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Synthesis of azacrown ethers modified with side-chains containing germanium

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Abstract

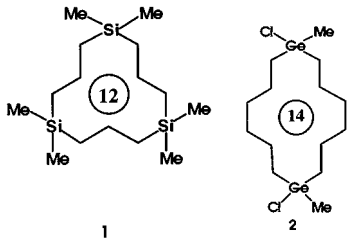
The reaction between ethanolamine (**4**) and tri- or tetraethylene tosylate (**5**) and (**13**) gave 9- and 12-membered monoazacrowns with a $-CH_2CH_2OH$ residue on nitrogen, **A-OH** and **B-OH**, together with 18- and 24-membered diazacrown ethers with the same substituent on nitrogen, **E-OH** and **F-OH.** If 2-(2-aminoethoxy)ethanol (**12**) was used in the reaction described above, instead of **4**, the final products, **G-OH** and **H-OH**, and **K-OH** and **L-OH**, have a longer side chain, $-CH_2CH_2OCH_2CH_2OH$, on nitrogen (Route 1). A series of reactions involving bromoethanol (**6**) and diethanolamine (**9**) formed, with **5** or **13**, 18- and 24-membered monoazacrowns with the shorter substituent as described above, a 15-membered monoazacrown ether **C-OH** and an 18-membered **D-OH**. If 2-(2-chloroethoxy)ethanol (**14**) is used instead of **6**, **I-OH** and **J-OH** are obtained (Route 2′). All these hydroxy azacrown ethers were made to react with 3-trimethylgermylpropionic acid (**18**) to give the corresponding germanium-containing **A**–**L**. A preliminary investigation was carried out on the cation transport capability of these germanium-containing azacrown ethers to observe whether germanium might enhance their cation transporting capability. © 2001 Published by Elsevier Science B.V.

Keywords: Cation transport; Diazacrown ether; Esterification; H-tube test; Hydrogermylation; Monoazacrown ether; Organogermanium compounds

1. Introduction

Ever since the commencement of the chemistry of crown ethers [1], their capability to capture and transport cations with sizes comparable to the size of the crown cavity has attracted considerable attention. Azacrown ethers have been known to possess the same capability [2], and in a way, are more suitable than crown ethers themselves in that it is possible to introduce a variety of side chains on nitrogen so that the modification of the nature of the cavity is more feasible. In this regard, many reports have been published on the synthesis and cation transport experiments [3].

Meanwhile, it was also known that some cyclic compounds containing Group 14 element(s) such as silicon or tin exhibit anion capturing/transporting capabilities. One example is the 1,1,5,5,9,9-hexamethyl-1,5,9-trisilacyclododecane (**1**), which showed the anion transport capability [4]. We have also shown that 1,8-dichloro-1,8-dimethyl-1,8-digermacyclotetradecane (**2**) [5] and 1,12-dichloro-1,12-dimethyl-1,12-digermacyclo-docosane (**3**) [6] transport chloride anions selectively.



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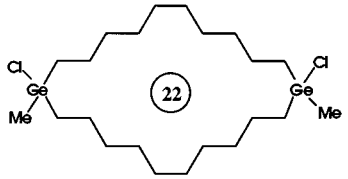

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It occurred to us that if the cation capturing/transporting property of azacrown ethers and the anion capturing/transporting property of organogermanium compounds could be combined, then the cation capturing/transporting property of the azacrown might be affected, and hopefully enhanced, by the presence of germanium. The latter might capture/transport the counteranion of the cation that is trapped by the azacrown ethers. With this prospect in mind, we decided to prepare a series of azacrown ethers that have sidechains modified with germanium.

The idea of ditopic ligands which capture/transport cations and anions simultaneously is not new. For instance, Tasker et al. reported some ligands that capture transition metal cation and its counteranion simultaneously [7]. Beer et al. reported a tripod tris(amidobenzo-15-crown-5) sodium ion and an anion such as halide anions simultaneously [8]. For these ligands, and other ditopic ligands, the binding sites are usually a quaternary ammonium salt or an amide moiety; to the best of our knowledge, the idea of using germanium or any other Group 14 elements as the binding site of anions in the ditopic ligand is not known.

2. Results and discussion

2.1. Strategy of synthesis

Since the synthesis of azacrown ethers is well documented, the crucial point of synthesis of our target molecules is the introduction of a germanium moiety into the molecule. There are several methods available to achieve the incorporation of germanium:

1. Hydrogermylation of an alkene (Eq. (1)):

$$R-CH=CH_2 + R^1R^2R^3Ge-H \rightarrow R-CH_2-CH_2GeR^1R^2R^3 \quad (1)$$

2. Reaction between a lithio derivative of an organogermanium compound and a haloalkane (Eq. (2)):

$$R-X + R^1R^2R^3Ge-Li \rightarrow R-Ge\ R^1R^2R^3 + LiX \quad (2)$$

3. Esterification of an alcohol with a germanium-containing carboxylic acid or its derivative (Eq. (3)):

$$R\text{–}OH + R^1R^2R^3Ge \sim\sim COOH \rightarrow R^1R^2R^3Ge \sim\sim COOR + OH \quad (3)$$

Initially, we intended to synthesize the desired azacrown ethers by hydrogermylation. Although the attempt was successful, the yield was low, and it was difficult to obtain an analytically pure sample because of some contamination which was difficult to remove. For method (ii), some complication is inevitably involved in most cases, probably because of the high reactivity of the organolithium reagent.

Finally, we found that the last method is the one of choice because the reaction in general is cleaner than the other two methods, and hence the yield is reasonable.

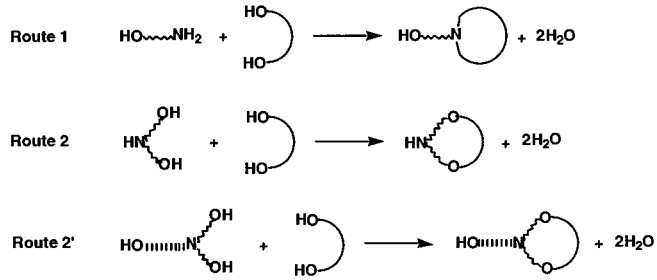
2.2. Synthesis of hydroxyazacrown ethers

Yet another advantage of using method (iii) is that the preparation of azacrown ethers having a terminal hydroxy group on nitrogen as the side chain is well known [9,10]. For the preparation of such hydroxyazacrown ethers, we have chosen two slightly different routes. In both the routes, the ring component is a polyethyleneglycol (as the tosylate) and the nucleophilic displacement occurring at the two termini of these is the key reaction for the ring closure.

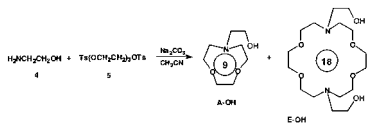
In Route 1, a hydroxy-amine is used as the nitrogen source and in this case the nucleophile is the nitrogen. The side chain on nitrogen of the azacrown ethers necessarily originates from the substituent on the nitrogen of the hydroxy-amine. By choosing the substituent, azacrown ethers with different side chains on nitrogen can be prepared.

In Route 2, a dihydroxy-amine is used as the nitrogen source and the two oxygen atoms of the hydroxy group will act as the nucleophiles that attack the two termini of glycol. The side chain on nitrogen of the dihydroxy-amine is necessarily the substituent on nitrogen of the azacrown ethers. It is difficult to introduce the substituent after the ring closure, and consequently a dihydroxy-amine with a substituent on nitrogen must be used (Route 2′). Here again, by choosing the substituents, azacrown ethers with different side chains on nitrogen can be prepared. The essence of Routes 1, 2 and 2′ are shown in Scheme 1 where the wavy line indicates alkyl or alkyloxy residues.

Typical examples of the preparation of hydroxyazacrown ethers are shown in the following schemes. Thus, by Route 1, a mixture of ethanolamine (**4**) and tri-



Scheme 1. The formation of azacrown ethers.



Scheme 2. Synthesis of hydroxyazacrown ether via Route 1.

ethyleneglycol ditosylate (**5**) was heated in MeCN in the presence of Na_2CO_3 to form a mixture of 9-membered *N*-(2-hydroxyethyl)-4-aza-9-crown-3 (**A-OH**) and 18-membered *N*,*N*′-bis(2-hydroxyethyl)-4,13-diaza-18-crown-6 (**E-OH**), which was separated by gel permeation chromatography (GPC) (Scheme 2). This route to **E-OH** is a modification of the method reported by Gatto and Gokel [11] although they used diiodide instead of ditosylate.

In practice, Route 2 is a little complicated because the NH function of the dihydroxy amine must be protected during the ring closure, and the protecting procedure was selected such that the protecting group would eventually be the side-chain on the nitrogen with the terminal hydroxy group (Route 2′). Thus, 2-bromoethanol (**6**) was treated with 1,2-dihydropyran (**7**) to give 2-bromoethylpyranyl ether (**8**). The pyranyl ether **8** was made to react with diethanolamine (**9**) to form the necessary nitrogen source, *N*-(2-pyranyloxyethyl)-diethanolamine (**10**). The cyclization proceeded smoothly between **10** and **5** to give the pyranyloxyethyl azacrown ether (**11**). Hydrolysis of **11** with aqueous (aq.) HCl gave the 15-membered *N*-(2-hydroxyethyl)-4-aza-15-crown-5 (**C-OH**) (Scheme 3).

This method is a modification of the one reported by Newkombe and Marsden [12]. Although many other methods have been reported, we almost exclusively used this method to prepare the monoazacrown ethers.

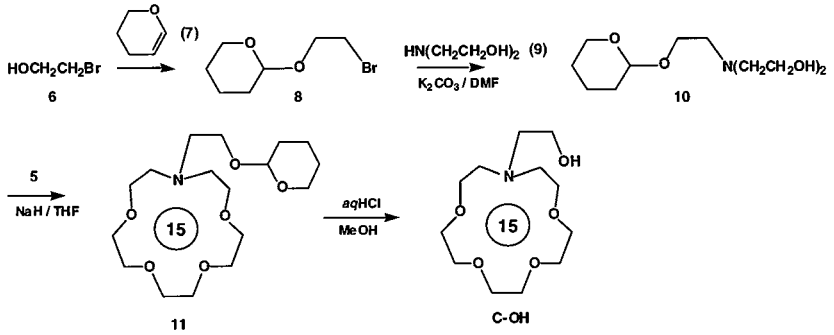
For synthesizing other azacrown ethers, one can use the other amine sources or ring sources. Thus, if tetraethyleneglycol ditosylate (**13**) is used instead of **5**, azacrown ethers with larger ring size can be prepared. If 2-(2-aminoethoxy)ethanol (**12**) is used instead of **4**, an azacrown ether with a longer substituent on nitrogen will be obtained. As shown in Scheme 4, the reaction between **12** and **13** gave the 12-membered hydroxy monoazacrown ether (**H-OH**) and the 24-membered dihydroxy diazacrown ether (**L-OH**), both of which have a longer side-chain on nitrogen.

The same strategy can be applied to Route 2. Thus, a combined use of 2-(2-chloroethoxy)ethanol (**14**) instead of **6**, and of **13** instead of **5** gave the 18-membered hydroxymonoazacrown (**J-OH**) via its pyranyl ether (**17**) (Scheme 5).

