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Solvent Extraction Studies of New *bis*-Sulfonamide Group-Containing Podands

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Abstract. A number of new open chain *bis*-sulfonamides with 2, 3 and 4 ether oxygen atoms were synthesized and their Na^+ and K^+ extractability was tested. For these types of ligands, both sulfonamide protons are ionized and two aqueous phase cations are complexed in the extraction. The ligand–cation complexes are composed of the ligand in a dianion form, a metal cation and tetramethylammonium hydroxide (TMA) as the co-cation in a ratio of 1 : 1 : 1 when TMA is present, or of ligand and metal cation in a ratio of 1 : 2 when only metal hydroxide is present in the aqueous solution. The influence of different substituents on the phenyl amide group on extractability and extraction selectivity was investigated. An X-ray crystal structure was obtained for the podand containing four ether oxygen atoms. The properties of open-chain ligands were compared with the analogous macrocyclic compounds.

Key words. Solvent extraction, sodium, potassium, sulfonamide, crystal structure.

1. Introduction

Macrocyclic ligands containing proton-ionizable sulfonamide groups as part of a macroring cavity have been studied [1–4] and found to be effective transport agents for alkali metal cations [3, 4]. These ligands also possess ionophoric ability and have been studied in ion-selective membrane electrodes [5, 6]. Generally, polydentate macrocyclic ligands form more stable complexes than the corresponding open chain ligands. This phenomenon is known as the 'macrocyclic effect'. Occasionally, however, the noncyclic ligands appear to be superior complexing agents as compared to the analogous macrocyclic compounds as determined by ion extraction studies or by membrane transport experiments [7, 8]. This paper describes the synthesis of open chain *bis*-sulfonamide compounds **1–14** (Scheme 1) and a study of their cation selectivity in solvent extraction. Also, the cation extractability of the open chain ligands is compared with that of the analogous macrocyclic compounds **15** and **16** (Figure 1).

2. Experimental

Infrared (IR) spectra were obtained on a Beckman Acculab 2 spectrometer. The proton nuclear magnetic resonance (NMR) spectra were obtained on a JEOL

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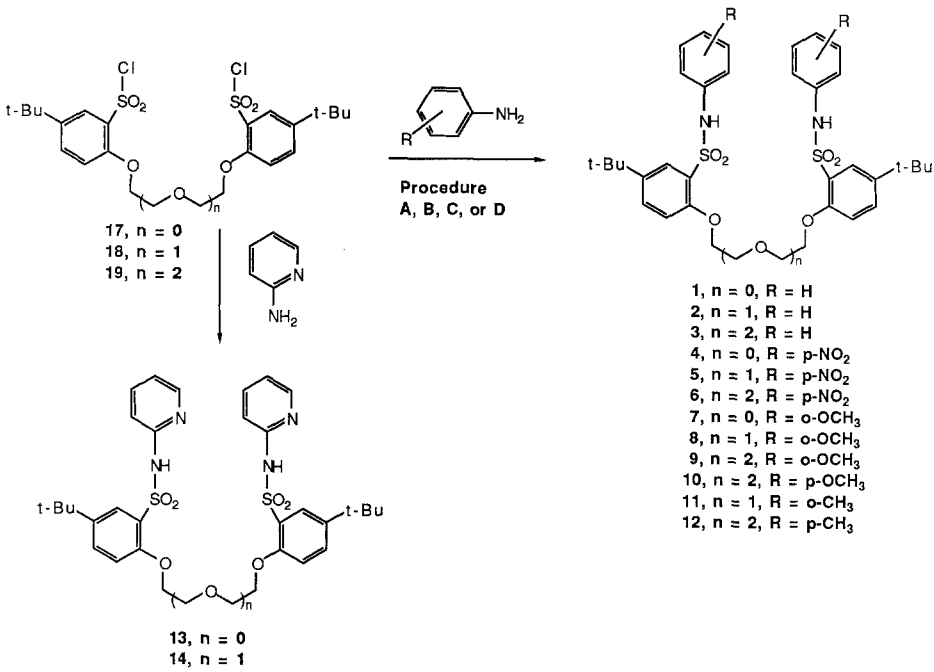

Scheme 1. Preparation of New *bis*-Sulfonamides.

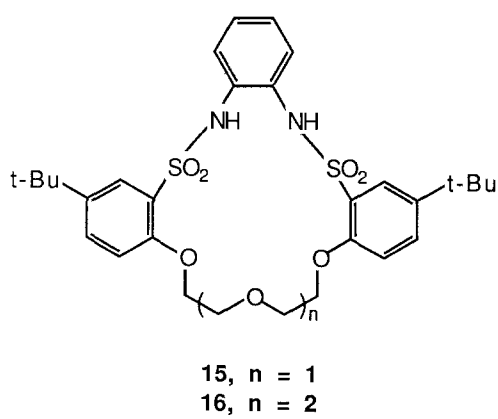

Fig. 1. Macrocylic *bis*-Sulfonamides.

