PURIFICATION OF WASTE WATER WITH CROWN ETHERS ANCHORED ON A SOLID SUPPORT

Report to the

Water Research Commission

by

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WRC Report No : 1173/1/03
ISBN No : 1-77005-057-4

July 2003

Executive summary

Back ground

A new technique to purify waste water from SA mines and factories was developed. The importance of a solution to the general world wide problem to purify water cheaply, and effectively, is highlighted by the fact that UNESCO has identified contamination of earth's fresh water supplies as the biggest threat to man's survival on earth. This is put in perspective when one realises that UNESCO estimates that only 0.007 % of water on earth is still capable and simultaneously available (i.e. not to deep underground, not frozen on polar ice caps etc.) to support human life. The remainder is too contaminated with salts and metals to support human life (quoted from UNESCO'S web page: htpp://www.unesco.org). It is, therefore, important to maintain existing fresh water supplies and to purify large industrial volumes of waste water. Purification of industrial waste water, however, presents a large problem. Reverse osmosis, or other technologies are currently used to *partially* remove sulphate, chloride, sodium, calcium, phosphate and other ions from industrial effluents by fractionating the water into a clean portion and one in which the contaminants are concentrated to 10% or more. Either the contaminated fraction is stored in sludge dams or dams with a high salt content to slowly evaporate, or more expensive purification processes (e.g. distillation) are used. Eventually, contaminated water from the waste water reservoirs seeps into the ground, and contaminates underground water reservoirs. Such underground water reservoirs eventually become unfit for human consumption or to support life in general (i.e. bore holes become useless). The poisonous nature of the water in the sludge dams also poses a major threat to the entire ecological system in which they are situated. For example, no fish will live in it. Birds and small mammals become poisoned when they drink it, they die, and an entire life chain is disturbed. Trees and vegetation will die. A technology which can remove all contaminants from wastewater after techniques such as reverse osmosis, membrane technology partially cleaned it, is highly desirable.

We began developing such a technology and funding to develop it further should be top priority. Our strategy involves identification of a suitable ligand that can bind a target metallic cation, in this study the sodium cation, strongly but reversibly. To bind sodium cations, the crown ether family of ligands was identified. In order to handle this sodium cation scavenging moiety in a convenient way during the purification of water, the crown ether was anchored on a suitable support system, here an elastomeric (rubber-like) polymer. To make this material work as sodium cation scavenging device it needs to be circulated through contaminated water, given

enough time to bind the contaminant cations, and then it must be transported to a collecting vessel where the contaminating cations must be released and recovered from the support. If this process can be achieved in a cyclic way economically, it will complement existing membrane technology by taking over the cleaning of polluted waste water after membrane technology concentrated impurities into a smaller volume of water. It provides for the eventual recovery of all water contaminated in industrial processes. When such technology becomes fully operational, greatly improved opportunities will be created, many of these economic.

Aims of study

To achieve this goal, the aims of this study was as shown below. All the aims were realised.

1. Synthesis and modification of crown ethers and other macrocycles.

Since crown ethers are the molecules that was chosen to bind the sodium cation contaminants in waste water, they were chemically modified to allow polymer anchoring.

2. Test the effectivity of synthesised crown ethers as contaminant scavangers

This task was done routinely to establish if a newly synthesised compound was an effective contaminant scavenger.

3. Develop suitable polymers on which the crown ethers may be anchored

A polymeric solid support was chosen as the tool required to transport the contaminants from the contaminated water reservoir to a suitable site for precipitation.

4. Anchor the crown ethers on the polymers

Suitable methods to bind the crown ethers to the polymeric solid support were developed

5. Develop techniques to allow release of the contaminants from the polymeric carriers.

Once the contaminants have been trapped by the polymer bound crown ethers, they need to be release again under controlled conditions at a previously determined site. Factors that may be used to influence the release of the contaminants are heat (up to 60 C), UV light irradiation and pH changes. Precisely how pH control may be utilised to induce release of the contaminants from the polymers were researched.