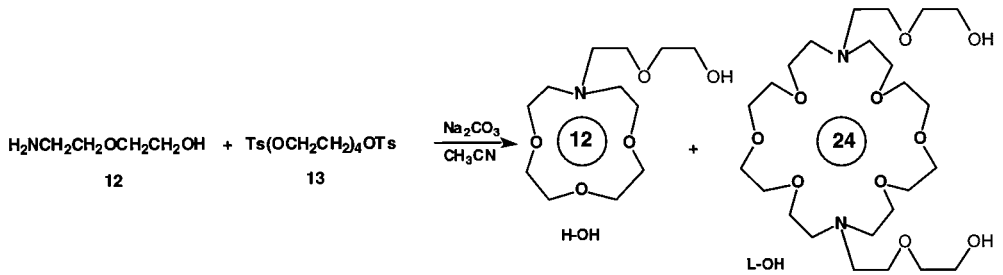
Thus, akin to the synthesis of the azacrown ether skeleton, we used only two methods modified from the methods outlined in Refs. [11,12]. The details of the synthesis will be given in Section 3.

2.3. Incorporation of germanium moiety into azacrown ethers

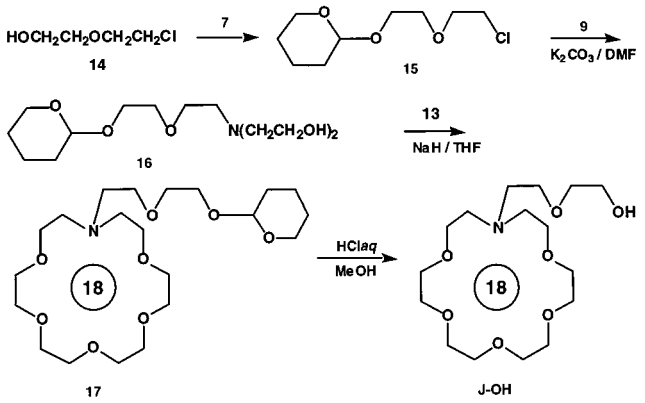
We have chosen 3-(trimethylgermyl)propionic acid $(CH_3)_3GeCH_2CH_2COOH$ (**18**), as the carboxylic acid to be used in Eq. (3). Hydrogermylation of acrylic acid



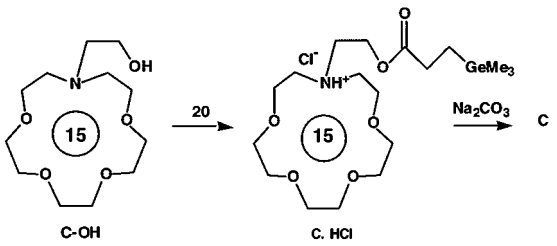
Scheme 3. Synthesis of azacrown ether via Route 2′.



Scheme 4. Synthesis of hydroxyazacrown ethers with longer side chain on nitrogen via Route 1.



Scheme 5. Synthesis of hydroxyazacrown ethers with longer side chain on nitrogen via Route 2′.



Scheme 6. Incorporation of germanium with acid chloride.

with trichlorogermane $HGeCl_3$ gives 3-trichlorogermylpropionic acid (**19**) and the subsequent Grignard reaction of **19** with methyl magnesium iodide gives **18** (Eq. 4), e.g.

$$\begin{aligned} CH_2=CHCOOH + HGeCl_3 \\ \rightarrow Cl_3GeCH_2CH_2COOH\ (\mathbf{19}) \\ Cl_3GeCH_2CH_2COOH + 3CH_3MgI \\ \rightarrow (CH_3)_3GeCH_2CH_2COOH\ (\mathbf{18}) + 3MgClI \end{aligned} \quad (4)$$

Initially we used 3-trimethylgermylpropionyl chloride $(CH_3)_3GeCH_2CH_2COCl$ (**20**), for the esterification process (Schotten–Baumann reaction). However, it turned out that the reaction proceeded smoothly, but the azacrown ethers formed the hydrogen chloride salt, which requires neutralization with Na_2CO_3, consequently making the following separation/purification procedures more tedious (Scheme 6).

Incorporation of the germanium moiety was achieved by the reaction of the hydroxyazacrown ethers and **18** in $CHCl_3$ in the presence of 4-aminopyridine and dicyclohexylcarbodiimide (DCC). The yields are generally reasonable.

All trimethylgermylpropionates of monoazacrown ethers are listed in Fig. 1, while the similar derivatives of the diazacrowns are given in Fig. 2.

2.4. Attempted hydrogermylation

Hydrogermylation is one of the most common reactions for incorporating germanium into organic compounds if the precursor, an appropriate alkene, is easily obtained. In fact, the reaction between allyl bromide (**21**) and **9** gave allyldiethanolamine (**22**), which was made to react with **5** to give *N*-allyl-4-aza-15-crown-5 (**23**). The hydrogermylation of **23** with triphenylgermane (**24**) in the presence of a catalytic amount of H_2PtCl_6 gave the desired product, *N*-(3-triphenylgermylpropyl)-4-aza-15-crown-5 (**25**) as shown in Scheme 7. The yield was low, and it was extremely difficult to obtain an analytically pure sample from the reaction mixture.

2.5. Characterization

The characterization of the prepared hydroxy azacrown ethers (**A-OH**–**L-OH**) and their germaesters (**A**–**L**) was carried out mostly based on ^1H- and ^{13}C-NMR spectra together with mass spectrometric analysis.

For instance, the characterization of the 18-membered monoazacrown **D-OH** and **D**, 18-membered diazacrowns **E-OH** and **E**, and the 24-membered diazacrowns **F-OH** and **F** will be described.

Mass spectra of all alcohols **A-OH**–**L-OH** and their precursors were recorded in the electron impact (EI) mode. All of these showed molecular ion peaks as indicated in Section 3.

However, for germanium compounds **A**–**L**, the EI mode mass spectra are not always very clear-cut, mostly because of excessive fragmentation. In particular, the characteristic pattern owing to the isotope distribution of germanium was largely obscured. Some ten years ago, matrix-assisted laser desorption ionization (MALDI) mass spectrometry [13] was introduced for the analysis of high molecular weight natural products, such as proteins. A substantial improvement was achieved by a combination of MALDI and time-of-flight (TOF) techniques [14] and recently, delayed ion extraction (DE) technique was introduced to MALDI-TOF mass spectrometry [15], which improved the resolution and accuracy of mass spectra such that the isotopically resolved peaks could be observed. It occurred to us that this DE MALDI-TOF technique might be a powerful tool for the analysis of organogermanium compounds by showing the isotopic distribution of germanium clearly.

The whole DE MALDI-TOF mass spectra and the expansion of the $[M+H]^+$ peak of **D** are shown as an example of compounds containing one germanium atom in Fig. 3a and b, respectively. Fig. 4a and b shows, respectively, the whole DE MALDI-TOF mass spectra and the expansion of the $[M+H]^+$ peak of **E** as an example of compounds containing two germa-

nium atoms. The usefulness of DE MALDI-TOF spectra in characterizing organogermanium compounds is obvious.

In ^{1}H-NMR spectra, all the azacrown ethers exhibit a large multiplet centered on δ 3.60–3.65 owing to the ring protons adjacent to oxygen. The signal of the $-CH_2OH$ methylene of the side chain is also in this region. There are two types of methylene group adjacent to nitrogen: one is in the ring and the other in the side chain. Based on the intensity, it is clear that the ring methylene is in the low-field region.

All the esters **D**, **E** and **F** exhibited a feature common to the ester side chain. The strong signal at very high field is certainly because of the three methyl groups bonded to germanium. The methylene proton bonded to germanium comes next, and in esters, the two types of methylene group adjacent to nitrogen are degenerate. The signal of the ring methylene adjacent to oxygen is as much the same as that of the precursor. Finally, the $-CH_2OCO-$ methylene signal appears at the lowest field. The discussion above is summarized in Fig. 5.

The assignment of ^{1}H-NMR spectra of **A**, **B** and **C**, and their precursors can be made in a similar manner. The assignment for azacrowns with longer side chain also follows a similar strategy.

The assignment of ^{13}C-NMR spectra is also more or less straightforward. The methylene carbons adjacent to oxygen resonate at around δ 70 while those adjacent to nitrogen are around δ 54–57. The signal of the $-CH_2OH$ methylene carbon is at the lower field (ca. δ 59) compared with ring methylene, and on esterification it moves to low field (δ 72). It is easy to identify the carbon nuclei belonging to the side chain. The whole discussion is summarized in Fig. 6.

The assignment of the NMR spectra of azacrown ethers with longer side chains is exemplified by the case of **K-OH** and **K**. The ring- and side-chain methylene protons adjacent to oxygen have as much the same chemical shifts as their monoaza analogs. The ring- and side-chain methylene protons adjacent to nitrogen have slightly different chemical shifts for **K-OH**, which are degenerate for **K**. The same is true for their ^{13}C-NMR

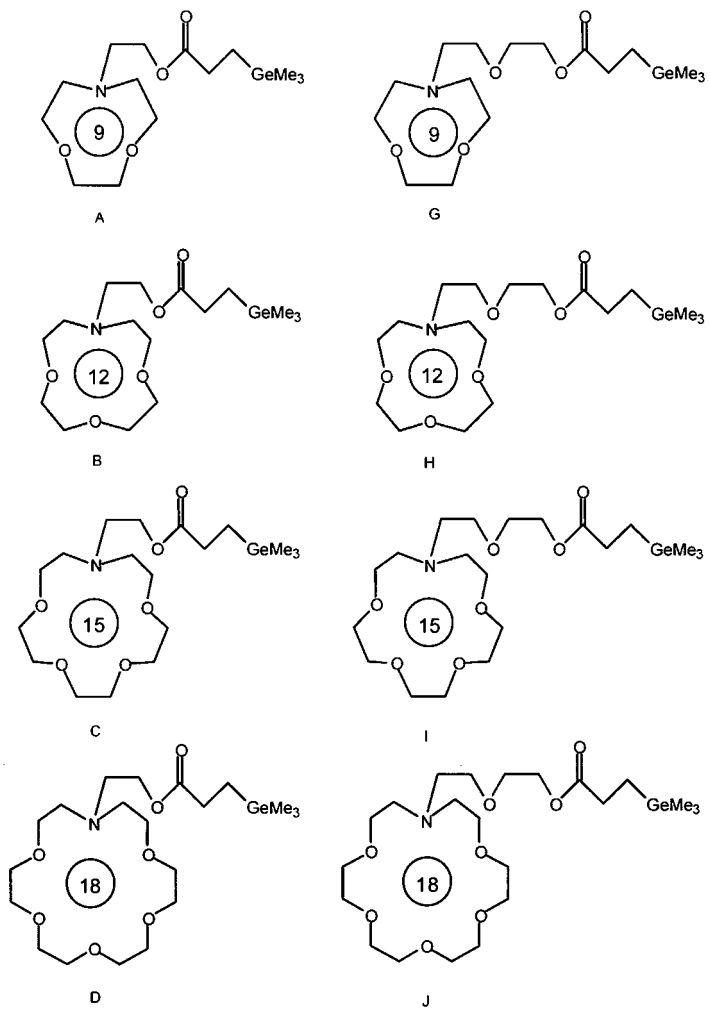


Fig. 1. Prepared monoazacrowns with germanium-containing side-chains.