FX-90Q spectrometer in $CDCl_3$ (Aldrich). Elemental analyses were performed by MHW Laboratories, Phoenix, Arizona. Melting points were taken on a Thomas-Hoover melting point apparatus and are uncorrected. Starting sulfonyl chlorides **17**, **18** and **19** (see Scheme 1) were prepared as reported in [1, 2]. The substituted anilines and aminopyridines were used as purchased from Aldrich. All other organic reagents and solvents used for the synthetic and solvent extraction work were

reagent grade and were used as purchased (KOH from Spectrum, NaOH from Anachemica – carbonate free, TMA from Aldrich and HNO_3 and CH_2Cl_2 from Fisher).

2.1. PREPARATION OF *BIS*-SULFONAMIDES **1–14** (SCHEME 1)

The *bis*-sulfonamides were prepared as follows.

Procedure A: A 15 mL solution containing 2 mmoles of *bis*-sulfonyl chloride **17**, **18**, or **19**, 4 mmoles of the appropriate amine and 4 mmoles of dry pyridine in dry toluene were refluxed for about 2 h. The solution was cooled, washed with 10 mL of 1M aqueous hydrochloric acid followed by 10 mL of water, dried over anhydrous magnesium sulfate and the solvent was removed under reduced pressure to give the crude product. The product was recrystallized from the appropriate solvent. See Table I for the solvent conditions, yields and physical properties of the new *bis*-sulfonamides.

Procedure B: *bis-p*-Nitroanilide **4** was prepared using equivalent amounts of *bis*-sulfonyl chloride **17** and *p*-nitroaniline in dry pyridine. The product crystals separated when the solution was allowed to stand overnight.

Procedure C: Triethylamine and benzene were used rather than pyridine and toluene as in Procedure A. The solution was refluxed for 5 h and left standing for 20 h. The product was isolated by silica gel chromatography using methylene chloride/acetone in a 1/1 volume ratio as eluant.

Procedure D: A two-fold excess of the amine was used in benzene or methylene chloride. The mixture was refluxed for 20 h. The precipitated amine hydrochloride was filtered and the filtrate was evaporated under reduced pressure. The oily residue crystallized upon adding ethyl ether.

Compounds **15** and **16** (Figure 1) were obtained as described in [1, 3].

2.2. X-RAY STRUCTURAL DETERMINATION OF **9**

A suitable crystal of **9**, crystallized from isopropyl alcohol, was mounted on a Nicolet R3 automated diffractometer which used graphite monochromated Mo K_α radiation ($\lambda = 0.71073$ Å). The lattice parameters and orientation matrix were calculated using a least-squares procedure involving 22 carefully centered reflections with $7.95 < 2\theta < 17.4$. Crystal data and experimental conditions for intensity data collection and the structure solution are summarized in Table II. A variable scan rate $\theta - 2\theta$ scan procedure was used to measure the intensities. The structure was solved using the direct method program SOLV. All computer programs used in the solution, refining and displaying of the structure are contained in the SHELXTL [9] program package. The difference map showed the presence of a disordered solvent molecule located about a center of inversion. The fact that the solvent molecule was disordered and its atoms had large thermal motion explains the difficulty in finding all of the nonhydrogen atoms in the map. Only three of the four atoms were found.

In the refinement process, all benzene groups were considered as rigid bodies. Disorder in the tertiary butyl group bonded to benzene, C(B31)—C(B36), was resolved using a difference map. It was also possible to resolve the disorder for the methoxy carbon associated with the C(B41)—C(B46) benzene. Positions for

Table I. Yields and physical properties of compounds **1–14**[a]