Methodology

In order to modify crown ethers to allow it to be anchored onto a solid support benso-15-crown-5 derivatives were synthesised and functionalised to have an aldehyde, nitro, amino, alcohol, halide or carboxylic acid group on them. This provided a handle to anchor it on the polymer.

The effectivity of selected crown ethers as sodium cation scavenging devices were tested by measuring the amount of sodium cations it could remove from a standard stock solution utilising analytical techniques such as flame photometry. The solid support required to anchor the crown ether sodium cation scavengers on, involved developing techniques to polymerise hydroxy-terminated polybutadiene into a rubber-like elastomer via diisocyanate curing. The polymerisation of epichlorohydrin, and its functionalisation to have amino, isocyanate and carboxylated side chains were also explored. This provided us with handles to which the crown ethers may be anchored. Methods to chemically bind the crown ethers to the polymers involved the reactions between amines and isocyanates, amines and carboxylic acids, alcohols and isocyanates, amines and halogens. In essence the crown ethers was attached to the solid support via linking units of monomeric (e.g. isophorone diisocyanate) or polymeric (e.g. polyvinyl alcohol) nature. Finally, the effectiveness of sodium release from the polymer-anchored crown ether device under different acid conditions were researched by determining how much cations was released from the cation scavenging device under specific acidic conditions. The method of detecting sodium cations was again flame photometry.

Results

All the above aims were successfully explored. The best sodium cation scavenging devices were found to be those that had polymeric linking groups between solid support and crown ether. Systems that allowed dendrimer technology of the third order to exponentially increase the loading capacity of crown ethers on the solid support were especially effective. Specifically, when the linking groups were a dendrimer constructed from a di-isocyanate coupled to polyvinyl alcohol, which was in turn coupled to an isocyanate-containing polymer, 92% removal of all sodium cations from a 10 cm^3 sample of 200 ppm stock solution was achieved in a single extraction experiment. The device performed optimally at ca 50-60 ^oC. Repetitive experiments showed that the device did not loose activity after 10 extraction cycles. The capacity of the present device is approximately 1.5g/m^2 surface area of the scavenging device.

Conclusions and Recommendations for Further Research

During the period 2000 –2002 we have set ourselves the goal of developing the science required to develop a new means of cleaning factory wastewater. This new process is distinctly different from current state of the art ion exchange or membrane technology. We have developed procedures to synthesise an elastomeric polymeric support, synthesise Na^+ scavenging devices in the form of crown ether derivatives, and we developed the science required to heavily coat the surface of the solid support with the crown ether Na^+ scavenging molecules. In particular we used dendrimer technology adapted to polymer systems and we called these starburst molecules. The design of our device is provided in schematic form providing details of the system on page 41, **Figure 12**.

Although this research program succeeded to develop the science required to manufacture a device that is capable of transferring 76-92% of the available Na^+ cations from a 200 ppm Na^+ solution, and release half of this amount again in a previously determined reservoir in a single cycle, the density of Na^+ cations on the solid support is still low: only about 1.5 g / m^2. Also, the present technology only supports Na^+ removal from water. To improve the loading capacity, and to expand the technology to also include other cations including heavy metals, it is recommended that

1) Funding be made available to develop the technology to increase the density of Na^+ loading by expanding the order of the existing starburst structure from 3 to 6.
2) Devices be developed that can remove (and selectively recover) other metals from aqueous solution including magnesium (pollutant), lead (poison), platinum and silver (precious metals), copper and cobalt (economically important but scarce metals in South Africa) cations.
3) The present technology be expanded to include inputs from engineering institutions to test and develop this new technology on pilot plant scale and beyond.

Acknowledgements

The research in this report emanated from a project funded by the Water Research Commission and entitled

"PURIFICATION OF WASTE WATER WITH CROWN ETHERS ANCHORED ON A SOLID SUPPORT"

The Steering Committee responsible for this project consisted of the following persons:

Dr G Offringa	Water Research Commission (Chairman)
Mr P. Smit	Water Research Commission (KSA Co-ordinator)
Mrs M Hinsch/alt Mrs LA Boyd	Department of Water Affairs and Forestry
Mrs WC DuPlessis	University of the Free State (Secretary)
Prof SS Basson	University of the Free State
Prof JC Swarts	University of the Free State
Dr JC Roos	University of the Free State
Dr EWA Cukrowska	University of the Witwatersrand
Prof RD Sanderson/alt Dr EP Jacobs	University of Stellenbosch

The financing of the project by the Water Research Commission and the contribution of the members of the Steering Committee is acknowledged gratefully.

