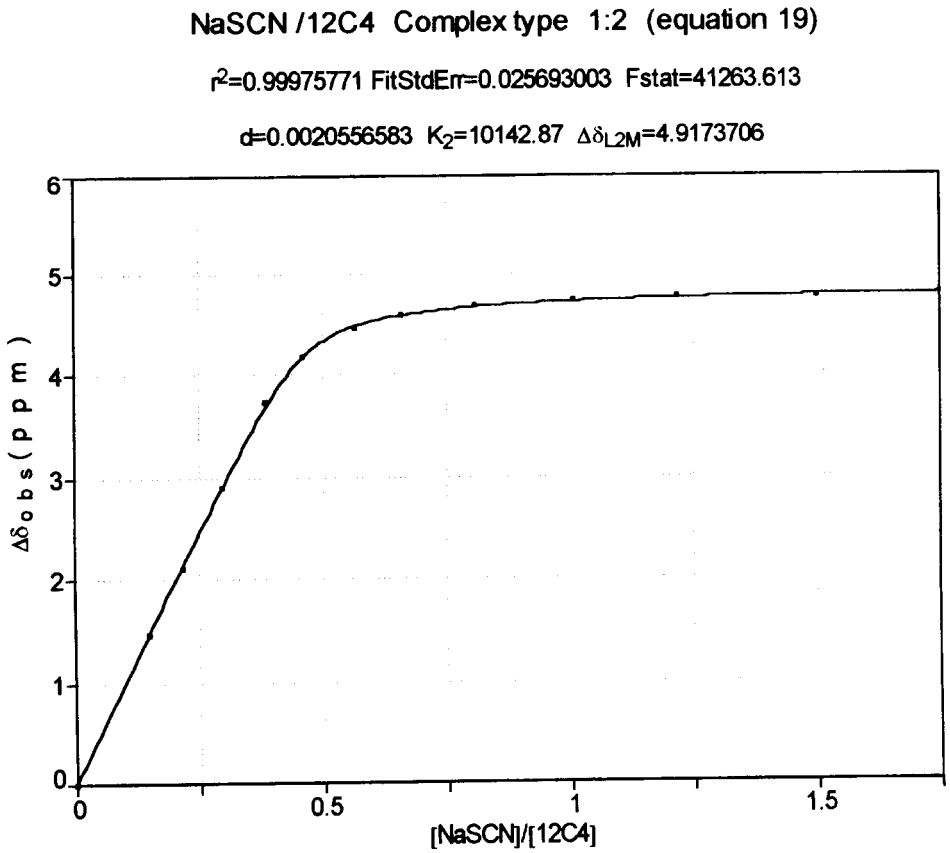


Figure 5. Fitting curves for 12C4/NaSCN complexation.

23], the two complex types could be detected, with the 1 : 2 complex being always predominant. Our result for the stability constant (log K) lies within an average difference of 0.26 when compared with previously published results [16, 21] for the 1 : 2 complex Na/12C4 studied in CH_3OH.

Substituting 12C4 with the methylurazolyle group, the new crown ether analog obtained shows an important decrease of the complexing capacity toward sodium cation. We observe a different complex type, 1 : 1, with a very small stability constant (Table I). The 1 : 2 stoichiometry for the complex with mC4 seems to be energetically unfavorable presumably due to the steric hindrance exerted by the substituent.

In the case of the 15C5 crown ether we have only the 1 : 1 complex, as previously observed in the literature by different methods [13, 24–28]. Our result for the stability constant (log K) lies within an average difference of 0.13 when compared with previously published results [13, 24, 26, 28] for the 1 : 1 complex Na/12C4