Compd.	Method of synthesis (solvent)	Yield (%)	Solvent for crystal	m.p. [°C]	IR(NH) [cm^{-1}]	NMR Spectra (δ) [ppm]
1	A (Tol)	63	Tol	205–06	3280	1.28(*s*, 18 H), 4.5(*s*, 4 H), 7.05(*d*, 2 H) 7.15(*m*, 10 H), 7.45(2*d*, 2 H), 7.95 (*d*, 2H), 8.45[b](*s*, 2 H)
2[c]	C (CH_2Cl_2)	25	AcOH	173–75	3280	1.2(*s*, 18 H), 3.93(*m*, 4 H), 4.23(*m*, 4 H), 6.9–8.33(*m*, 16 H), 9.7[b](*s*, 2 H)
3	D (Bnz)	50	EtOEt	170–71	3300	1.24(*s*, 18 H), 3.72(*s*, 8 H), 4.16(*m*, 4 H) 6.76–7.7(*m*, 16 H), 7.95[b](*s*, 2 H)
4	B (Pyr)	33	Pyr	261–63	3260	1.28(*s*, 18 H), 4.50(*s*, 4 H), 7.05(*d*, 2 H), 7.20(*d*, 4 H), 7.63(2*d*, 2 H) 8.03(*d*, 4 H), 8.15(*d*, 2 H), 9.15[b](*s*, 2 H)
5	A (Tol)	80	MeOH	213–15	3310	1.28(*s*, 18 H), 4.15(*m*, 4 H), 4.35(*m*, 4 H), 6.85(*d*, 2 H), 7.25(*d*, 4 H), 7.5(2*d*, 2 H) 7.9(*d*, 2 H), 7.95(*d*, 4 H) 8.35[b](*s*, 2 H)
6	C (Bnz)	40	Acetone	158–59	3250	1.30(*s*, 18 H), 3.95(*s*, 8 H), 4.3(*s*, 4 H), 6.9(*d*, 2 H), 7.45(*m*, 6 H), 7.82(*s*, 2 H), 8.02(*d*, 4 H), 8.55[b](*s*, 2 H)
7	A (Tol)	57	AcCN	213–15	3290	1.2(*s*, 18 H), 3.5(*s*, 6 H), 4.55(*s*, 4 H), 6.5–7.8(*m*, 14 H), 7.55[b](*s*, 2 H)
8	A (Tol)	60	*i*-PrOH	134–35	3275	1.2(*s*, 18 H), 3.6(*s*, 6 H), 4.05(*m*, 4 H), 4.2(*m*, 4 H), 6.5–7.0(*m*, 8 H) 7.25–7.5, (*m*, 4 H), 7.65[b](*s*, 2 H), 7.7(*d*, 2 H)
9	A (Bnz, 24 h)	50	*i*-PrOH	67–9	3220 3300	1.24(*s*, 18 H), 3.6(*s*, 6 H), 3.72(*s*, 4 H), 3.86(*m*, 4 H), 4.15(*m*, 4 H), 6.6–7(*m*, 8 H), 7.28–7.48(*m*, 4 H), 7.76[b](*s*, 2 H)
10	A (Bnz, 30 h)	71.5	Acetone	176–77	3280	1.20(*s*, 18 H), 3.6(*s*, 6 H), 3.67(*s*, 8 H), 4.2(*s*, 4 H), 6.72(*d*, 4 H), 6.87(*d*, 2 H), 7.13(*d*, 4 H), 7.45(*d*, 2 H), 7.62(*s*, 2 H), 7.85[b](*s*, 2 H)
11	A (Tol)	60	*i*-PrOH	153–55	3320	1.25(*s*, 18 H), 2.25(*s*, 6 H), 4.00(*m*, 4 H), 4.15(*m*, 4 H), 6.7(*d*, 2 H), 6.85–7.05(*m*, 8 H), 7.15[b](*s*, 2 H), 7.4(2*d*, 2 H), 7.7(*d*, 2 H)
12	A (Bnz)	73	MeOH	188–90	3250	1.2(*s*, 18 H), 2.2(*s*, 6 H), 3.48(*s*, 8 H), 4.04(*m*, 4 H), 6.8–7.66(*m*, 14 H), 7.86[b](*s*, 2 H)
13	A (Tol)	40		272–74	d	1.30(*s*, 18 H), 4.20(*s*, 4 H), 6.75–8.15(*m*, 16 H)
14	A (Tol)	80	DMF	250–51	d	1.24(*s*, 18 H), 4.05(*m*, 4 H), 6.72–7.2(*m*, 6 H), 7.4–8.1(*m*, 10 H)

[a] All new compounds gave a satisfactory combustion analysis (0.3%).
[b] Signal disappeared upon addition of D_2O.
[c] Prepared as in Ref. [3].
[d] *N*-Pyridylsulfonamides do not exhibit the normal N—H band between 3100 and 3400 cm^{-1} [18]