This project was only possible with the co-operation of many individuals and institutions. The author therefore wish to record his sincere thanks to the following:

Dr HG Koortzen	University of the Free State
Dr TM Botha	University of the Free State
Mr K Du Toit	Sastech

CONTENTS

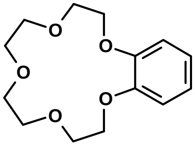
CONTENTS

List of Tables

List of Figures

List of Reaction Schemes

List of Symbols and Abbreviations

benzo-15-crown-5	This trivial nomenclature is used throughout this report to indicate 2,3-benzo-1,4,7,10,13-pentaoxacyclopentadec-2-ene, the IUPAC name for the compound having the structure 
DMF	dimethyl formamide
HTPB	hydroxy-terminated polybutadiene
LD_{50}	50% lethal dosage
PECH	polyepichlorohydrin
Ts	toluenesulphonyl
〰	This symbol is used to indicate that a polymer is cross-linked.

1. Introduction: Ultimate goal of study

The ultimate goal of this research program is to prepare the components of a device that is capable of removing salts such as sodium chloride or sodium sulphate from factory wastewater. For this purpose a solid support is required to which may be anchored a suitable complexing agent that is capable of selectively but reversibly binding contaminating sodium cations. The solid support may be in the form of beads, balls, or any suitably engineered form, but for the purpose of developing the science required to make such material, during this study, an elastomeric polymeric water-insoluble support that can inter alia operate as a conveyer belt was chosen. Crown ether sodium cation scavenging derivatives were then anchored onto this support. To envisage how this device may work, **Figure 1** is instructive. This diagram helps to visualise how a water-insoluble elastomeric solid support, covered on the surface by a material that can trap a targeted water-soluble polluting ion, here crown ethers for the sodium cation, may look like and operate. It operates by picking up the Na^+ contaminant from contaminated water, shown here as a brine-like wastewater ***lake*** that stocks pollutants, but it can for instance also be a outlet stream at a factory. The trapped contaminants may then be released under suitable conditions in a small ***recovery reservoir***. The concentration of the pollutant in the ***recovery reservoir*** will increase with time until eventually it begins to precipitate. Hence the reservoir has the capability of recovering contaminants in a pure form and in the solid state. This pre-designed reservoir will be very small, perhaps 2 x 2 x 2 m.