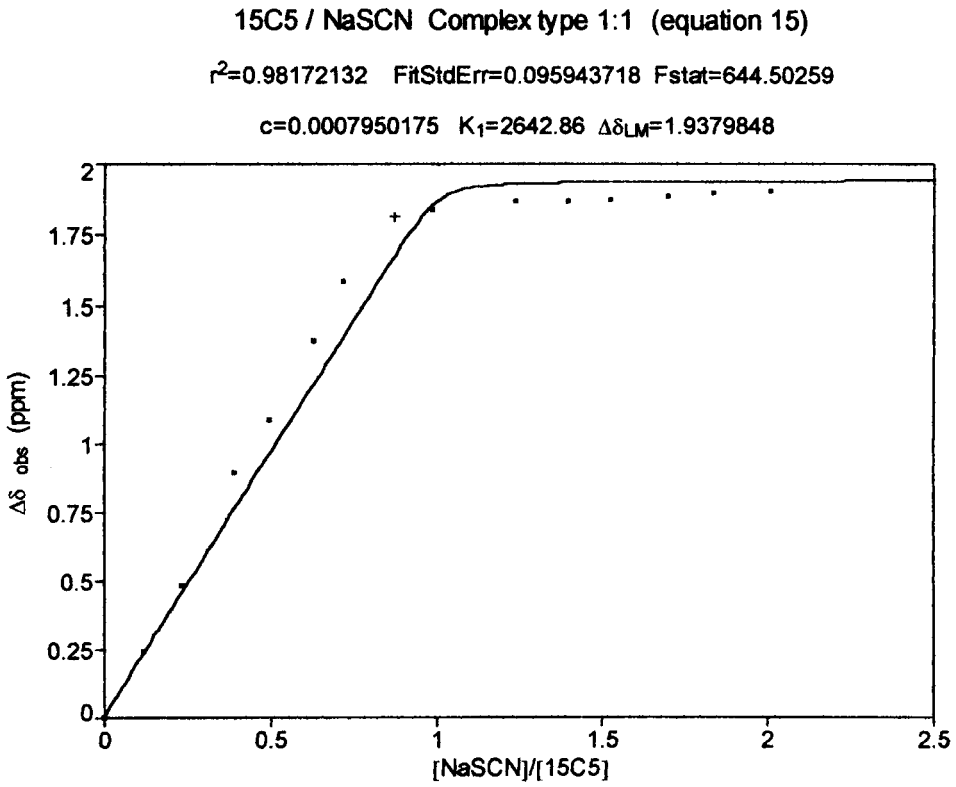


Figure 6. Fitting curves for 15C4/NaSCN complexation.

studied in CH_3OH. Substitution with the methylurazolyle group does not change the complex type, but the stability constant is diminished.

The substituent effects are more important for 12C4 than for 15C5 (Table I). In both cases, the stability constant of the crown ether analogue-NaSCN complex, in deuterated methanol solution, is smaller than that of the unsubstituted crown ether.

3.3. X-RAY CRYSTALLOGRAPHIC STRUCTURE

The NMR results obtained in solution for the 1 : 1 complex of mC5-NaSCN (**V**) have been confirmed by single crystal X-ray diffraction measurements.

Figure 9 shows the ORTEP structure for the NaSCN complex. Crystallographic data are presented in Table II, while atomic parameters, atomic bond lengths, bond angles and selected torsion angles are available as supplementary material.

For the complex of mC5 (**IV**) with NaSCN, i.e., **V**, the feature of interest in the structure concerns the torsion angles in the O—C—C—O and C—O—C—C units (Table III).

Table II. Crystallographic data for the mC5-NaSCN complex (**V**)

Formula	$C_{15}H_{20}O_4N_4Na$
Fw	320.35
Crystal system	Orthorhombic
Space group	Pbca
a (Å)	13.373 (1)
b (Å)	16.002 (1)
c(Å)	18.318 (1)
V (Å^3)	3920.0 (8)
Z (molecules per unit cell)	9
D_m (Mg m^{-3})	1.250
Crystal dimensions (mm^3)	0.20 × 0.20 × 0.20
Radiation (λ, Å)	X-ray, 0.71073
Octants measured	h (0 to 16), k (0 to 19), k (0 to 22)
Max θ (°)	25.41
Temperature (°C)	25
No. of measured reflections	4452
No. of independent reflections	3987
No. of observed reflections	2776
R_f	0.060
R_w	0.089
S	2.957
No. of parameters	239

Table III. Selected torsion angles (°) for the for mC5-NaSCN complex (**V**)

C(14)—O(3)—C(16)—C(24)	165.6	C(25)—O(6)—C(26)—C(18)	−141.8
C(23)—O(5)—C(27)—C(25)	177.2	C(19)—O(7)—C(22)—C(14)	88.0
C(26)—O(6)—C(25)—C(27)	166.1	C(18)—O(8)—C(24)—C(16)	174.7
C(22)—O(7)—C(19)—C(23)	−165.6	O(3)—C(14)—C(22)—O(7)	59.5
C(24)—O(8)—C(18)—C(26)	172.2	O(7)—C(19)—C(23)—O(5)	63.3
C(16)—O(3)—C(14)—C(22)	177.1	O(3)—C(16)—C(24)—O(8)	−62.0
C(27)—O(5)—C(23)—C(19)	179.4	O(8)—C(18)—C(26)—O(6)	59.8
		O(6)—C(25)—C(27)—O(5)	−64.2