Table II. Crystal and experimental data for **9**

Formula	$C_{40}H_{52}N_2O_{10}S_2 \cdot (CH_3)_2CHOH$
Formula weight	845.20
$F(000)$	1808
Crystal Size, mm	$0.4 \times 0.3 \times 0.3$
Space group	$P2_1/a$
a, Å	16.183(6)
b, Å	16.391(6)
c, Å	17.646(7)
β, deg.	106.84(3)
V, Å^3	4480(3)
Z	4
d_x, g/cc	1.25
d_{ob}, g/cc	1.22
μ, cm^{-1}	1.63
$\sin\theta/\lambda$	0.50
Total unique data	4591
observed	2360
R_m	0.016(57)
R	0.10
R_w	0.13
GOF	1.62
Max and min. peaks in the ΔF map	0.58, −0.40

hydrogen atoms bonded to carbon atoms in the benzene rings and in the O—C—C—O groups were calculated based on known molecular geometry. These atoms were allowed to ride on their bonded carbon atoms and their isotropic thermal parameters were set equal to 1.2 times the initial equivalent isotropic thermal parameter of the bonded carbon atoms and were not refined. Positions for hydrogen atoms of methoxy carbons and tertiary butyl carbons were not included in the calculations and these carbon atoms and O(2ME) were refined isotropically. The remaining heavy atoms of **9** were refined anisotropically. The three partial atoms of the solvent molecule were also refined isotropically. It was possible to locate the hydrogen atom bonded to N(1) in a difference map but not the one bonded to N(14). Atomic scattering factors were obtained from Volume 4 of the *International Tables for X-Ray Crystallography* [10].

2.3. EXTRACTION EXPERIMENTS

Single and competitive extraction of Na^+ and K^+ from H_2O to CH_2Cl_2 using the synthesized podands as extraction agents was assessed. Aqueous sodium and potassium hydroxide solutions were used. Distilled, deionized water was used in all experiments. The ligands were dissolved in methylene chloride. The extraction experiments were performed at 22°C by stirring 4 mL of the aqueous phase with 4 mL of the organic phase for 30 minutes [11–13]. Several experiments using 1 mM, 3 mM, or 5 mM solutions of ligands in CH_2Cl_2 and aqueous solutions of varying pH values were performed. The following aqueous solutions were used:

(a) Aqueous 5 mM NaOH or KOH with TMA (tetramethylammonium hydroxide) in distilled deionized water. Varying amounts of TMA were used to adjust the pH to values of either 14, 13 or 12. Solutions of pH 12 were checked for pH with a glass–reference combination electrode (Sargent Welch). The pH 13 and 14 solutions were assumed to be pH 13 or 14 from the amount of TMA added and approximate pH measurements.
(b) Aqueous mixtures of NaOH, KOH, TMA (concentrations: 5 mM, 5 mM, 1 M, respectively) were used in competitive extraction experiments with ligands **1**, **3**, **7**, **11** and **16**.
(c) Either aqueous 0.5M NaOH or 0.5M KOH in deionized distilled water (pH $\approx$ 13.7) was used in experiments with ligands **3**, **15** and **16**.
(d) Aqueous mixtures (1 : 1) of 1M NaOH and 1M KOH were used in experiments with ligands **3**, **15** and **16**.

Compounds **13** and **14** are insoluble in methylene chloride and were not used for extraction experiments.

Upon equilibration, the two phases were allowed to separate for about 2 h. For experiments a and b [using solutions (a) and (b) with TMA present], a portion of the aqueous phase was analyzed for the appropriate metal by atomic absorption spectrophotometry. The concentration of the metal in the aqueous phase before extraction was established in the same way. The amount of TMA extracted into the organic phase was established by a proton-NMR method in the following manner. First, the organic layer, after being carefully separated, was evaporated to dryness and $CDCl_3$ was added. Second, the relative amounts of TMA and the ligand were determined from the ratio of the NMR peaks at $\delta = 3.2$ (TMA) and $\delta = 4.1$ (ligand).

The extractabilities (f, defined as the fraction of the total amount of metal ion originally present which is extracted into the organic phase) for Na^+ and K^+ with each ligand were calculated from three separate experiments, at the appropriate pH value. The distribution ratio of the metal ion between organic and aqueous phases (D_{M+}) for each experiment with TMA present was calculated as follows (Equation 1):

$$D_{M+} = \frac{[M \cdot TMA \cdot H_{2n-2}L_{n,org}]}{[M^+_{aq}]} = \frac{f}{1-f} \tag{1}$$

Such extraction studies were carried out at 3 different ligand concentrations (1, 3 and 5 mM) and enabled the determination of the ligand to cation complex stoichiometry [12, 13]. A 1 : 1 ligand : M^+ stoichiometry existed in each complex. Several examples of the log D_{M+} vs. log (ligand concentration) plots yielding a slope of 1 are given in Figure 2.