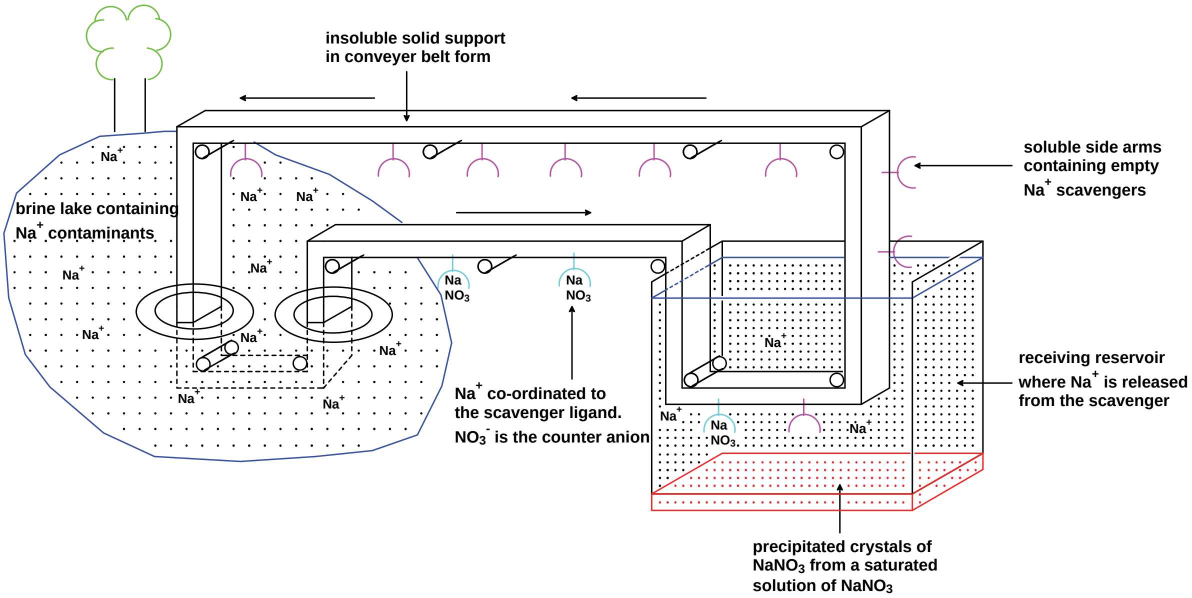


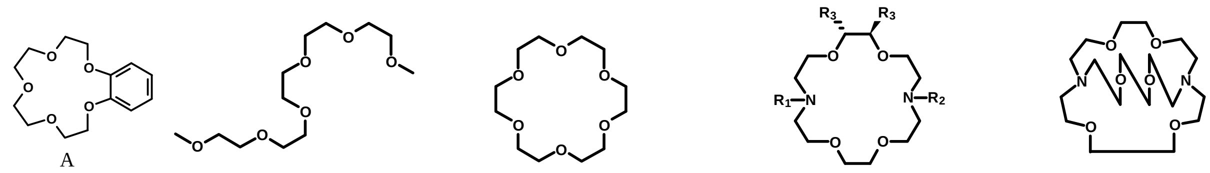
Figure 1: Schematic design of a device that can selectively recover contaminants from wastewater. Drawing not to scale. The brine lake holding the contaminated water may cover several thousands of square meters, while the receiving reservoir must be small, perhaps covering an area as small as only 5 m^2.

2. Literature survey

Since the discovery of crown ethers by Pedersen,[1] in the late 1960's, many researchers have investigated this class and related macrocyclic compounds for their ability to complex cations, anions and neutral compounds. Crown ethers[1] or coronands[2] (**Figure 2**) are macrocyclic ligands that only contain oxygen atoms as donor atoms. Due to the cumbersome IUPAC names of these macrocycles, e.g. 2,3-benzo-1,4,7,10,13-pentaoxacyclopentadec-2-ene for **A**, trivial names such as benzo-15-crown-5 for **A**, will be used throughout this document. Trivial names consist of:

i. The substituents on the macrocyclic ring, e.g. the benzo group of **A**.
ii. The number of atoms in the macrocyclic ring, e.g. 15 for **A**.
iii. The base name ‘crown’.
iv. The number and type of donor atoms in the macrocyclic ring, e.g. 5 for **A**.

Crown ethers are known for their complexation preference for alkali and alkaline earth metal cations.[1] Many factors have been found that influence the selectivities of macrocycles, including macrocyclic cavity dimensions; shape and topology; substituent effects; conformational flexibility/rigidity; and donor atom type, number and arrangement.



A

B K^+, log *K* (MeOH) = 2.30

C K^+, log *K* (MeOH) = 6.32

D $R_1 = (CH_2CH_2O)_2CH_3$, $R_2 = CH_3$, $R_3 = H$, K^+, log *K* (MeOH) = 4.80

E n = 0, K^+, log *K* (MeOH) = 10.49

Figure 2: Benzo-15-crown 5, **A**, a podand, **B,** crown ether, **C**, lariat ether, **D,** and cryptand, **E**.