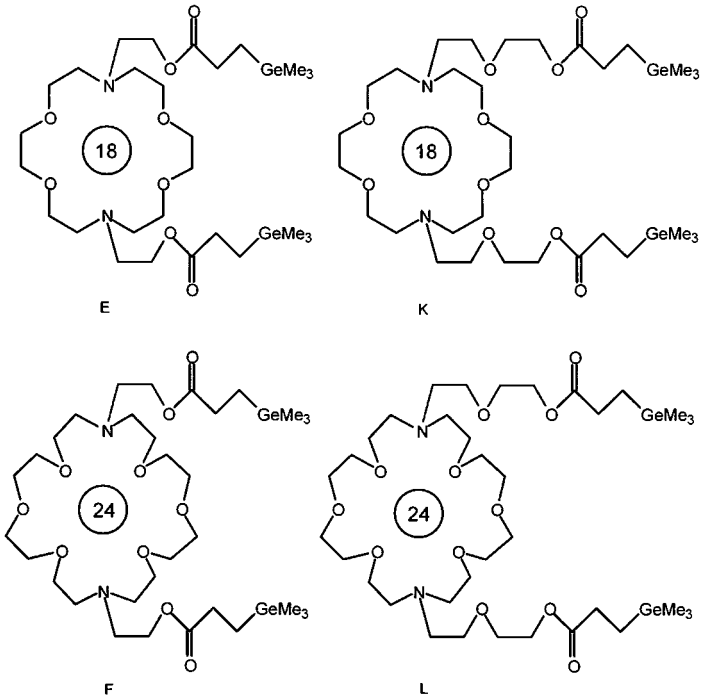


Fig. 2. Prepared diazacrowns with germanium-containing side-chains.

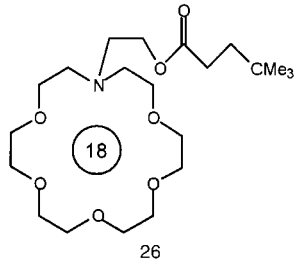
spectra also; two types of methylene carbons adjacent to oxygen cannot be differentiated although the shift values of these carbons adjacent to the nitrogen are slightly different. Here again the germanium-containing side chain(s) can be identified easily by NMR spectra. The results are summarized in Fig. 7.

2.6. Cation transport experiments

A preliminary series of cation transport experiments was carried out by the H-tube test for all azacrown ethers with germanium-containing side chains [16]. The device used is illustrated in Fig. 8 and the observations have been summarized below.

1. When alkali metal chlorides are used, the cation transport capability of our azacrown ethers is in parallel with the conventional azacrown ethers. Thus, the 15-membered azacrown ethers transport Na^+, and the 18-membered azacrown ethers transport K^+.
2. When alkali metal nitrates are used, the 18-membered azacrown ethers transport K^+.
3. When the transport of K^+ by 18-membered azacrown ethers was measured, the largest amount of transport was observed when the counteranion was iodide.

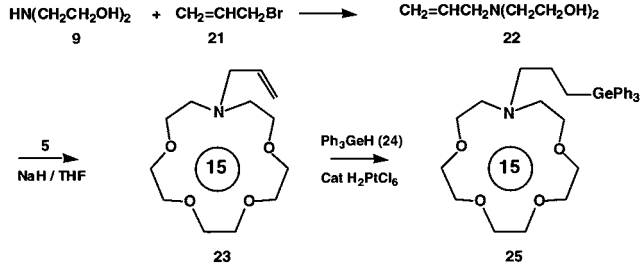
However, we have to admit that it is rather difficult to assess the role of germanium in the cation transport by azacrown ethers. It will be necessary to prepare the whole series of azacrown ethers such as **26**, the carbon analog of **D**, with a carbon atom instead of germanium. The role of the side-chains carrying the germanium moiety cannot be assessed before some conclusion can be obtained. Research along this line is in progress in our laboratory.



3. Experimental

All manipulations were performed under an inert atmosphere of nitrogen or argon. Dry, oxygen-free solvents were employed throughout. Diethyl ether was distilled from sodium before use. Tetrahydrofuran (THF) and MeCN were dried by LAH and molecular sieve, respectively.

IR spectra were determined with a JASCO FTIR-300 spectrometer. ^{1}H-NMR spectra were determined on a JEOL EX-400 spectrometer operating at 400 MHz, and the chemical shifts were reported in δ (ppm) with



Scheme 7. Synthesis of a germaazacrown ether via hydrogermylation.

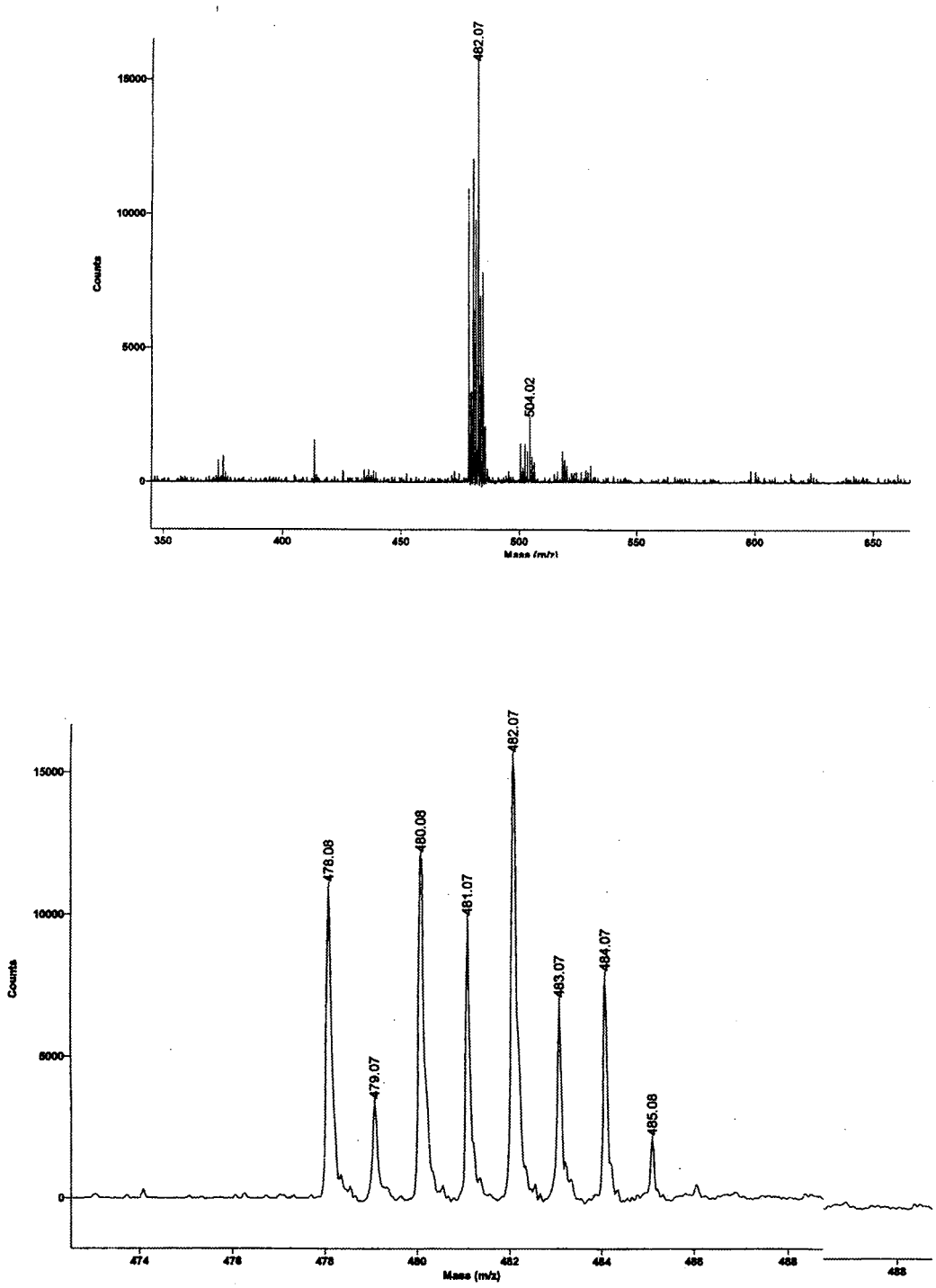


Fig. 3. (a) Mass spectrum of **D** (full). A peak at 504.02 is owing to $[M + Na]^+$. (b) Mass spectrum of **D** (expansion).

respect to Me_4Si. ^{13}C-NMR spectra were determined on a JEOL EX-400 spectrometer operating at 100 MHz and the chemical shifts were reported in δ (ppm) with respect to Me_4Si. Mass spectra were recorded on JEOL NS-MP09 mass spectrometer operating in the EI mode at 70 eV or on a PerSeptive Bioystems DE MALDI-TOF mass spectrometer, Voyager Elite XL. Atomic absorption spectra were determined with a Hitachi 12-8100 Polarized Zeeman atomic absorption spectrometer.

*3.1. N-(2-Hydroxyethyl)-4-aza-9-crown-3 (**A-OH**) and N,N′-bis(2-hydroxyethyl)-4,13-diaza-18-crown-6 (**E-OH**)*

A solution of ethanolamine (**4**) (2.70 g, 44.2 mmol), triethylenegylcol ditosylate (**5**) (17.60 g, 38.4 mmol) and

Na_2CO_3 (17.68 g, 166.8 mmol) in MeCN (370 ml) was stirred vigorously under reflux for 24 h. The reaction mixture was cooled and filtered, and the filtrate was concentrated in vacuo. The residue was dissolved in H_2O. The aqueous solution was repeatedly extracted with $CHCl_3$. The combined organic phase was dried over $MgSO_4$, concentrated in vacuo, and then column chromatographed (Al_2O_3) by eluting with $CHCl_3$–2-propanol = 10:1, followed by separation by GPC to give **A-OH** (0.89 g, 13.2%) and **E-OH** (1.34 g, 20.0%) both as pale yellow oil.