It was also found that the amount of the TMA extracted into the CH_2Cl_2 phase was the same as the amount of Na^+ or K^+ extracted by the ligand (for example, for **11**, $f_{K+} = 40\%$, $f_{TMA} = 38 \pm 4\%$). The same experiment carried out with a blank organic layer showed no extraction of either TMA or K^+. In an experiment with no metal cation but 1M TMA in the aqueous solution, the TMA extracted into the organic phase by **11** (0.005M) was equivalent to only 15% of the amount of the ligand. This amount is much smaller than that extracted with either K^+ (40%) or

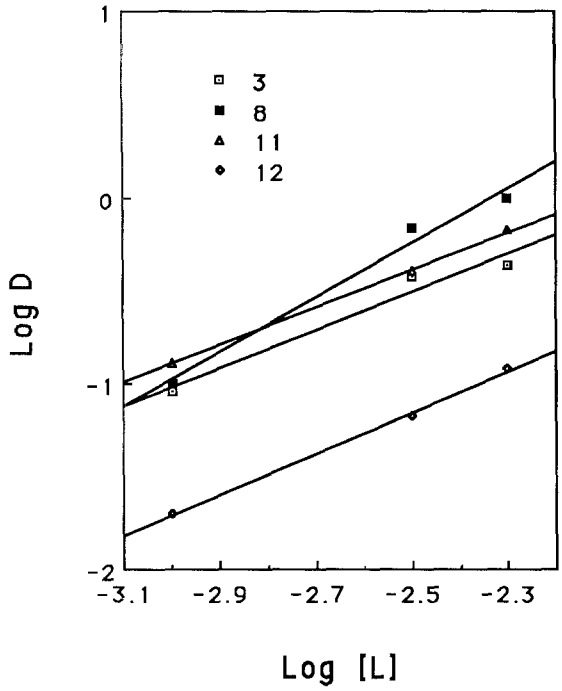

Fig. 2. Plot of log D (distribution ratio) versus log $[L]_{org}$ for the solvent extraction of K^+ in the presence of TMA with ligands **3**, **8**, **11**, **12** (experiment a).

Na^+ (78%) also present in the aqueous phase. In an experiment of type b with **3**, the amount of TMA extracted into the organic phase ($10 \pm 1\%$) was the same as the sum of Na^+ and K^+ ions (9.9%) extracted. The extraction equilibrium constant expression (K_{ex}) for Equation (2), where H_2L is a ligand with two ionizable protons, can be formulated as Equation (3). Equations (1) and (3) are combined to form Equation (4).

$$M^+_{aq} + TMA^+_{aq} + H_2L_{org} = M^+ \cdot TMA^+ \cdot H_{2n-2}L_{n,org} + 2\,H^+_{aq} \tag{2}$$

$$K_{ex} = \frac{[M \cdot TMA \cdot H_{2n-2}L_n]_{org}[H^+]^2_{aq}}{[M^+]_{aq}[TMA^+]_{aq}[H_2L]^n_{org}} \tag{3}$$

In Equation (4) $C = K_{ex} \cdot [TMA^+]/[H^+]^2 = \text{const.}$ since the excess amounts of TMA and OH^- allow for nearly constant pH values and TMA concentrations to be maintained in the experiments under consideration.

$$\log D_{M^+} = \frac{[M \cdot TMA \cdot H_{2n-2}L_n]}{[M^+]} = n \cdot \log[H_2L]_{org} + \log C \tag{4}$$

A least squares linear regression analysis allowed the values of log C and the accompanying standard deviations to be determined from plots like those in Figure 2.

For experiments c and d (no TMA present), after separation of the two layers, the cations were re-extracted from the organic phase into aqueous 0.1M HNO_3. The water phase was then analyzed for the appropriate metal ion by atomic absorption spectrophotometry. In the experiment with **7** (5 mM solution) where only one cation was present in high concentration (1M solution of potassium ion), over 90% of the ligand molecules were involved in the extraction with the ligand : metal cation ratio being 1 : 2. Hence, extractions performed without TMA present can be described by Equations (5) and (6).

$$2\,M^+_{aq} + H_2L_{org} = M_2L_{org} + 2\,H^+_{aq} \tag{5}$$

$$K_{ex} = \frac{[M_2L]_{org}[H^+]^2_{aq}}{[M^+]^2_{aq}[H_2L]_{org}} \tag{6}$$

3. Results and Discussion

The purpose of this study was to investigate Na^+ and K^+ solvent extraction mediated by the open-chain *bis*-sulfonamide compounds in the presence and absence of TMA and to determine the nature of the extractive complex. We were also interested in comparing the extractive complexation behavior of the open chain and macrocyclic *bis*-sulfonamides.