The question that arises is what effect does ring formation has on the binding strength of poly(ethyleneoxy) compounds with cations? The answer to this question can be illustrated by the comparison of thermodynamic data, such as the stability constants (log *K*) between a podand, crown ether, lariat ether, cryptand and a cation. The log *K* (MeOH) for the interaction between the podand **B** and K^+ is 2.30, compared to 6.32 for the interaction between the crown ether **C**, 4.80 for the interaction between **D** and 10.49 for the interaction between the cryptand **E** and K^+, respectively. It is clear that the more preorganised the molecule becomes, i.e. from linear, such as the case with the podand (least preorganised) to bicyclic, such as the case with the cryptand (most preorganised), the interaction of the ligand with the cation produced a more stable complex. The principle of preorganisation in its original formulation states: "the smaller the changes in organisation of host, guest, and solvent required for complexation, the stronger will be the binding of the guest species".[3]

It is thus very important to have a ring, or cyclic structure, to obtain a more stable cation-ligand complex. Ring size plays a further role in how strong ligand-cation interaction is. Ring size can be changed in two ways: by increasing the size of the ring without changing the amount of donor atoms, and by increasing the amount of donor atoms. For the first possibility, it was found that changes in the structure from **F**, n=0 to **F,** n = 1 changed the affinity of these molecules towards Li^+ and Na^+. For n = 0, K (MeOH) = 2.01 and 2.06, for Li^+ and Na^+ respectively. For the interaction of **F** with n = 1, log K $(MeOH)_{Li}$ = 2.34 and log K $(MeOH)_{Na}$ = 1.63, respectively.[3] Thus, despite the same amount of donor atoms in their macrocyclic rings, i.e. 4 oxygen donor atoms, it is evident that **F**, n = 1, prefer Li^+ above Na^+, while **F**, n = 0 do not exhibit a cation preference between Li^+ and Na^+. The amount of donor oxygen atoms also play a role. Crown ethers with 4 oxygen atoms prefer mostly Li^+ (e.g. **F**or **H**, n=1). With 5 oxygen atoms, Na^+ is prefered: **H**, n = 2 have log K_{Na} = 3.37. With n = 3, K^+ or Pb^{2+} is preferred (log K_K = 6.32, log K_{Pb} = 5.49), while n = 4 leads to a complex that prefers Rb (log K_{Rb} = 7.37).

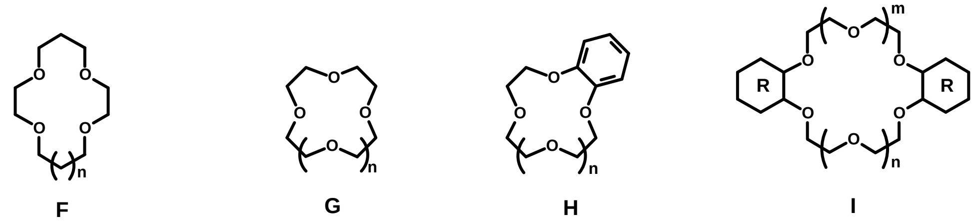


Figure 3: Structural differences in crown ethers

The selectivity of crown ethers with different size for specific cations can be traced to the radius of cations and the diameter of the cavity in each macrocycle. The cation radii of selected cations are listed in **Table 1**, while **Table 2**, lists cavity dimensions of specific classes of crown ethers. The listed data imply, for example, that all the crown ethers that contain 14-members in their macrocyclic ring contain cavities with dimensions between 1.20 – 1.50 Å. Furthermore, if one have a need to bind K^+, one needs to find a crown ether with a cavity size comparable or larger than that of the cation. The ionic diameter of K^+ is 1.38 Å. Thus, crown ethers with a cavity size larger than 1.38 Å, such as 15-crown-5, 18-crown-6 and 21-crown-7 would be able to house the desired cation. Logically, if the cavity is very large, binding is poor. Just the right size will allow efficient orbital overlap and hence good binding. The cavity size is not the only factor in determining which cation would be complexed, but as a general rule, it gives a good idea of which crown ether can be used to complex a desired cation.

Table 1. Selected metal cation diameters.

Cation	Ionic Diameter, Å	Cation	Ionic Diameter, Å
Mg^{2+}	0.72	Ba^{2+}	1.35
Li^{+}	0.76	K^{+}	1.38
Ca^{2+}	1.00	Rb^{+}	1.52
Na^{+}	1.02	Cs^{+}	1.67
Ag^{+}	1.15	NH_4^{+}	2.84
Sr^{2+}	1.18		

Table 2. The cavity diameter for selected macrocyclic ring sizes.