A-OH. ^{1}H-NMR ($CDCl_3$): δ 2.79 (t, 2H, chain-NCH_2), 2.84 (t, 4H, ring-NCH_2), 3.60 (m, 10H, OCH_2, OH). ^{13}C-NMR ($CDCl_3$): δ 55.19 (ring-NCH_2), 58.63 (chain-NCH_2), 59.01 (CH_2OH), 72.80 and 73.09 (CH_2O). IR (neat, NaCl, cm^{-1}): 3409. EIMS; m/z (%

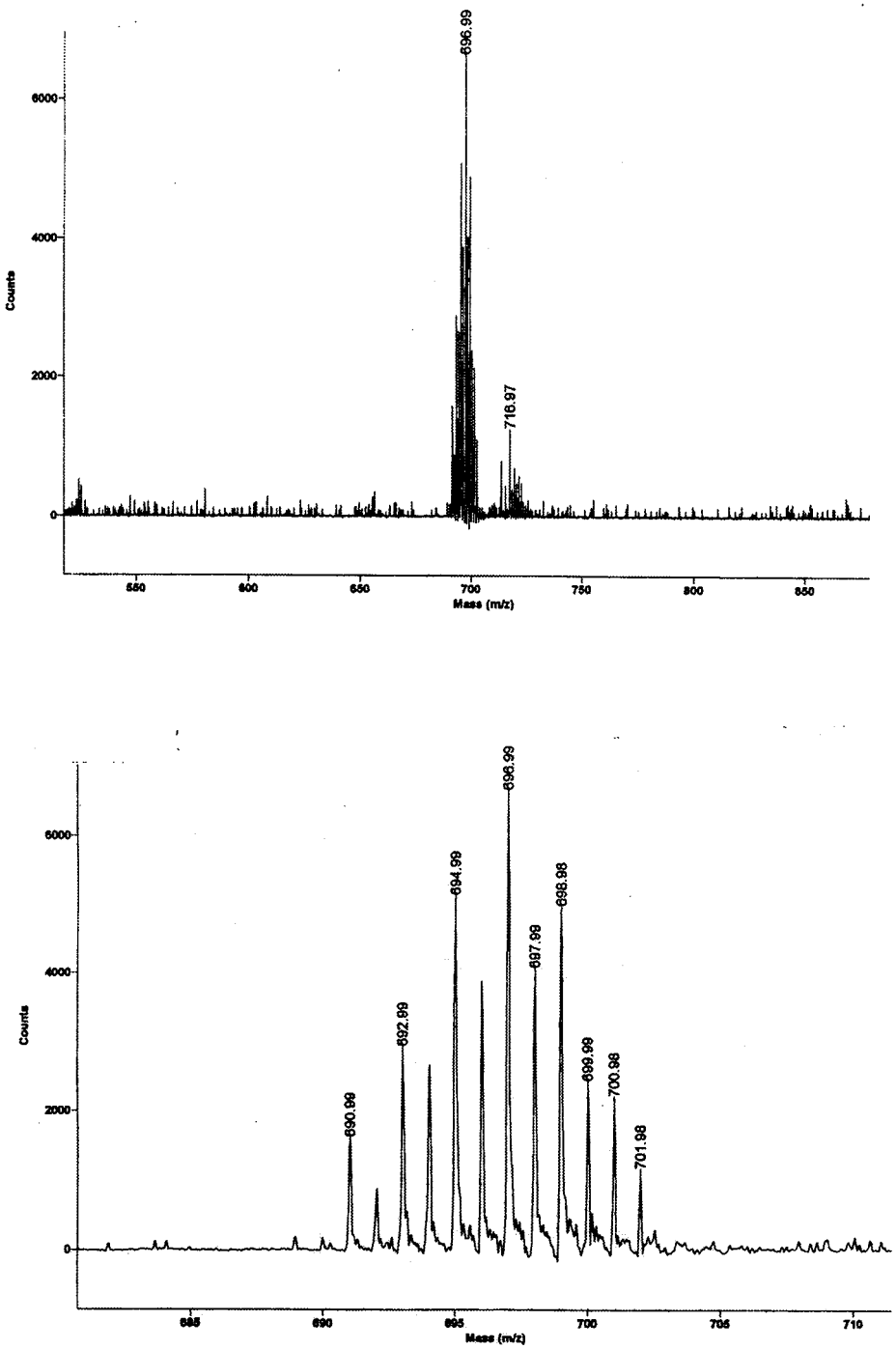


Fig. 4. (a) Mass spectrum of **E**. A peak at 716.97 is owing to $[M + Na]^+$. (b) Mass spectrum of **E** (expansion).

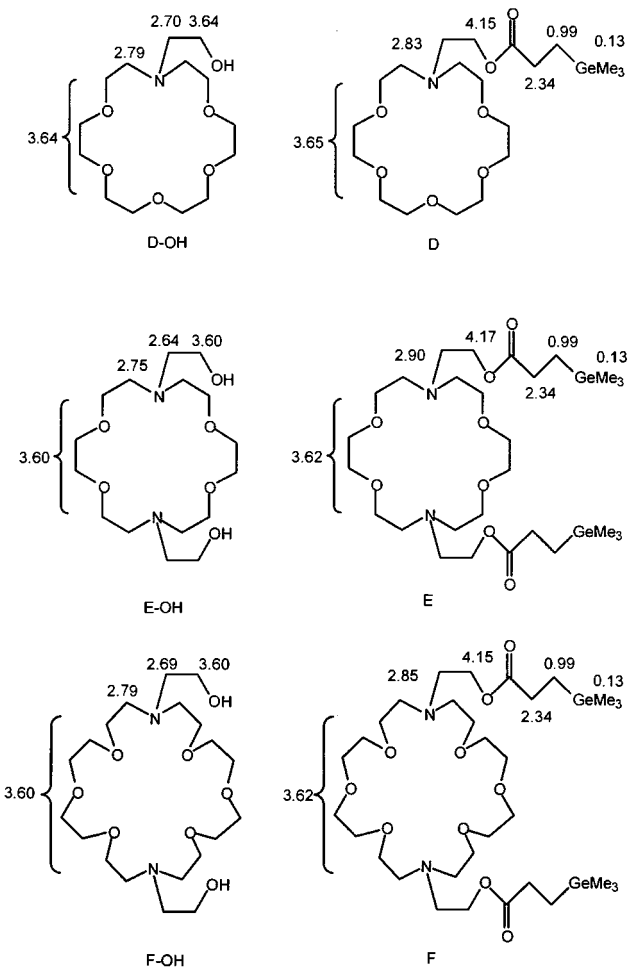


Fig. 5. Assignment of ^{1}H-NMR spectra of some azacrown ethers.

relative intensity): 175 ([M$^+$], 8.87) ($C_8H_{17}O_3N$, 175.23).

E-OH. ^{1}H-NMR ($CDCl_3$): δ 2.64 (t, 4H, chain-NCH_2), 2.75 (t, 8H, ring-NCH_2), 3.60 (m, 20H, OCH_2, OH). ^{13}C-NMR ($CDCl_3$): δ 55.13 (ring-NCH_2), 57.36 (NCH_2), 59.38 (CH_2OH), 69.81 and 70.65 (CH_2O). IR (neat, NaCl, cm^{-1}): 3425. EIMS; m/z (% relative intensity): 350 ([M$^+$], 10.20) ($C_{16}H_{34}O_6N_2$, 350.46).

Gatto and Gokel [11] obtained **E-OH** by the reaction of substituted amine and the diiodide as the NaI complex. On the contrary, our method directly yielded the desired product **E-OH**.

*3.2. N-(2-Hydroxyethyl)-4-aza-12-crown-4 (**B-OH**) and N,N′-bis(2-hydroxyethyl)-7,19-diaza-24-crown-8 (**F-OH**)*

The preparation of **B-OH** and **F-OH** are essentially identical to that of **A-OH** and **E-OH** [17]. From **4** (1.57 g, 25.7 mmol), tetraethylenegylcol ditosylate (**13**) (10.79 g, 21.5 mmol) [18] and Na_2CO_3 (10.16 g, 95.6 mmol) in 30 ml MeCN, **B-OH** (1.76 g, 37.3%) and **F-OH** (0.41 g, 4.3%) were obtained as pale yellow oil.

B-OH. ^{1}H-NMR ($CDCl_3$): δ 2.67 (t, 4H, chain-CH_2N), 2.71 (t, 8H, ring-CH_2N), 3.63 (m, 15H, OCH_2, OH). ^{13}C-NMR ($CDCl_3$): δ 55.13 (ring-CH_2N), 57.02 (chain-CH_2N), 59.27 (CH_2OH), 69.31, 70.46 and 70.65 (CH_2O). IR (neat, NaCl, cm^{-1}): 3388 (s). EIMS; m/z (% relative intensity): 219 ([M$^+$], 5.8) ($C_{10}H_{21}O_4N$, 219.28).

F-OH. ^{1}H-NMR ($CDCl_3$): δ 2.69 (t, 4H, chain-CH_2N) 2.79 (t, 8H, ring-CH_2N) 3.60 (m, 30H, OCH_2, OH). ^{13}C-NMR ($CDCl_3$): δ 54.62 (ring-CH_2N), 57.02 (chain-CH_2N), 59.27 (CH_2OH), 69.61, 70.36 and 70.58 (CH_2O). IR (neat, NaCl, cm^{-1}): 3190. EIMS; m/z (% relative intensity): 438 ([M$^+$], 5.8) ($C_{20}H_{42}O_8N_2$, 438.56).

The alcohols **B-OH**, **C-OH** and **D-OH** were prepared by the reaction of the corresponding azacrown with ethylene oxide. The ^{1}H-NMR data reported are in good agreement with our data [17].

*3.3. N-(2-Hydroxyethyl)-4-aza-15-crown-5 (**C-OH**)*

The preparation was carried out by the method described in the literature [17]. A mixture of 2-bromoethanol (**6**) (6.52 g, 4.98 mmol) and *p*-toluenesufonic acid (TsOH) (1.13 g, 5.90 mmol) was added dropwise to dihydropyran (**7**) (8.55 g, 102 mmol) at 0 °C and stirred continuously for 12 h. Aq. $NaHCO_3$ (10%, 100 ml) was added and the mixture was extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was distilled in vacuo (80 °C, 8 Torr) to give a colorless oil of 2-bromoethylpyranyl ether (**8**) (9.22 g, 82.2%).

8. ^{1}H-NMR ($CDCl_3$): δ 1.52–1.90 (m, 6H, py-CH_2), 3.46–3.53 (m, 3H, CH_2O), 3.54–4.04 (m, 3H, CH_2O) 4.66–4.68 (m, 1H, CH). ^{13}C-NMR ($CDCl_3$): δ 19.38 (py-CH_2) 25.46 (py-CH_2), 30.52 (py-CH_2 or CH_2Br), 30.96 (py-CH_2 or CH_2Br), 62.30 (CH_2O), 67.55 (CH_2O), 98.8 (CH). IR (neat, NaCl, cm^{-1}): 2943.A mixture of **8** (1.96 g, 9.37 mmol), diethanolamine (**9**) (1.02 g, 9.70 mmol) and K_2CO_3 (1.55 g, 11.2 mmol) was stirred in DMF (15 ml) for 24 h. DMF was removed under reduced pressure, and the solid was filtered. The filtrate was dissolved in CH_2Cl_2, dried and evaporated. By distillation in vacuo (140 °C, 2 Torr), a colorless oil of *N*-2-(pyranyloxyethyl)diethanolamine (**10**) (1.32 g, 60.4%) was obtained.

10.^{1}H-NMR ($CDCl_3$): δ 1.51–1.82 (m, 6H, py-CH_2), 2.69–2.73 (m, 6H, NCH_2), 3.54–3.94 (m, 10H, CH_2O), 4.54–4.57 (m, 1H, CH). ^{13}C-NMR ($CDCl_3$): δ 20.52 (py-CH_2), 25.26 (py-CH_2), 30.92 (py-CH_2), 54.31 (CH_2N; to be side chain), 57.48 (CH_2N; to be ring), 59.73(CH_2O; to be ring), 63.83 and 67.01 (CH_2O), 100.13 (CH). IR (neat, NaCl, cm^{-1}): ν(OH) 3391.