The structural study of **9** was initiated to obtain the conformation of the molecule in order to better understand the changes that must occur during the complexation process. A computer drawn representation of the molecule is shown in Figure 3. The bond lengths and angles for the atoms in the chain portion of **9** are listed in Table III. For clarity, the disordered atoms in the less populated sites of the tertiary butyl group bonded to the C(31)—C(36) benzene were omitted in Figure 3 as were C(2MB), a disordered methoxy carbon on the C(B41)—C(B46) benzene, the solvent molecule and all the hydrogen atoms. The molecule has a linear

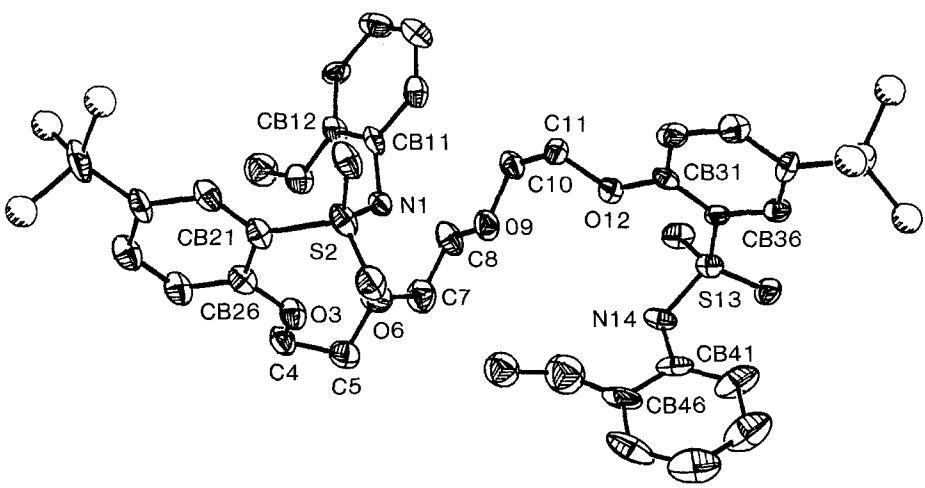

Fig. 3. Computer drawing of **9** with hydrogen atoms, the solvent molecule and one of each disordered atoms omitted for clarity.

Table III. Selected bond lengths and angles and torsion angles in **9** with e.s.d. values in parentheses

1	2	3	1–2(Å)	1–2–3 (deg.)
C(B11)	N(1)	S(2)	1.45(1)	121.0(7)
N(1)	S(2)	C(B21)	1.620(9)	107.4(4)
S(2)	C(B21)		1.753(9)	–
C(B26)	O(3)	C(4)	1.36(1)	118.1(8)
O(3)	C(4)	C(5)	1.42(1)	107(1)
C(4)	C(5)	C(6)	1.49(2)	107(1)
C(5)	O(6)	C(7)	1.42(2)	117(1)
O(6)	C(7)	C(8)	1.40(2)	111(1)
C(7)	C(8)	O(9)	1.44(3)	113(1)
C(8)	O(9)	C(10)	1.37(2)	113(1)
O(9)	C(10)	C(11)	1.43(2)	110(1)
C(10)	C(11)	O(12)	1.48(2)	108(1)
C(11)	O(12)	C(B31)	1.44(2)	119.2(9)
O(12)	C(B31)		1.37(1)	–
C(B36)	S(13)	N(14)	1.73(1)	105.9(4)
S(13)	N(14)	C(B41)	1.65(1)	122.0(9)
N(14)	C(B41)		1.44(1)	–
O(S1)	S(2)	O(S2)	1.42(1)	120.4(5)
O(S2)	S(2)		1.419(9)	–
O(S3)	S(13)	O(S4)	1.451(8)	119.0(5)
O(S4)	S(13)		1.416(9)	–

Torsion Angles (deg.)

O(3)—C(4)—C(5)—O(6)	−61(1)
C(4)—C(5)—O(6)—C(7)	−157(1)
C(5)—O(6)—C(7)—C(8)	−180(1)
O(6)—C(7)—C(8)—O(9)	70(2)
C(7)—C(8)—O(9)—C(10)	−177(1)
C(8)—O(9)—C(10)—C(11)	−178(1)
O(9)—C(10)—C(11)—O(12)	71(1)

arrangement with a large degree of flexibility in the backbone chain. The nitrogen atoms are far apart but it appears that the molecule could easily wrap around a metal cation. Unfortunately, it has not been possible to grow crystals of metal ion complexes of any of these podands.