Macrocycle	Cavity Diameter, Å
14-crown-4	1.20 – 1.50
15-crown-5	1.70 – 2.20
18-crown-6	2.60 – 3.20
21-crown-7	3.40 – 4.30

The next question that comes to mind is what would happen when the macrocyclic ring would be made more rigid, by attaching for example a benzene ring? The addition of two benzo groups, as in **I** (**Figure 3**), rigidifies the crown ether and it also reduces the donicity of the attached oxygen atoms.[4] This can clearly be observed by comparing the interaction between **G** (n = 3) and **I** (n = 3) and K^+. The log *K* (MeOH) values changed from 6.32 to 5.00 in moving from **G** to **I**, implying that the affinity of **I** for the K^+ has dropped by about 20 % as compared to the affinity of **G** for the same cation. However, compounds such as **H** and **I** is much easier to modify chemically by introducing side chains due to the much higher reactivity of the aromatic benzene ring compared to that of an alkyl group.

The complexation of cations by macrocyclic ligands is thus not as straightforward as one would expect. Factors such as the presence of a cyclic structure, the structural arrangement of the donor atoms and the presence of rigid groups, must all be considered to ascertain the viability of ligands as complexons for cations.

Many of the crown ethers are known to have biological effects.[4] In terms of how poisonous they are, the LD_{50} value (50% oral lethal dosage) for crown ether **G** (n = 2) and **I** (m = n = 1) were reported as 3.15 g/kg and 300 mg/kg respectively. The LD_{50} reported for aspirin in mice is 1.10 g/kg, and for strychnine sulphate 5 mg/kg.[4] Especially 15-crown-5 derivatives would thus not pose a poisonous threat to ecosystems when it is used with normal care in a water purification procedure.

Acording to Hansch's series of lipophilia,[5] crown ethers earn a 'zero', and this makes it soluble in both lipophilic media, e.g. benzene or chloroform; and in hydrophilic media, e.g. water or short chain alcohols. This universal solubility is due to the unique structure of the macrocyclic ring of the crown ether. Each lipophilic ethylene group is associated with a highly hydrophilic oxygen atom. Although they show this universal solubility, the orientation of the crown ether ring in solution will drastically be influenced by the nature of the solvent used (**Figure 4**). For instance when hydrophilic solvents are used, e.g. water or short chain alcohols, the highly hydrophilic oxygen atoms are directed outwards and a lipophilic nucleus is formed (**Figure 4a**). When lipophilic solvents are used, e.g. benzene or chloroform, the lipophilic CH_2 groups are directed outwards and the oxygen atoms are forced inside the cavity of the macrocyclic ring (**Figure 4b)**. In the latter case, a hydrophilic and electronegative cavity is produced, and this cavity is suitable for complexations of cations, such as K^+, even in organic lipophylic media.