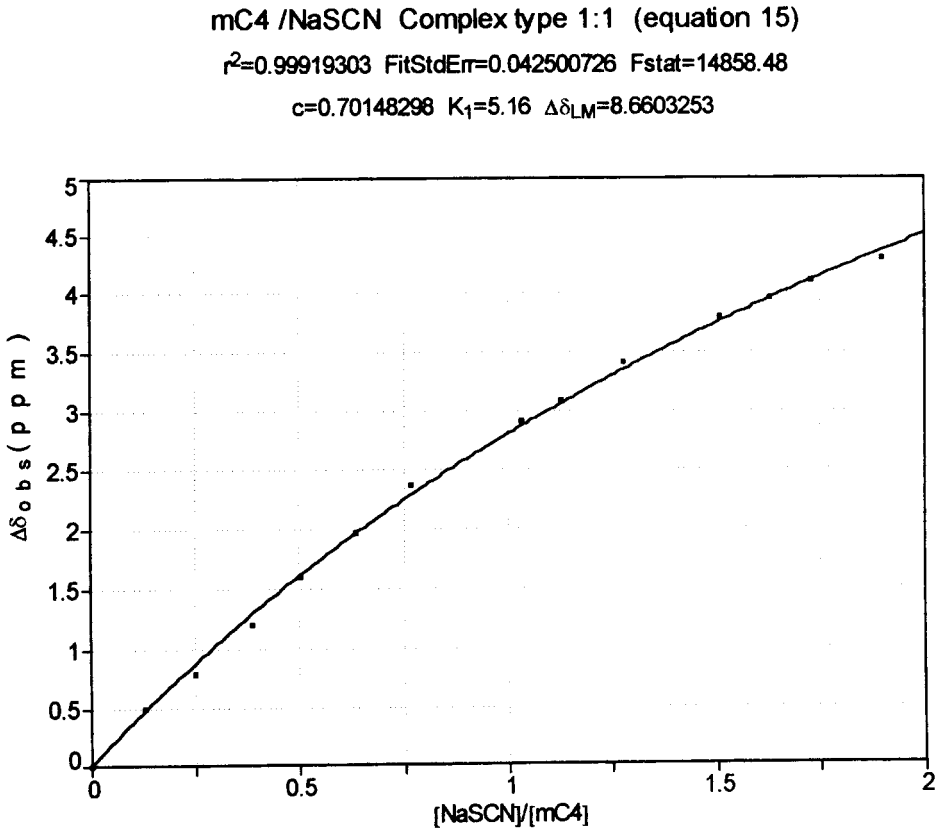


Figure 7. ^{13}C complexation shifts ($\Delta\delta$) of the substituted macrocyclic carbon atom of mC4 at different NaSCN concentration – fitting curve.

The "normal" disposition for the O—C—C—O moieties in polyethers [29–30] is gauche (torsion angles $\cong$60°), while that for the C—O—C—C moieties is trans (torsion angles $\cong$180°).

In the crystal complex **V**, the O—C—C—O torsion angles in the range 59.8°–64.2° are the values usually observed for cyclic polyether complexes, but for the C—O—C—C torsion angles two important deviations are noteworthy: C(19)—O(7)—C(22)—C(14) at 88° and C(25)—O(6)—C(26)—C(18) at 141.8°. As a result the average O···O distance is as short as 2.75 Å which represents a van der Waals contact. The five ether oxygen atoms are not in a planar arrangement, and lie above and below their mean plane by different distances: −0.909 Å for O(3), −0.5658 Å for O(5), 0.4346 Å for O(6), 0.3919 Å for O(7), −0.1698 Å for O(8).