To a suspension of sodium hydride (NaH) (1.09 g, 45.3 mmol) in THF (80 ml), a THF (50 ml) solution of

10 (3.81 g, 16.3 mmol) was added dropwise and the mixture was stirred for 30 min. A THF (50 ml) solution of **5** (7.44 g, 16.2 mmol) was added to the mixture within 20 min. The resultant mixture was stirred further for 75 h. The mixture was filtered, and the filtrate was extracted with $CHCl_3$ and dried over $MgSO_4$. The solvent was removed, and the residue was purified by column chromatography (Al_2O_3, $CHCl_3$) to give colorless oil of *N*-(2-pyranyloxyethyl)-4-aza-15-crown-5 (**11**) (2.44 g, 7.02 mmol, 43.4%).

11. ^{1}H-NMR ($CDCl_3$): δ 1.55 (m, 6H, py-CH_2), 2.80 (t, 2H, chain-CH_2N), 2.84 (t, 4H, ring-CH_2N), 3.6 (m, 20H, CH_2O), 4.63 (m, CH, 1H). ^{13}C-NMR ($CDCl_3$): δ 19.66, 25.56 and 30.78 (py-CH_2), 55.16 (ring-CH_2N), 56.01 (chain-CH_2N), 62.31 (CH_2O), 65.86 (CH_2O), 70.13, 70.20, 70.45 and 71.02 (ring-CH_2O), 98.96 (CH). IR (neat, NaCl, cm^{-1}): 2941, 2867.

A mixture of **11** (1.30 g, 3.74 mmol), MeOH (8 ml) and aq. HCl (6 mol l^{-1}, 2 ml) was stirred for 12 h followed by the addition of Na_2CO_3 and stirred again. The solvent was removed and the residue was dissolved in H_2O, which was extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$, and the solvent was removed under reduced pressure to give the faintly yellow oil of **C-OH** (0.56 g, 2.13 mmol, 57.0%).

C-OH. ^{1}H-NMR ($CDCl_3$): δ 2.67 (t, 2H, chain-CH_2N), 2.76 (t, 4H, ring-CH_2N), 3.64 (m, 20H, CH_2O). ^{13}C-NMR ($CDCl_3$): δ 55.55 (ring-CH_2N), 57.92 (chain-CH_2N), 59.39 (CH_2OH), 69.99, 70.13, 70.53 and 70.77 (CH_2O). IR (neat, NaCl, cm^{-1}): ν(OH) 3270. EIMS; *m*/*e* (% relative intensity): 263 ([M^+], 9.59) ($C_{12}H_{25}O_5N$, 263.33).

The ^{1}H-NMR data are in agreement with those given in Ref. [11].

3.4. *N*-(2-Hydroxyethyl)-4-aza-18-crown-6 (**D-OH**)

The synthesis of **D-OH** is essentially identical to that of **C-OH** except that tetraethyleneglycol ditosylate (**13**) was used instead of **5**. To a suspension of NaH (2.65 g,

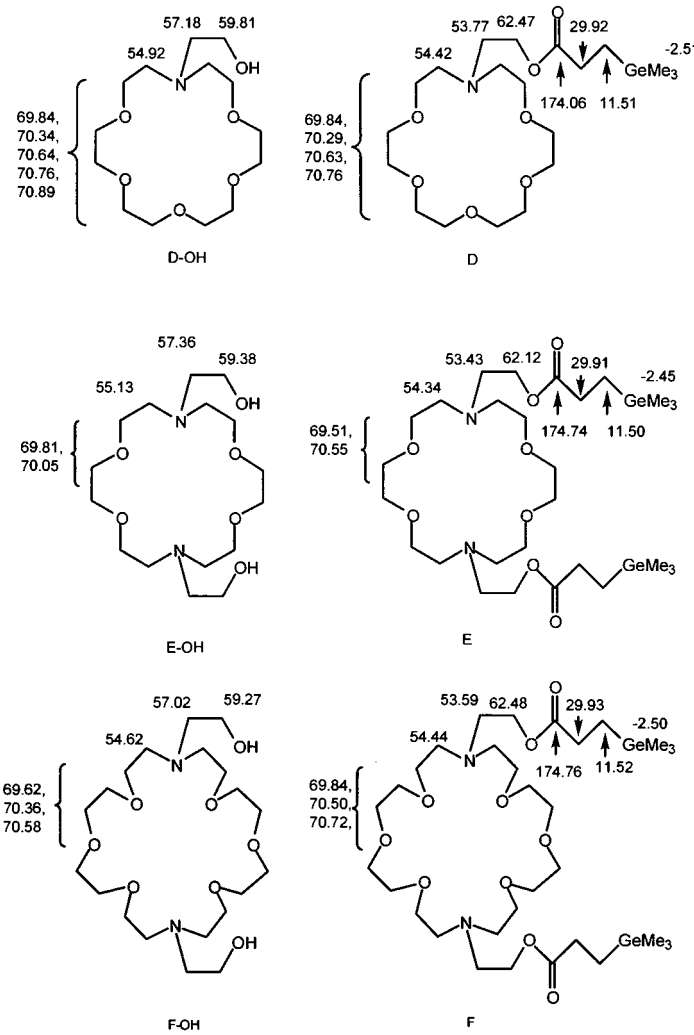


Fig. 6. Assignment of ^{13}C-NMR spectra of some azacrown ethers.

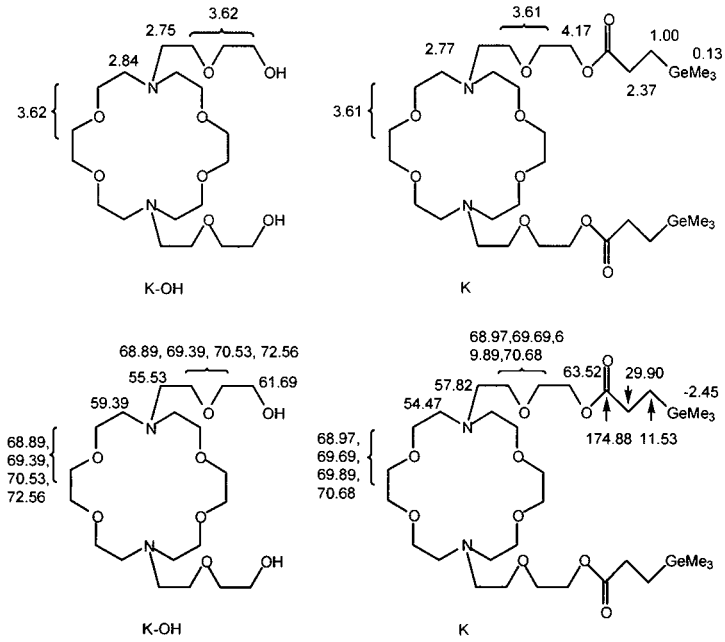


Fig. 7. Assignment of ^{1}H- and ^{13}C-NMR spectra of **K-OH** and **K**.

110.4 mmol) in THF (350 ml), a THF (50 ml) solution of **10** (10.47 g, 44.9 mmol) was added dropwise and stirred for 30 min. A THF solution (100 ml) of **13** (22.49 g, 4.47 mmol) was added dropwise to the mixture within 20 min. The resulting mixture was stirred further for 69 h. The mixture was filtered, and the solvent was removed. The residue was dissolved in H_2O, extracted with $CHCl_3$ and dried over $MgSO_4$. The solvent was removed, and the residue was purified by column chromatography (Al_2O_3, $CHCl_3$) to give a colorless oil of *N*-(2-pyranyloxyethyl)-4-aza-18-crown-6 (**27**) (8.49 g, 21.7 mmol, 45.8%).

27. ^{1}H-NMR ($CDCl_3$): δ 1.55 (m, 6H, py-CH_2), 2.80 (t, 2H, chain-NCH_2) 2.84 (t, 4H, ring-NCH_2) 3.70 (m, 24H, OCH_2), 4.60 (m, CH, 1H). ^{13}C-NMR ($CDCl_3$,): δ 19.69, 25.57 and 30.79 (py-CH_2), 54.67 (ring-CH_2N), 55.04 (chain-CH_2N), 62.34 and 65.79 (CH_2O), 69.90, 70.39, 70.76, 70.86 and 98.97 (ring-CH_2O).

The acid-catalyzed hydrolysis of **27** to **D-OH** was carried out in a similar manner as that for **C-OH**. Thus, from **27** (1.76 g, 4.50 mmol), yellow oil of **D-OH** (0.39 g, 3.03 mmol, 67.2%) was obtained.

D-OH. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 2.70 (t, 2H, chain-CH_2N), 2.79 (t, 4H, ring-CH_2N), 3.64 (m, 24H, CH_2O). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 54.92 (ring-CH_2N), 57.18 (chain-CH_2N), 59.32 (CH_2OH), 69.84, 70.34, 70.64 70.76 and 70.89 (CH_2O). IR (neat, NaCl, cm^{-1}): 3219. EIMS; *m/e* (% relative intensity): 306([M^+], 4.14) ($C_{14}H_{29}O_6N$, 307.39).

The ^{1}H-NMR data are in agreement with those in Ref. [11].

*3.5. N-{2-(2-Hydroxyethoxy)ethyl}-4-aza-9-crown-3 (**G-OH**) and N,N′-bis{2-(2-hydroxyethoxy)ethyl}-4,13-diaza-18-crown-6 (**K-OH**)*

The method used in the preparation of **G-OH** and **K-OH** is identical to that for **A-OH** and **E-OH** except that 2-(2-aminoethoxy)ethanol (**12**) was used instead of **4**. Thus, from **12** (2.44 g, 23.2 mmol), **5** (9.04 g, 19.7 mmol) and Na_2CO_3 (9.08 g, 85.7 mmol), a pale yellow oil of *N*-{2-(2-hydroxyethoxy)ethyl}-4-aza-9-crown-3 (**G-OH**) (0.46 g, 10.7%) and *N,N′-bis*{2-(2-hydroxyethoxy)ethyl}-4,13-diaza-18-crown-6 (**K-OH**) (0.46 g, 10.6%) were obtained.

G-OH. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 2.83 (t, 2H, chain-NCH_2), 2.92 (t, 4H, ring-NCH_2), 3.70 (m, 10H, OCH_2). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 54.85 (ring-NCH_2), 56.50 (chain-NCH_2), 61.73 (CH_2OH), 68.92, 72.00, 72.25 and 72.25 (OCH_2). IR (neat, NaCl, cm^{-1}): ν(OH) 3422. EIMS; *m/z* (% relative intensity): 219 ([M^+], 6.41) ($C_{10}H_{21}O_4N$, 219.28).

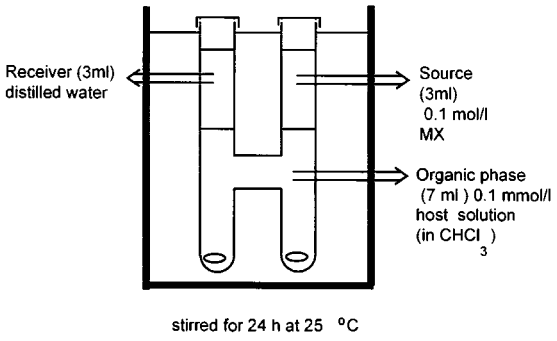


Fig. 8. Cation transport experiment.