The macrocyclic compounds (**15** and **16**) analogous to these podands require both protons to be ionized in order to form extractive complexes [1–4]. The open chain ligands **1**–**12** also require high pH values (pH = 14) in the aqueous phase in order for extraction of alkali metal cations to occur. Apart from ligands **4**–**6**, the extraction of Na^+ and K^+ from an aqueous phase of pH = 13 and lower was negligible. This fact provides further support for the idea that both protons must be ionized for complex formation with alkali cations since pK_{a_1} for these *bis*-sulfonamides should be about 9 [14] and pK_{a_2} should be about 3 pK_a units higher than pK_{a_1}. Ligands **4**–**6**, which extracted metal ions at pH values down to 12, possess

strong electron withdrawing nitro groups in the para positions of the *N*-phenyl units which would cause the sulfonamides to be more acidic [14]. The pK_{a_1} value to remove the first proton in nitro ligands **4**–**6** should be about 7.5–8 and pK_{a_2} about 3 pK_a units higher [14]. Hence, it appears that both protons need to be ionized in order to form alkali metal cation complexes with these ligands as well.

Our results confirm that when TMA is present, the extractive *bis*-sulfonamide ligand–metal ion complexes were composed of the ligand in a dianion form, a metal cation and a TMA cation in a ratio of 1 : 1 : 1. After ionization of both protons, we believe that a complex of the ligand with one metal cation is formed where the ligand is wrapped around the cation, and one TMA cation is associated with the 1 : 1 complex outside the pseudocavity as a cocation. This neutral species would be readily extracted into the organic phase. Without the metal cation, the ligand conformation, possibly linear (see the above crystal structure determination of **9**), does not match the size of the large TMA cation which makes complex formation with two TMA molecules relatively difficult. This is confirmed by the fact that only a small amount of TMA is extracted by these ligands without K^+ or Na^+ being present (see experimental section). The partition coefficient for TMA between water and the organic solvent (methylene chloride) without a complexing ligand present is negligible. In a blank extraction experiment, TMA was not detected in the organic layer.

The log *C* values (see experimental section) for Na^+ and K^+ in the presence of TMA (type a experiments) for each of the ligands studied are given in Table IV. A comparison of selectivity for K^+ over Na^+ of the ligands **1**–**9**, expressed as the

Table IV. Log C^a values for the extractions of Na^+ and K^+ by **1**–**12**, **15**, **16** carried out in the presence of TMA[b]

	log *C*	
Ligand	Na^+	K^+
1	1.4 ± 0.2	0.7 ± 0.1
2	2.3 ± 0.1	1.9 ± 0.2
3	0.8 ± 0.1	2.1 ± 0.1
4	2.0 ± 0.3	2.6 ± 0.3
5	3.1 ± 0.1	2.9 ± 0.2
6	2.4 ± 0.1	2.5 ± 0.1
7	2.5 ± 0.1	1.9 ± 0.2
8	2.5 ± 0.1	2.4 ± 0.1
9	1.0 ± 0.1	1.9 ± 0.1
10	1.5 ± 0.1	1.6 ± 0.2
11	3.5 ± 0.1	2.5 ± 0.1
12	1.3 ± 0.1	1.3 ± 0.1
15	1.4 ± 0.1	1.2 ± 0.1
16	1.3 ± 0.1	1.3 ± 0.1

[a] $C = K_{ex}[1M\ TMA]/([1 \times 10^{-14}\ M\ H^+])^2$ for $M^+_{aq} + TMA^+_{aq} + H_2L_{org} = complex_{org} + 2H^+_{aq}$.
[b] Tetramethylammonium cation.

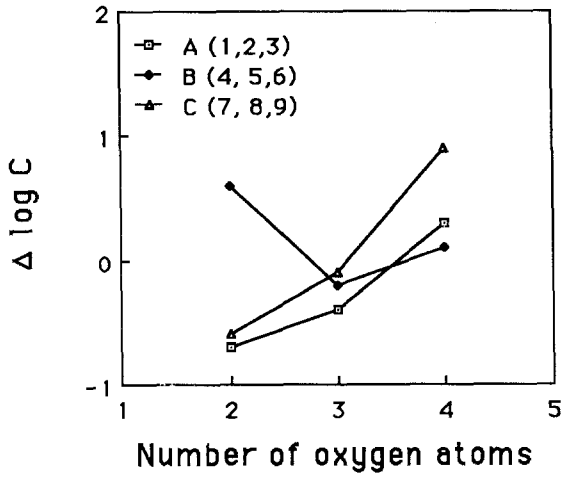

Fig. 4. Plot of ion selectivities (Δ log *C*) obtained from experiments (a) (with TMA as cocation) as a function of the number of oxygen atoms in the polyether chain.