The Na^+ cation is situated 0.965 Å out of this mean plane. The conformation found in the complexed macrocycle allows the Na^+ ion to interact with the five ether oxygen atoms of one crown unit, with one oxygen from the methylurazolyl

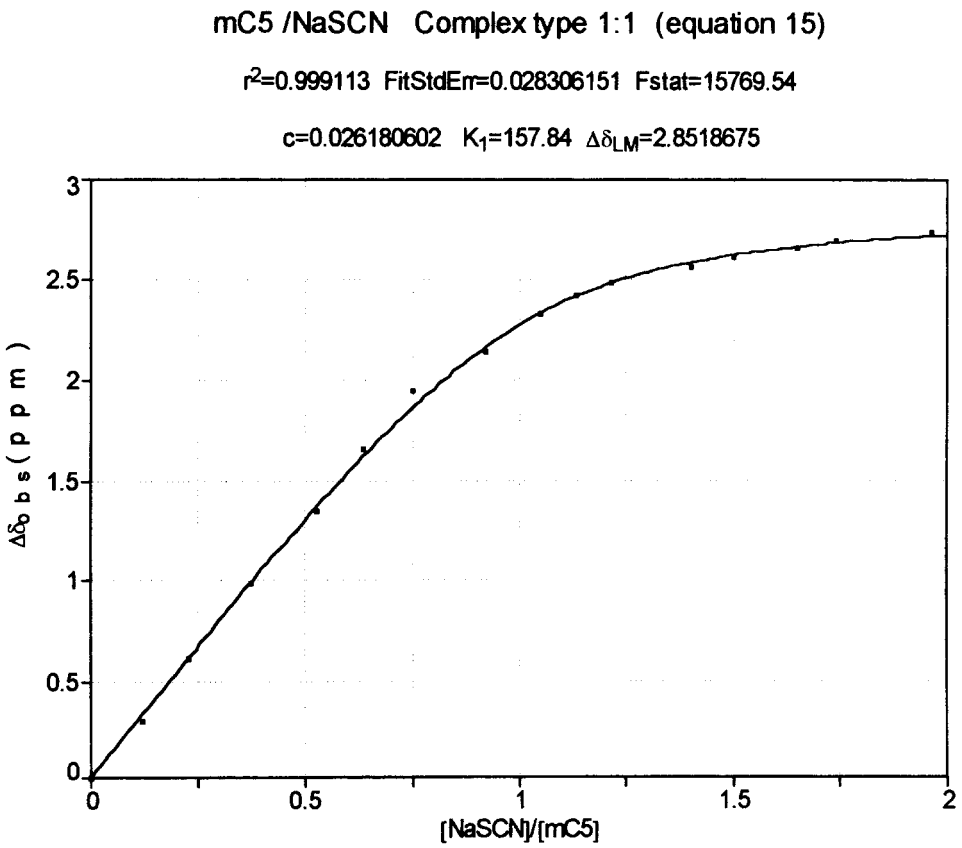


Figure 8. ^{13}C complexation shifts ($\Delta\delta$) of the substituted macrocyclic carbon atom of mC5 at different NaSCN concentration – fitting curve.

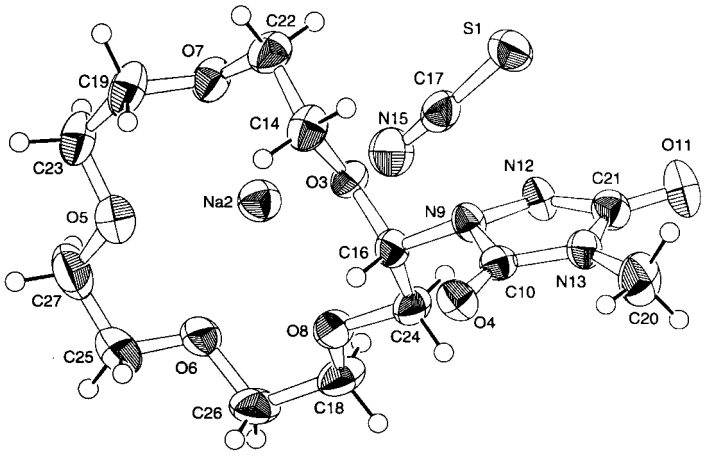


Figure 9. ORTEP plot diagram for the mCs-NaSCN complex (**V**).