K-OH. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 2.75 (t, 4H, chain-NCH_2), 2.84 (t, 8H, ring-NCH_2), 3.62 (m, 30H, OCH_2). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 54.39 (ring-NCH_2), 55.53 (chain-NCH_2), 61.69 (CH_2OH), 68.89, 69.39, 70.53 and 72.56 (OCH_2). IR (neat, NaCl, cm^{-1}): 3327. EIMS; *m/e* (% relative intensity): 438 ([M^+], 4.87) ($C_{32}H_{66}O_{10}N_2$, 438.56).

3.6. N-{2-(2-Hydroxyethoxy)ethyl}-4-aza-12-crown-4 (H-OH) and N,N′-bis{2-(2-hydroxyethoxy)ethyl}-7,19-diaza-24-crown-8 (L-OH)

The preparation of **H-OH** and **L-OH** was carried out in a similar manner as described in Section 3.5 except that **13** was employed instead of **5** as the ring source.

Thus, to a refluxing mixture of Na_2CO_3 (4.77 g, 45.4 mmol) in MeCN (250 ml), **12** (18.37 g, 173.3 mmol) was added and the reflux was continued for 1 h, to which a MeCN solution (80 ml) of **13** (20.07 g, 39.9 mmol) was added dropwise. After refluxing for 24 h, the solid was filtered, and the solvent was removed under reduced pressure. Water was added and the mixture was extracted with $CHCl_3$. The organic layer was dried and removed under reduced pressure. The residue was chromatographed on alumina ($CHCl_3$–2-propanol = 10:1) and separated by GPC to give a pale yellow oil of *N*-{2-(2-hydroxyethoxy)ethyl}-4-aza-12-crown-4 (**H-OH**) (3.05 g, 25.5%) and *N*,*N*′-bis{2-(2-hydroxyethoxy)ethyl}-7,19-diaza-24-crown-8 (**L-OH**) (0.75 g, 5.14%).

H-OH. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 2.71 (t, 2H, chain-NCH_2), 2.76 (t, 4H, ring-NCH_2), 3.63 (m, 18H, OCH_2). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 55.47 (ring-NCH_2), 56.36 (chain-NCH_2), 61.04 (CH_2OH), 69.23, 69.83, 70.20, 70.87 and 72.31 (OCH_2). IR (neat, NaCl, cm^{-1}): 3309. EIMS; *m/z* (% relative intensity): 263([M^+], 7.60) ($C_{12}H_{25}O_5N$, 263.33).

L-OH. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 2.79 (t, 4H, chain-NCH_2), 2.82 (t, 8H, ring-NCH_2), 3.63 (m, 36H, OCH_2). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 54.34 (ring-NCH_2), 55.28 (chain-NCH_2), 61.62 (CH_2OH), 69.02, 69.37, 70.38, 70.64 and 72.48 (OCH_2). IR (neat, NaCl, cm^{-1}): 3384. EIMS; *m/z* (% relative intensity): 526 ([M^+], 5.71) ($C_{24}H_{50}O_{10}N_2$, 526.67).

3.7. N-{2-(2-Hydroxyethoxy)ethyl}-4-aza-15-crown-5 (I-OH)

A mixture of 2-(2-chloroethoxy)ethanol (**14**) (17.25 g, 138.4 mmol) and TsOH (0.01 g) was added dropwise to **7** (23.15 g, 275.2 mmol) at 0 °C and stirred continuously for 12 h. Aq. $NaHCO_3$ (10%, 100 ml) was added and the mixture was extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was distilled in vacuo (80 °C, 8 Torr) to give a colorless oil of 2-(2-hloroethoxy)ethylpyranyl ether (**15**) (24.45 g, 84.7%).

15. ^{1}H-NMR ($CDCl_3$): δ 1.51–1.87 (m, 6H, py-CH_2), 3.48–3.97 (m, 10H, CH_2O), 4.63–4.65 (m, 1H, CH). ^{13}C-NMR ($CDCl_3$): δ 19.61, 25.53 and 30.70 (py-CH_2), 42.79 (CH_2Cl), 62.30, 66.68, 70.66 and 71.37 (CH_2O), 98.95(CH). IR (neat, NaCl, cm^{-1}): 2943.

A mixture of **15** (12.52 g, 60.0 mmol), **9** (6.31 g, 60.0 mmol) and K_2CO_3 (10.77 g, 78.0 mmol) was stirred in DMF (100 ml) for 42 h. The DMF was removed under reduced pressure, and the solid was filtered. The filtrate was dissolved in CH_2Cl_2, dried and evaporated. By distillation in vacuo (180 °C, 3 Torr), a colorless oil of *N*-{2-(2-pyranyloxyethoxy)ethyl}diethanolamine (**16**) (8.42 g, 48.2%) was obtained.

16. ^{1}H-NMR ($CDCl_3$): δ 1.55–1.83 (m, 6H, py-CH_2), 2.69–2.73 (m, 6H, CH_2N), 3.50–3.91 (m, 12H, CH_2O), 4.15–4.58 (m, 1H, CH). ^{13}C-NMR ($CDCl_3$): δ 19.95, 25.11 and 30.61 (py-CH_2), 54.03 and 57.07 (CH_2N), 59.45, 59.45, 63.10 and 66.29 (CH_2O), 99.51(CH). IR (neat, NaCl, cm^{-1}): 3399.

To a suspension of NaH (1.21 g, 50.5 mmol) in THF (200 ml), a THF (50 ml) solution of **16** (4.87 g, 17.6 mmol) was added dropwise and the mixture was stirred. A THF (80 ml) solution of **5** (8.54 g, 18.6 mmol) was added to the mixture within 20 min. The resultant mixture was stirred further for 36 h at room temperature (r.t.). The mixture was filtered, and H_2O was added to the filtrate, which was extracted with $CHCl_3$, and the organic layer was dried over $MgSO_4$. The solvent was removed, and the residue was purified by column chromatography (Al_2O_3, $CHCl_3$) to give a colorless oil of *N*-{2-(2-pyranyloxyethoxy)ethyl}-4-aza-15-crown-5 (**28**) (3.70 g, 9.68 mmol, 55.5%).

28. ^{1}H-NMR ($CDCl_3$): δ 1.55 (m, 6H, py-CH_2), 2.80 (t, 2H, chain-NCH_2), 2.84 (t, 4H, ring-NCH_2), 3.6 (m, 20H, CH_2O), 4.63 (m, CH, 1H). ^{13}C-NMR ($CDCl_3$): δ 19.66, 25.56 and 30.78 (py-CH_2), 55.16 (ring-NCH_2), 56.01 (chain-NCH_2), 62.31, 65.86, 70.13, 70.20, 70.45 and 71.02 (CH_2O), 98.96 (CH).

A mixture of **28** (1.05 g, 2.68 mmol), MeOH (14 ml) and aq. HCl (6 mol l^{-1}, 2 ml) was stirred for 12 h. Na_2CO_3 was added and stirred thoroughly. The solvent was removed and the residue was dissolved in H_2O, and the mixture was extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$, and the solvent was removed under reduced pressure to give a faintly yellow oil of **I-OH** (0.40 g, 1.03 mmol, 48.6%).

I-OH. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 2.78 (t, 2H, chain-NCH_2), 2.84 (t, 4H, ring-NCH_2), 3.63 (m, 23H, OCH_2). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 54.93 (ring-NCH_2), 56.31 (chain-NCH_2), 61.66 (CH_2OH), 68.96, 69.40, 70.01, 70.23, 70.82 and 72.43 (OCH_2). IR (neat, NaCl, cm^{-1}): 3258. EIMS; *m/z* (% relative intensity): 306 ([M^+], 10.0) ($C_{14}H_{29}O_6N$, 307.38).

The alcohols **I-OH** and **J-OH** were prepared by the reaction of the corresponding azacrowns with 2-chloroethanol. Neither the yield nor the spectroscopic data are described in the literature [19].

3.8. N-{2-(2-Hydroxyethoxy)ethyl}-4-aza-18-crown-6 (J-OH)

To a suspension of NaH (2.65 g, 110.4 mmol) in THF (350 ml), a THF (50 ml) solution of **16** (10.47 g, 44.9 mmol) was added dropwise and the mixture was stirred for 30 min following with an addition of a THF (80 ml) solution of **13** (22.49 g, 44.7 mmol) to the mixture. The resultant mixture was stirred further for 69 h at r.t. The mixture was filtered, and H_2O was added to the filtrate, which was extracted with $CHCl_3$, and the organic layer was dried over $MgSO_4$. The solvent was removed, and the residue was purified by column chromatography (Al_2O_3, $CHCl_3$) to give a colorless oil of *N*-{2-(2-pyranyloxyethoxy)ethyl}-4-aza-18-crown-6 (**17**) (5.78 g, 16.16 mmol, 45.8%).

17. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.55 (m, 6H, CH_2), 2.80 (t, 2H, chain-NCH_2), 2.84 (t, 4H, ring-NCH_2), 3.70 (m, 24H, OCH_2), 4.60 (m, 1H, OCHO). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 19.69, 25.57 and 30.79 (py-CH_2), 54.67 (ring-CH_2N), 55.04 (chain-CH_2N), 62.34 (CH_2OH), 65.79, 69.90, 70.39, 70.76, 70.86 and 70.86 (OCH_2), 98.97 (OCHO).

A mixture of **17** (1.03 g, 2.36 mmol), MeOH (10 ml) and aq. HCl (6 mol, 3 dm^{-3}) was stirred for 12 h. Na_2CO_3 was added and stirred further. The solvent was removed and the residue was dissolved in H_2O, and the mixture was extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$, and the solvent was removed under reduced pressure to give a faintly yellow oil of **J-OH** (0.45 g, 1.28 mmol, 54.3%).

J-OH. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 2.75 (t, 2H, chain-NCH_2), 2.83 (t, 4H, ring-NCH_2), 3.63 (m, 26H, OCH_2). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 54.52 (ring-NCH_2), 55.85 (chain-NCH_2), 61.83 (CH_2OH), 69.07, 69.49, 70.29, 70.67, 70.81 and 72.57 (OCH_2). IR (neat, NaCl, cm^{-1}): 3283. EIMS; *m*/*z* (% relative intensity): 350 ([M^+], 5.50) ($C_{16}H_{33}O_7N$, 351.44).

3.9. 3-Trimethylgermylpropionate of N-(2-hydroxyethyl)-4-aza-9-crown-3 (A)

3-Trimethylgermylpropionic acid (**18**) was prepared by the Grignard reaction of 3-trichlorogermyl propionic acid with methyl magnesium iodide. The germylpropionic acid was obtained by the hydrogermylation of acrylic acid with trichlorogermane [20].

Germylation of **A-OH**–**J-OH** with **18** can generally be achieved with the aid of DCC and 4-dimethylaminopyridine (**29**). Thus, a solution of **A-OH** (0.23 g, 1.31 mmol), **18** (0.36 g, 1.89 mmol) and **29** (0.23 g, 1.88 mmol) in $CHCl_3$ (10 ml) was cooled to 0 °C, and DCC (0.34 g, 1.65 mmol) was added. The resulting mixture was stirred for 24 h, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel using benzene–ethyl acetate (1:1) as the eluent. The yield was 0.29 g (0.83 mmol, 63.6%).

A. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 0.13 (s, 9H, Me_3Ge), 0.99 (m, 2H, $GeCH_2$), 2.35 (m, 2H, $GeCH_2CH_2$), 2.88 (m, 6H, NCH_2), 3.74 (m, 8H, OCH_2), 4.16 (t, 2H, $OCOCH_2$). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ −2.50 (Me_3Ge), 11.53 ($GeCH_2$), 29.96 ($GeCH_2CH_2$), 55.73 (chain-CH_2N), 55.84 (ring-CH_2N), 62.50 ($OCOCH_2$), 72.24 and 72.41 (CH_2O), 174.81 (C=O). IR (neat, NaCl, cm^{-1}): 1736. DE MALDI-TOFMS; *m*/*z*: 346.08, 348.08, 349.08, 350.07, 351.08, 352.07 ($C_{14}H_{29}O_4NGe$, 348.00).

3.10. 3-Trimethylgermylpropionate of N-(2-hydroxyethyl)-4-aza-12-crown-4 (B)

B was prepared under the similar conditions mentioned above from **B-OH** (0.24 g, 1.09 mmol), **18** (0.32 g, 1.68 mmol), **29** (0.21 g, 1.72 mmol) and DCC (0.34 g, 1.65 mmol) as a pale yellow oil (0.34 g, 0.87 mmol, 79.6%). The eluent used for chromatography was benzene–ethyl acetate = 1:1.

B. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 0.13 (s, 9H, Me_3Ge), 0.99 (m, 2H, $GeCH_2$), 2.33 (m, 2H, $GeCH_2CH_2$), 2.81 (t, 6H, CH_2N), 3.65 (m, 12H, CH_2O), 4.17 (t, 2H, $OCOCH_2$). ^{13}C-NMR ($CDCl_3$, 100 MHz): −2.51(Me_3Ge), 11.50 ($GeCH_2$), 29.93 ($GeCH_2CH_2$), 54.76 (chain-CH_2N), 55.36 (ring-CH_2N), 62.25 ($OCOCH_2$), 70.23, 70.31 and 71.06 (CH_2O), 174.74 (C=O). IR (neat, NaCl, cm^{-1}): 1736. DE MALDI-TOFMS; *m*/*z*: 390.09, 391.09, 392.09, 393.09, 394.08, 395.09, 396.09 ($C_{16}H_{33}O_5NGe$, 392.05).

3.11. 3-Trimethylgermylpropionate of N-(2-hydroxyethyl)-4-aza-15-crown-5 (C)

C was prepared from **C-OH** (0.27 g, 1.03 mmol), **18** (0.32 g, 1.68 mmol), **29** (0.17 g, 1.39 mmol) and DCC (0.32 g, 1.55 mmol) and **29** (0.17 g, 1.39 mmol) as a pale yellow oil (0.17 g, 1.39 mmol, 72.8%). The eluent used was $CHCl_3$–MeOH = 10:1.

C. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 0.13 (s, 9H, Me_3Ge), 0.99 (m, 2H, $GeCH_2$), 2.33 (m, 2H, $GeCH_2CH_2$), 2.81 (m, 6H, CH_2N), 3.66 (m, 16H, CH_2O), 4.14 (t, 2H, $OCOCH_2$). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ −2.38 (Me_3Ge), 11.65 ($GeCH_2$), 30.04 ($GeCH_2CH_2$), 54.79 (chain-CH_2N), 55.01 (ring-CH_2N), 62.55 ($OCOCH_2$), 70.10, 70.20, 70.44 and 71.00 (CH_2O), 174.77 (C=O). IR (neat, NaCl, cm^{-1}): 1735. DE MALDI-TOFMS; *m*/*z*: 434.06, 435.07, 436.06, 437.06, 438.06, 439.06, 440.06 ($C_{18}H_{37}O_6NGe$, 436.10).

3.12. 3-Trimethylgermylpropionate of N-(2-hydroxyethyl)-4-aza-18-crown-6 (D)

D was prepared from **D-OH** (0.57 g, 1.85 mmol), **18** (0.66 g, 3.46 mmol), DCC (0.27 g, 2.20 mmol) and **29** (0.60 g, 2.90 mmol) as a pale yellow oil (0.41 g; 0.94 mmol, 56.8%). The eluent used was $CHCl_3$–MeOH = 8:1.

D. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 0.13 (s, 9H, Me_3Ge), 0.99 (m, 2H, $GeCH_2$), 2.34 (m, 2H, $GeCH_2CH_2$), 2.83 (m, 6H, CH_2N), 3.65 (m, 20H, CH_2O), 4.15 (t, 2H, $OCOCH_2$). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ −2.51 (Me_3Ge), 11.51 ($GeCH_2$), 29.92 ($GeCH_2CH_2$), 53.77 (chain-CH_2N), 54.42 (ring-CH_2N), 62.47 ($OCOCH_2$), 69.84, 70.29, 70.63 and 70.76 (CH_2O), 174.76 (C=O). IR (neat, NaCl, cm(1): 1734. DE MALDI-TOFMS; *m*/*z*: 478.08, 479.07, 480.08, 481.07, 482.07, 483.07, 484.07, 485.08 ($C_{20}H_{41}O_7NGe$, 480.16).

3.13. 3-Trimethylgermylpropionate of N,N(-bis((2-hydroxyethyl))-4,13-diaza-18-crown-6 (E)

E was obtained from E-OH (0.37 g, 1.06 mmol), 18 (0.51 g, 2.67 mmol) and 29 (0.26 g, 2.10 mmol), DCC (0.48 g, 2.33 mmol) as a pale yellow oil (0.31 g, 0.46 mmol, 43.5 %%). The eluent used was $CHCl_3$–MeOH = 4:1. E. 1H-NMR ($CDCl_3$, 400 MHz): (0.13 (s, 18H, Me_3Ge), 0.99 (m, 4H, $GeCH_2$), 2.34 (m, 4H, $GeCH_2CH_2$), 2.90 (t, 12H, CH_2N), 3.62 (m, 16H, CH_2O), 4.17 (t, 4H, $OCOCH_2$). 13C-NMR ($CDCl_3$, 100 MHz): (2.50 (Me_3Ge), 11.50 ($GeCH_2$), 29.91 ($GeCH_2CH_2$), 53.43 (chain-CH_2N), 54.34 (ring-CH_2N), 62.12 ($OCOCH_2$), 69.51 and 70.55 (CH_2O), 174.74 (C(O). IR (neat, NaCl, cm(1): 1735. DE MALDI-TOFMS; *m*/*z*: 690.99, 692.99, 694.99, 696.99, 697.99, 698.98, 699.99, 700.98, 701.98 ($C_{28}H_{58}O_8N_2Ge_2$, 696.00).

3.14. 3-Trimethylgermylpropionate of N,N′-bis(2-hydroxyethyl)-7,19-diaza-24-crown-8 (F)

F was prepared from **F-OH** (0.22 g, 0.50 mmol), **18** (0.27 g, 1.42 mmol), **29** (0.17 g, 1.39 mmol) and DCC (0.29 g, 1.41 mmol) as a pale yellow oil (0.31 g, 0.46 mmol, 87.5%). The eluent used was $CHCl_3$–MeOH = 8:1.

F. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 0.13 (s, 18H, Me_3Ge), 0.99 (m, 4H, $GeCH_2$), 2.34 (m, 4H, $GeCH_2CH_2$), 2.85 (t, 12H, CH_2N), 3.62 (m, 24H, CH_2O), 4.15 (t, 4H, $OCOCH_2$). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ −2.50 (Me_3Ge), 11.52 ($GeCH_2$), 29.93 ($GeCH_2CH_2$), 53.59 (chain-CH_2N), 54.44 (ring-CH_2N), 62.48 ($OCOCH_2$), 69.84, 70.50 and 70.72 (CH_2O), 174.76 (C=O). IR (neat, NaCl, cm^{-1}): 1736. DE MALDI-TOFMS; *m*/*z*: 781.05, 783.06, 784.07, 785.06, 787.05, 789.05 ($C_{32}H_{66}O_{10}N_2Ge_2$, 784.10).

3.15. 3-Trimethylgermylpropionate of N-{2-(2-hydroxyethoxy)ethyl}-4-aza-9-crown-3 (G)

G was prepared (from **G-OH** (0.26 g, 1.19 mmol), **18** (0.33 g, 1.73 mmol), **29** (0.18 g, 1.47 mmol) and DCC (0.34 g, 1.65 mmol) as a pale yellow oil (0.33 g, 0.84 mmol, 70.7%). The eluent used was $CHCl_3$–MeOH = 8:1.

G. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 0.14 (s, 9H, Me_3Ge), 1.00 (m, 2H, $GeCH_2$), 2.37 (m, 2H, $GeCH_2CH_2$), 2.88 (m, 6H, CH_2N), ca. 3.6 (m, 12H, CH_2O), 4.22 (t, 2H, $OCOCH_2$). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ −2.50 (Me_3Ge), 11.50 ($GeCH_2$), 29.87 ($GeCH_2CH_2$), 55.96 (ring-CH_2N), 56.74 (chain-CH_2N), 63.46 ($OCOCH_2$), 68.90, 70.03, 72.26 and 72.54 (CH_2O), 174.83 (C=O). IR (neat, NaCl, cm^{-1}): 1736. DE MALDI-TOFMS; *m*/*z*: 390.07, 391.07, 392.06, 393.06, 394.06, 395.06, 396.06, 397.05 ($C_{16}H_{33}O_5NGe$, 392.05).

3.16. 3-Trimethylgermylpropionate of N-{2-(2-hydroxyethoxy)ethyl}-4-aza-12-crown-4 (H)

H was prepared from **H-OH** (0.25 g, 0.95 mmol), **18** (0.27 g, 1.42 mmol), **29** (0.17 g, 1.39 mmol) and DCC (0.28 g, 1.36 mmol) as a pale yellow oil (0.17 g, 0.39 mmol, 41.0%). The eluent used was $CHCl_3$–MeOH = 10:1.

H. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 0.13 (s, 9H, Me_3Ge), 1.00 (m, 2H, $GeCH_2$), 2.36 (m, 2H, $GeCH_2CH_2$), 2.78 (t, 6H, CH_2N), 3.65 (m, 16H, CH_2O), 4.21 (t, 2H, $OCOCH_2$). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ −2.50 (Me_3Ge), 11.49 ($GeCH_2$), 29.85 ($GeCH_2CH_2$), 55.53 (ring-CH_2N), 56.01 (chain-CH_2N), 63.48 ($OCOCH_2$), 68.93, 69.56, 70.17, 70.25 and 70.96 (CH_2O), 174.85 (C=O). IR (neat, NaCl, cm^{-1}): 1735. DE MALDI-TOFMS; *m*/*z*: 434.12, 435.12, 436.12, 437.12, 438.11, 439.12, 440.11 ($C_{18}H_{37}O_6NGe$, 436.10).