difference in the log *C* values as a function of the number of oxygen atoms in the polyether chain, is shown in Figure 4. Curve A concerns the unsubstituted *N*-phenyl ligands, curve B has *p*-nitro substituents and curve C has *o*-methoxy substituents on the *N*-phenyl groups. Although ligands containing three oxygen atoms in the chain (where $n = 1$) have good extractabilities (large log *C* values) in each case, they show little selectivity between sodium and potassium (Δ log *C* is small). Ligands with four oxygen atoms ($n = 2$) show K^+ selectivity (Δ log *C* is >0), while ligands with two oxygen atoms ($n = 0$) show Na^+ selectivity in the unsubstituted and *o*-methoxy substituted forms. This selectivity probably is due to a pseudocavity–cation size fit. However, the *para*-substituted ligands (**4–6, 10, 12**) show little selectivity no matter how many oxygen atoms are present. The nitro-substituted podands (**4–6**) all exhibited good extractabilities due to their higher acidity as expected. The lack of a decrease in extractability in substituting electron donating methoxy groups into the *ortho*-position is interesting. This factor can be observed by comparing log *C* values for ligands **1–3** with those for **7–9**. Probably, the methoxy oxygen atoms in the *ortho* positions are involved in complexation with the cations and the increased binding strength of the extra donor atoms offsets the slight decrease in acidity of the ligands.

Little extraction selectivity between K^+ and Na^+ was observed with sulfonamide macrocycles **15** and **16** with TMA as cocation. The smaller macrocycle showed a slight preference for Na^+ as one might expect, but the differences in the log *C* values are much greater for the analogous open-chain compounds.

The selectivities observed in competitive K^+ *vs.* Na^+ extractions in the presence of TMA are readily predicted from the log *C* values for single alkali cation extraction. This observation is illustrated for ligands **1**, **7**, **11**, and **16** in Table V. The similar selectivities in both the single and competitive extractions are readily apparent. The comparisons are seen to be even more exact when the amount of extraction in the competitive experiments are predicted from solving simultaneously

Table V. Comparison of the fraction (f) of K^+ and Na^+ extracted in single cation and competitive experiments with TMA present.[a]

Ligand		f Values (%)			
		Single		Competitive	
#	Concentration (mM)	Na^+	K^+	Na^+	K^+
1	5	10.0	2.4	6.3	2.0
3	5	2.3	30.9	–	–
7	5	40.8	16.4	38.1	13.1
11	5	78.0	40.0	58.5	19.3
16	5	8.9	8.3	10.2	10.1

[a] TMA = Tetramethylammonium cation. Aqueous phase contained 5 mM NaOH or 5 mM KOH or 5 mM of each and 1M TMA. Organic solvent was methylene chloride.

the K^+ and Na^+ log C expressions using the log C values determined from the single alkali cation extractions. The $Na^+ : K^+$ f values are predicted (based on log C data in Table IV) to be 9.9 : 2.2, 42 : 15, 69 : 18, and 8 : 8 for ligands **1**, **7**, **11**, and **16**, respectively. The ability to predict competitive alkali cation extractions from single cation extraction data, despite the experimental error in the single extractions, is further evidence for the idea that the alkali cation is complexed in the pseudocavity of the podand while the lipophilic TMA cation is coextracted outside the pseudocavity.

When TMA is not present to act as a cocation, extraction selectivity between Na^+ and K^+ using these podands disappears. An example of this can be seen from the data of Table VI for the extraction experiments of type c and d using podand **3**. It is most interesting that in the presence of TMA, **3** is selective for K^+ over Na^+ (see Tables IV and V), while in the absence of TMA, **3** lost its selectivity (see Table VI). This suggests that Na^+ is acting as the cocation when the lipophilic TMA is

Table VI. Extraction of Na^+ and K^+ in single cation and competitive experiments[a] without TMA being present.

Ligand		Concentration extracted			
		Single		Competitive	
#	Concentration (mM)	Na^+ (mM)	K^+ (mM)	Na^+ (mM)	K^+ (mM)
3	1	0.34	0.18	0.65	0.57
3	5	–	–	4.34	5.32
15	5	1.89	0.10	0.76	0.50
16	1	1.10	0.87	1.21	0.62

[a] Aqueous phase contained 0.5M NaOH, or 0.5M KOH, or 0.5M of each. Organic solvent was methylene chloride. Amount of extraction determined by back extraction into 0.1M HNO_3.

absent. One might expect that K^+ would be the better cocation since it has a smaller hydration energy than Na^+ [16, 17]. The sulfonamide macrocycles **15** and **16** actually exhibit greater or comparable $Na^+ : K^+$ selectivity without TMA present (compare Tables V and VI).

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