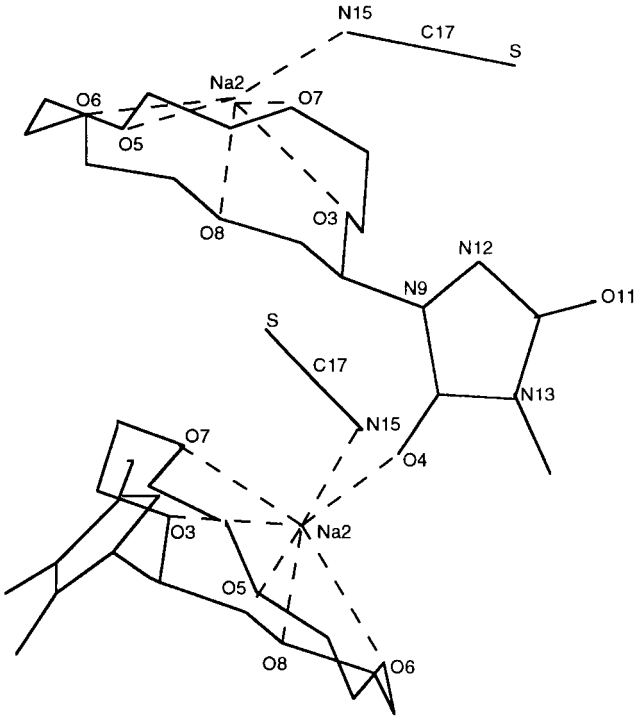


Figure 10. The interaction mode of the Na^+ ion in the mC5-NaSCN complex (**V**)

ring of a neighboring molecule $(1/2 + x, +y, 1/2 - z)$ and with the nitrogen atom of the SCN^- anion (see Figure 10).

The Na···O distance values (Table IV) for the six oxygen atoms involved in the complexation are slightly different (2.39–2.54 Å), and agree with the literature data [31].

4. Conclusions

The new crown ethers studied were found to form 1 : 1 complexes with NaSCN.

Substitution of 12C4 with the methylurazolyle group gave a different complex type, 1 : 1, the new crown ether analog obtained showing an important decrease of the complexation capacity towards sodium cation.

The NMR results obtained in solution for the 1 : 1 complex of mC5-NaSCN (**V**) have been confirmed by the single-crystal X-ray diffraction measurements.

For the usual 1 : 1 complexation of monocyclic crowns almost all carbon signals reveal upfield shifts [32]. It has been shown that the intensity of the upfield shifts on complexation depends initially on the extent of the conformational variations that take place for the effective formation of the complex [33–34].

Clearly, some additional experimental data are required in order to be able to comment further on the conformations of complex **V** compared with the uncom-

Table IV. Atomic bond distances (Å) for the for mC5-NaSCN complex (**V**)

Na(2)—O(3)	2.5462
Na(2)—O(4)*	2.4984
Na(2)—O(5)	2.3954
Na(2)—O(6)	2.5166
Na(2)—O(7)	2.4351
Na(2)—O(8)	2.5177
Na(2)—N(15)	2.5119

* The O(4) atom from the methylurazolyl cycle of a second molecule $(1/2 + x, +y, 1/2 - z)$.

plexed crown **IV**. Attempts are in progress to obtain the crystalline crown ether analogue **IV** in order to be able to carry out X-ray crystallographic studies.

Appendix

(A) *In the general case*, when both 1 : 1 and 1 : 2 complexes are present in the medium, the interaction between the ligand (L) and alkali metal ions (M) is defined by the equilibrium equations:

$$M + L \rightleftarrows LM \tag{1}$$

$$2L + M \rightleftarrows L_2M \tag{2}$$

and by the stability constants K_1 and K_2 associated with both complex types:

$$K_1 = [LM]/[L][M] \tag{3}$$

$$K_2 = [L_2M]/[L]^2[M] \tag{4}$$

If the exchange rate between the complexes and the isolated molecules is fast, the observed chemical shift δ_{obs} represents a weighted average of the chemical shifts corresponding to the three different species: the ligand (δ_L), the 1 : 1 complex (δ_{LM}) and the 1 : 2 complex (δ_{L_2M}). Then Equation (5) is valid:

$$\delta_{\text{obs}} = [L]/[L]_0 * \delta_L + [LM]/[L]_0 * \delta_{LM} + 2[L_2M]/[L]_0 * \delta_{L_2M} \tag{5}$$

where $[L]_0 = [L] + [LM] + 2[L_2M]$.