3.17. 3-Trimethylgermylpropionate of N-{2-(2-hydroxyethoxy)ethyl}-4-aza-15-crown-5 (I)

I was prepared from **I-OH** (0.13 g, 0.42 mmol), **18** (0.14 g, 0.73 mmol), **29** (0.08 g, 0.66 mmol) and DCC (0.15 g, 0.73 mmol) as a pale yellow oil (0.10 g, 0.42 mmol, 49.2%). The eluent used was $CHCl_3$–MeOH = 3:1.

I. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 0.13 (s, 9H, Me_3Ge), 0.99 (m, 2H, $GeCH_2$), 2.37 (m, 2H, $GeCH_2CH_2$), 2.88 (t, 6H, CH_2N), 3.66 (m, 20H, CH_2O), 4.23 (t, 2H, $OCOCH_2$). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ −2.53 (Me_3Ge), 11.40 ($GeCH_2$), 29.77 ($GeCH_2CH_2$), 54.85 (CH_2N), 62.23 ($OCOCH_2$), 67.73, 69.03, 69.84, 70.06 and 70.37 (CH_2O), 174.78 (C=O). IR (neat, NaCl, cm^{-1}): 1735. DE MALDI-TOFMS; *m*/*z*: 478.11, 479.11, 480.11, 481.11, 482.11, 483.11, 484.11 ($C_{20}H_{41}O_7NGe$, 480.16).

3.18. 3-Trimethylgermylpropionate of N-{2-(2-hydroxyethoxy)ethyl}-4-aza-18-crown-6 (J)

J was prepared from **J-OH** (0.13 g, 0.37 mmol), **18** (0.15 g, 0.79 mmol), **29** (0.08 g, 0.66 mmol) and DCC (0.15 g, 0.73 mmol) as a pale yellow oil (0.06 g, 0.11 mmol, 30.8%). The eluent used was $CHCl_3$–MeOH = 3:1.

J. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 0.14 (s, 9H, Me_3Ge), 1.00 (m, 2H, $GeCH_2$), 2.38 (m, 2H, $GeCH_2CH_2$), 2.88 (m, 6H, CH_2N), 3.65 (m, 24H, CH_2O), 4.22 (t, 2H, $OCOCH_2$). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ −2.48 (Me_3Ge), 11.50 ($GeCH_2$), 29.87 ($GeCH_2CH_2$), 54.58 (CH_2N), 63.47 ($OCOCH_2$), 68.95, 69.20, 70.21, 70.59 and 70.70 (CH_2O), 174.85 (C=O). IR (neat, NaCl, cm^{-1}): 1734. DE MALDI-TOFMS; *m*/*z*: 522.14, 523.14, 524.16, 525.16, 526.15, 527.14, 528.15 ($C_{22}H_{45}O_8NGe$, 526.23).

3.19. 3-Trimethylgermylpropionate of N,N′-bis{2-(2-hydroxyethoxy)ethyl}-4,13-diaza-18-crown-6 (K)

K was prepared from **10** (0.21 g, 0.48 mmol), **18** (0.26 g, 1.36 mmol), **29** (0.17 g, 1.39 mmol) and DCC (0.28 g, 1.36 mmol) as a pale yellow oil (0.18 g, 0.25 mmol, 51.6%). The eluent used was $CHCl_3$–MeOH = 6:1.

K. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 0.13 (s, 18H, Me_3Ge), 1.00 (m, 4H, $GeCH_2$), 2.37 (m, 4H, $GeCH_2CH_2$), 2.77 (t, 4H, chain-CH_2N), 2.84 (t, 8H, ring-CH_2N), 3.61 (m, 24H, CH_2O), 4.17 (t, 4H, $OCOCH_2$). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ −2.45 (Me_3Ge), 11.53 ($GeCH_2$), 29.90 ($GeCH_2CH_2$), 54.47 (ring-CH_2N), 54.82 (chain-CH_2N), 63.52 ($OCOCH_2$), 68.97, 69.69, 69.89 and 70.68 (CH_2O), 174.88 (C=O). IR (neat, NaCl, cm^{-1}): 1735. DE MALDI-TOFMS; *m*/*z*: 779.15, 781.15, 782.15, 783.15, 785.16, 787.15, 788.16, 789.14 ($C_{32}H_{66}O_{10}N_2Ge_2$, 784.10).

3.20. 3-Trimethylgermylpropionate of N,N′-bis{2-(2-hydroxyethoxy)ethyl}-7,19-diaza-24-crown-8 (L)

L was prepared (19.5%) from **L-OH** (0.28 g, 0.53 mmol), **18** (0.33 g, 1.73 mmol), **29** (0.19 g, 1.56 mmol) and DCC (0.35 g, 1.70 mmol) as a pale yellow oil (0.09 g, 0.10 mmol, 19.5%). The eluent used was $CHCl_3$–MeOH = 10:1.

L. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 0.13 (s, 18H, Me_3Ge), 1.00 (m, 4H, $GeCH_2$), 2.37 (m, 4H, $GeCH_2CH_2$), 2.81 (m, 12H, CH_2N), 3.62 (m, 36H, CH_2O), 4.20 (t, 4H, $OCOCH_2$). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ −2.45 (Me_3Ge), 11.53 ($GeCH_2$), 29.89 ($GeCH_2CH_2$), 54.56 (ring-CH_2N), 54.73 (chain-CH_2N), 63.52 ($OCOCH_2$), 68.95, 69.66, 69.84, 70.52 and 70.76 (CH_2O), 174.88 (C=O). IR (neat, NaCl, cm^{-1}): 1736. DE MALDI-TOFMS; *m*/*z*: 867.06, 869.06, 871.06, 872.06, 873.05, 875.07, 876.06, 877.05 ($C_{36}H_{74}O_{12}N_2Ge$, 872.20).

3.21. Attempted germylation of C-OH with 3-(trimethylgermyl) propionyl chloride

A solution of **C-OH** (0.46 g, 1.75 mmol) in $CHCl_3$ (12 ml) was refluxed, to which a solution of **20** (0.53 g, 2.53 mmol) in $CHCl_3$ (10 ml) was added dropwise. Heating was continued for 24 h. The solvent was removed under reduced pressure and the residue was purified by GPC to give a pale yellow liquid of **C.hydrochloride** (0.71 g, 1.50 mmol, 85.9%).

C.hydrochloride. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 0.14 (b, 9H, CH_3Ge), 1.00 (b, 2H, CH_2Ge), 2.38 (b, 2H, CH_2CH_2Ge), 3.16 (b, 6H, NCH_2), 3.68 (b, 16H, OCH_2), 4.23 (b, 2H, $COOCH_2$). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ −2.55 (CH_3Ge), 11.40 ($GeCH_2$), 29.77 (CH_2CH_2Ge), 54.85 (CH_2N), 63.23 ($COOCH_2$), 67.73, 69.83, 70.06 and 70.31 (CH_2O), 174.77 (CO).

Neutralization of **C.hydrochloride** with Na_2CO_3 gave **C** after purification (Yield: 28%). The spectroscopic data of **C** thus obtained are essentially identical with those of **C** obtained with the method described in Section 3.11.

3.22. Attempted hydrogermylation of an allylazacrown ether

To a solution of **9** (22.1 g, 210 mmol) and Na_2CO_3 (1.20 g, 106 mmol) in MeCN (250 ml), a solution of allyl bromide (**21**) (30.3 g, 250 mmol) was added dropwise, and the reaction mixture was stirred for 24 h. After cooling, CH_2Cl_2 (50 ml) was added and the solid was filtered. The organic layer was dried and removed under reduced pressure. The residue was distilled in vacuo (150 °C, 7 Torr) to give a colorless oil of *N*-allyldiethanolamine (**22**) (17.9 g, 58.6%).

22. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 2.61–2.68 (m, 4H, NCH_2), 3.19–3.21 (m, 2H, CH_2=CH–CH_2), 3.60–3.62 (m, 4H, –CH_2O), 4.07 (s, 2H, OH), 5.15–5.26 (m, 2H, CH_2=CH–CH_2), 5.81–5.91 (m, 1H, CH_2=CH–CH_2). ^{13}C–NMR ($CDCl_3$, 100 MHz): δ 55.70 (NCH_2), 57.61 (CH_2=CH–CH_2), 59.45 (CH_2O), 118.03 (CH_2=CH–CH_2), 134.86 (CH_2=CH–CH_2). IR (neat, NaCl, cm^{-1}): ν(C–N) 1446, 1419, 1361, 1041.

Sodium hydride (3.09 g, 128 mmol) in THF (120 ml) was refluxed, to which a solution of **22** (3.61 g, 24,8 mmol) in THF (50 ml) was added dropwise. Refluxing was continued for 20 h. Water was added, and THF was removed under reduced pressure. The residue was extracted with $CHCl_3$. The solvent was removed, and the residue was purified by column chromatography (Al_2O_3, $CHCl_3$) and GPC to give *N*-allyl-4-aza-15-crown-5 (**23**) as a yellow oil (2.70 g, 42%).

23. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 2.72 (m, 4H NCH_2), 3.16–3.17 (m, 2H, CH_2=CH–CH_2), 3.62–3.76 (m, 16H, OCH_2), 5.05–5.13 (m, 2H, CH_2=CH–CH_2), 5.82–5.92 (m, 1H, CH_2=CH–CH_2). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 54.16 (NCH_2), 59.99 (CH_2=CH–CH_2), 69.88, 70.15, 70.41 and 70.99 (OCH_2) 117.46 (CH_2=CH–CH_2) 135.81 (CH_2=CH–CH_2). IR (neat, NaCl, cm^{-1}): ν(C–N) 1431, 1041.

A mixture of **23** (0.50 g, 1.54 mmol) and triphenylgermane (**24**) (3.32 g, 1.23 mmol) was heated with continuous stirring in the presence of a catalytic amount of $H_2PtCl_6 \cdot 2H_2O$ at 111 °C for 48 h. The solid was filtered, and the residue was dissolved in $CHCl_3$ (20 ml). The organic layer was dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residue was purified with GPC to give *N*-[(3-triphenyl)germyl]propyl-4-aza-15-crown-5 (**25**) (0.04 g, 5.8%).

25. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.46–1.51 (m, 2H), 1.65–1.73 (m, 2H), 2.56–2.60 (m, 2H), 2.68–2.71(m, 4H, NCH_2CH_2O), 3.56–3.68 (m, 16H, CH_2O), 7.30–7.39 (m, 6H, Ph), 7.44–7.49 (m, 9H, Ph). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 11.47, 22.28, 54.35, 59.78 (NCH_2), 69.88, 70.15, 70.26 and 70.83 (OCH_2) 128.20, 128.88, 134.93 and 137.12 (Ph).

3.23. Cation transport experiments

Cation transport experiments were carried out by the H-tube test (Fig. 8). Thus, in the bottom of the H-tube, a $CHCl_3$ solution of azacrown ether **A**–**L** (1 mmol dm^{-3}; 7 ml) was added and in the right arm of the H-tube (source phase), an aqueous salt solution (100 mmol dm^{-3}; 3 ml) was added. In the left arm of the H-tube (receiving phase) pure H_2O was taken. A small magnetic bar was placed in the bottom of each arm and stirred continuously. The whole tube was kept at 25 °C for 24 h. The amount of cations in the receiving arm was measured by atomic absorption spectroscopy. The blank test was also performed where no host was dissolved in the organic layer.

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