The induced chemical shift by complex formation $\Delta\delta_{\text{obs}} = \delta_{\text{obs}} - \delta_L$ is obtained from Equation (6):

$$\Delta\delta_{\text{obs}=[LM]/[L]_0} * \Delta\delta_{LM} + 2[L_2M]/[L]_0 * \Delta\delta_{L_2M} \tag{6}$$

where $\Delta\delta_{LM} = \delta_{LM} - \delta_L$ and $\Delta\delta_{L_2M} = \delta_{L_2M} - \delta_L$.

It can be observed that the induced chemical shift depends on the degree of transformation of the ligand into the 1 : 1 complex ($\alpha_1 = [LM]/[L]_0$) and the 1 : 2 complex ($\alpha_2 = 2[L_2M]/[L]_0$). The expansion of the stability constants K_1 and K_2 in terms of total degree of transformation of the ligand ($\alpha = \alpha_1 + \alpha_2$), and the initial ratio of the concentrations of the metal ion and ligand $X = [M]_0/[L]_0$ gives:

$$K_1 = \alpha_1/\{[X - -(\alpha + \alpha_1)/2](1 - \alpha)[L]_0\} \tag{7}$$

$$K_2 = (\alpha - \alpha_1)/\{2[X - (\alpha + \alpha_1)/2](1 - \alpha)^2[L]_0^2\} \tag{8}$$

The α_1 parameter can be individually evaluated as a function of K_1 and K_2 using Equations (7) and (8). When these expressions are made equal, the following third order equation results:

$$\alpha^3 - (2 + \mathbf{a} + 2X)\alpha^2 + [1 + \mathbf{a}(1 + \mathbf{b}) + (4 + \mathbf{a})X]\alpha - (2 + \mathbf{a})X = 0 \tag{9}$$

where $\mathbf{a} = K_1/(K_2[L]_0)$ and $\mathbf{b} = 1/(K_1[L]_0)$.

The real root of the Equation (9) gives a solution of physical significance. This can be obtained by using the following set of function $F1$—$F8$ (Equation (10)), written in *C* language:

$$\begin{aligned}
F1 &= -2/27 * (2 + \mathbf{a} + 2 * X)\,\hat{}\,3 + 1/3 * (2 + \mathbf{a} + 2 * X)(1 + \mathbf{a} \\
&\quad * (1 + \mathbf{b}) + (4 + \mathbf{a}) * X) - (2 + \mathbf{a}) * X \\
F2 &= 1 + \mathbf{a} * (1 + \mathbf{b}) + (4 + \mathbf{a}) * X - 1/3 * (2 + \mathbf{a} + 2 * X)\,\hat{}\,2 \\
&\quad \Delta = (F1/2)\,\hat{}\,2 + (F2/3)\,\hat{}\,3 \\
F3 &= IF(\Delta.GT.0, -F1/2 + SQRT((F1/2)\,\hat{}\,2 + (F2/3)\,\hat{}\,3), \\
&\quad SQRT((ABS(F2/3))\,\hat{}\,3)) \\
F4 &= IF(\Delta.LT.0, -F1/F3/2, 1) \\
F5 &= IF(\Delta.GT.0, -F1/2 - SQRT((F1/2)^2 + (F2/3)\,\hat{}\,3), \\
&\quad ACOS(F4)) \\
F6 &= IF(F3.LT.0, -(ABS(F3))\,\hat{}\,(1/3), ABS(F3)\,\hat{}\,(1/3)) \\
F7 &= IF(F5.LT.0, -(ABS(F5))\,\hat{}\,(1/3), ABS(F5)\,\hat{}\,(1/3)) \\
F8 &= IF(\Delta.GT.0, F6 + F7 + 1/3 * (2 + \mathbf{a} + 2 * X), \\
&\quad (2 * ABS(F3)\,\hat{}\,(1/3) * COS(F5/3 + 2/3 * PI)) \\
&\quad +1/3 * (2 + \mathbf{a} + 2 * X))
\end{aligned} \tag{10}$$

The solution $\alpha = F8(\mathbf{a}, \mathbf{b}, X)$ of Equation (9) allows one to derive the values for the degree of transformation of the ligand, α_1 and α_2:

$$\alpha_1 = (1 - F8)(2X - F8)/(2\mathbf{b} + (1 - F8)) \quad \text{and} \quad \alpha_2 = F8 - \alpha_1 \tag{11}$$

Now Equation (6) can be written as a function of $[M]_0/[L]_0$ having four parameters **a**, **b**, $\Delta\delta_{LM}$ and $\Delta\delta_{L_2M}$:

$$\begin{aligned}\Delta\delta_{\text{obs}} &= (1-F8)(2X-F8)/(2\mathbf{b}+(1-F8)) * \Delta\delta_{LM} \\ &\quad +((F8-(1-F8)(2X-F8))/(2\mathbf{b}+(1-F8)) * \Delta\delta_{L_2M} \quad (12)\end{aligned}$$

(B) *In the particular case* when only the 1 : 1 complex is formed, Equation (6) reduces to:

$$\Delta\delta_{\text{obs}} = \alpha_1 * \Delta\delta_{LM} \quad (13)$$

The stability constant K_1 is written as a function of α_1 and initial ratio X, yielding a second order equation:

$$\alpha_1^2 - (1+\mathbf{c}+X)\alpha_1 + X = 0 \quad (14)$$

where $\mathbf{c} = 1/(2K_1[L]_0)$.

The substitution of the real root α_1 in Equation (13) leads to the following two parameter (**c** and $\Delta\delta_{LM}$) theoretical function:

$$\begin{aligned}\Delta\delta_{\text{obs}} &= \{1/2+\mathbf{c}+X/2-[(1/2+\mathbf{c})^2+(\mathbf{c}+1/2)X+(X/2)^2]^{1/2} \\ &\quad * \Delta\delta_{LM} \quad (15)\end{aligned}$$

(C) *In the case* when only the 1 : 2 complex is formed, Equation (6) reduces to:

$$\Delta\delta_{\text{obs}} = \alpha_2 * \Delta\delta_{L_2M} \quad (16)$$

Expanding K_2 in terms of α_2 and X, a third equation is obtained:

$$\alpha_2^3 - 2(1+X)\alpha_2^2 + (1+4X+\mathbf{d})\alpha - 2X = 0 \quad (17)$$

where $\mathbf{d} = 1/(K_2[L]_0^2)$.

As in case (**A**) the following function set $F1$–$F8$ determines the root α_2 = F8(**d**, X) with physical significance of the Equation (17):

$$\begin{aligned}F1 &= -2X + 2/3 * (1+X) * (1+\mathbf{d}+4 * X) - 16/27 * (1+X)^3 \\ F2 &= 1+\mathbf{d}+4 * X - 4/3 * (1+X)^2 \\ \Delta &= (F1/2)\,\hat{}\,2 + (F2/3)\,\hat{}\,3 \\ F3 &= IF(\Delta.GT.0, -F1/2 + SQRT(\Delta), SQRT((ABS(F2/3))\,\hat{}\,3)) \\ F4 &= IF(\Delta.LT.0, -F1/F3/2, 1) \\ F5 &= IF(\Delta.GT.0, -F1/2 + SQRT(\Delta), ACOS(F4)) \\ F6 &= IF(F3.LT.0, -(ABS(F3))\,\hat{}\,(1/3), ABS(F3)\,\hat{}\,(1/3)) \\ F7 &= IF(F5.LT.0, -(ABS(F5))\,\hat{}\,(1/3), ABS(F5)\,\hat{}\,(1/3)) \\ F8 &= IF(\Delta.GT.0, F6+F7+2/3 * (1+X), (2 * ABS(F3)\,\hat{}\,(1/3) \\ &\quad * COS(F5/3+2/3 * PI)) + 2/3 * (1+X)) \\ \alpha_2 &= F8(\mathbf{d}, X) \quad (18)\end{aligned}$$

and Equation (16) is written as a function of X, having two parameters **d** and $\Delta\delta_{L_2M}$

$$\Delta\delta_{\text{obs}} = F8 * \Delta\delta_{L_2M} \tag{19}$$

The experimental titration curves $\Delta\delta_{\text{obs}} = f(X)$, obtained by changing $[M]_0$ while $[L]_0$ is kept constant, can be fitted using theoretical functions (12), (15) or (19) as a user function into an iterative fitting program based on the least squares method. This permits the determination of the stability constants and the relative chemical shifts for 1 : 1 and 1 : 2 complexes.

References

1. C. J. Pedersen: *Angew. Chem. Int. Ed. Engl.* **27**, 1021 (1988).
2. J. M. Lehn: *Angew. Chem. Int. Ed. Engl.* **27**, 90 (1988); *Supramolecular Chemistry*, 1st edn, VCH Verlagsgesellschaft (1995).
3. D. J. Cram: *Angew. Chem. Int. Ed. Engl.* **27**, 1009 (1988).
4. L. F. Lindoy: *The Chemistry of Macrocyclic Ligand Complexes*, Cambridge University Press, Cambridge (1989).
5. S. Stoss, E. Kleinpeter, and H. J. Holdt: *Mag. Reson. Chem.* **29**, 999 (1991).
6. G. Gokel: *Crown Ethers and Cryptands*, Royal Society of Chemistry, Cambridge (1991).
7. S. Stoss, W. Schroth, and E. Kleinpeter: *Mag. Reson. Chem.* **30**, 425 (1992).
8. R. M. Izatt, K. Pawlak, J. S. Bradshaw, and R. L. Bruening: *Chem. Rev.* **91**, 1721 (1991).
9. F. W. Wehrli and S. Wehrli: *J. Magn. Reson.* **44**, 197 (1981).
10. E. Schmidt, A. Hourdakis, and A. I. Popov: *Inorg. Chim. Acta* **52**, 91 (1981).
11. M. Shamsipur and A. I. Popov: *J. Am. Chem. Soc.* **101**, 4051 (1979).
12. A. M. Alstanei: Ph.D. Thesis, Bucharest (1998).
13. G. Gokel, D. Goli, C. Minganti, and L. Echegoyen: *J. Am. Chem. Soc.* **105**, 6786 (1983).
14. D. Diamond, M. I. Cinoman, and G. N. Gokel: *J. Am. Chem. Soc.* **105**, 586 (1983).
15. G. Gokel: *Chem. Rev.* **21**, 39 (1992).
16. E. Amble and E. Amble: *Polyhedron* **2**, 1063 (1983).
17. D. Salvatierra, C. Diez, and C. Jaime: *J. Incl. Phenom.* **27**, 215 (1997).
18. R. D. Rogers, A. H. Bond, W. G. Hipple, A. N. Rollins, and R. F. Henry: *Inorg. Chem.* **30**, 2671 (1991).
19. E. A. Babaian, M. Huff, F. A. Tibbals, and D. C. Hrncir: *J. Chem. Soc. Chem. Commun.* 306 (1990).
20. J. Krane, E. Amble, J. Dale, and K. Daasvatn: *Acta Chem. Scand.* **B34**, 255 (1980).
21. M. Buschamann: *J. Solution Chem.* **16**, 181 (1987).
22. J. Massaux, J. Desreux, and G. Duyckaerts: *J. Chem. Soc., Dalton Trans.* 865 (1980).
23. B. L. Haymore, J. D. Lamb, R. M. Izatt, and J. J. Christensen: *Inorg. Chem.* **21**, 1598 (1982).
24. J. Lamb, R. Izatt, C. Swain, and J. Christiensen: *J. Am. Chem. Soc.* **102**, 475 (1980).
25. K. Ruhlandt-Senge and U. Muller, *Acta Crystallogr. C* **47**, 182 (1991).
26. K. Arnold, L. Echegoyen, and G. Gokel: *J. Am. Chem. Soc.* **109**, 3713 (1987).
27. A. W. Coleman, F. Villain, A. Navaza, H. Galons, and M. Miocque: *J. Incl. Phenom.* **10**, 423 (1991).
28. D. Dishong and G. Gokel: *J. Am. Chem. Soc.* **105**, 586 (1983).
29. A. C. Coxon, D. A. Laidler, R. B. Pettman, and J. F. Stoddart: *J. Am. Chem. Soc.* **100**, 8260 (1978).
30. M. J. Bovill, D. J. Chadwick, and I. O. Sutherland: *J. Chem. Soc., Perkin Trans. 2*, 1529 (1980).

31. P. Groth: *Acta Chem. Scand.* **A 35**, 721 (1981).
32. E. Kleinpeter, S. Stos, M. Gabler, and W. Schroth: *Magn. Reson. Chem.* **27**, 676 (1989).
33. J. Dale: *Isr. J. Chem.* **20**, 3 (1980).
34. G. W. Buchanan, V. M. Reynolds, K. Bourque, and C. Bensimon: *J. Chem. Soc. Perkin Trans. 2* 707 (1995).