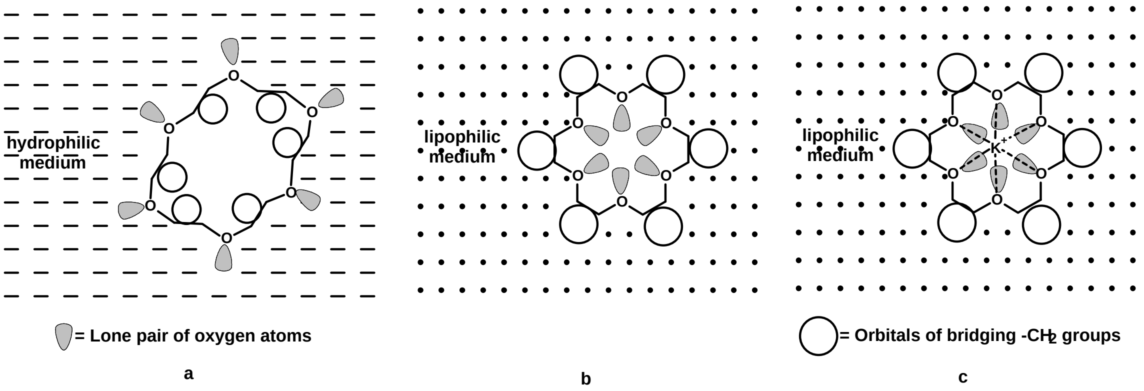
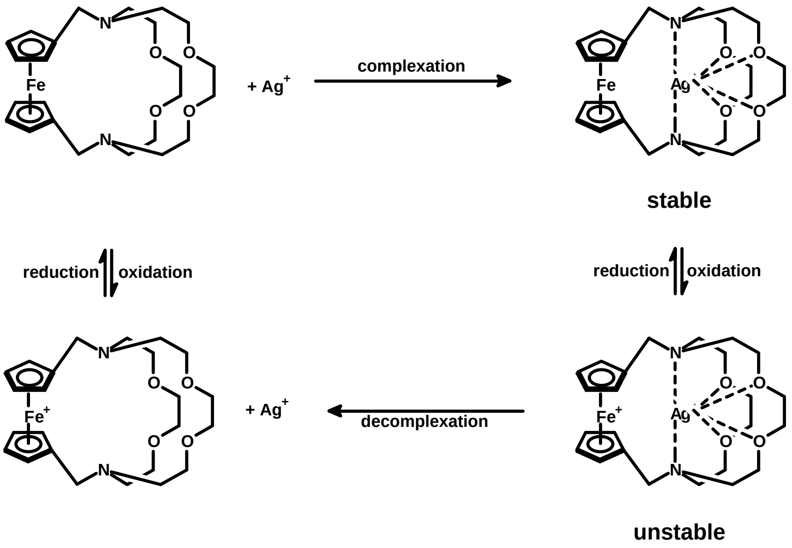


Figure 4: The influence of both lipophilic and hydrophilic media on the orientation of the 18-crown-6 macroring in both hydrophilic (a) and lipophilic (b) media, and the subsequent formation of a hydrophilic cavity that is suitable for the inclusion of cations (c), such as K^+.

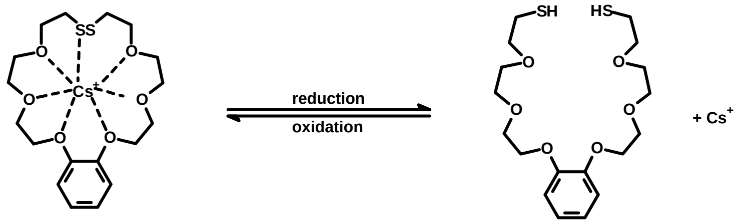
Macrocycles usually form 1:1 metal:macrocyclic ligand complexes, but, depending on the ratio of the diameter of the cavity and metal cation diameter, 1:2 and 2:3 complexes are also possible. The 1:1 complexes consists of the metal cation bound in the cavity of the macrocycle, and the most stable complex is considered to form when all the donor atoms in the macrocycle participate in the complexation of the cation. This is the ideal situation, but is not always the case, because the metal cation may have directed valencies that preclude bonding to all the donor atoms, or it may be too large or too small to fit "exactly" in the cavity. When **H**, n=3, forms a complex with K^+; the six oxygen atoms of the host form a ring around the equator of the spherical K^+. The apical positions are unoccupied in this situation. Since the host's donor atoms do not normally interact in the axial positions, many crown ether complexes have a counteranion or solvent molecule(s) in the co-ordination sphere.[4]

In order for crown ethers to be used in a cyclic way to transport cations from one phase to another, it is important to establish how cations may be released from their crown ether hosts. Three main methods are known: Redox induced cation release, light induced cation release and pH change induced cation release.

To achieve redox switching, the redox switchable compound must contain an active redox-responsive moiety close to the cation, or anion, binding site. Beer *et al.*[6] showed that reducible, or oxidisable, redox-active macrocycles can electrochemically recognise cationic (metal, ammonium) and anionic (halides, nitrate, phosphate, hydrogen sulphate) as guest species. These systems can be designed to electrochemically recognise the binding of a metal guest cation between the receptor site and the redox-active centre.[7] Ferrocene substituted macrocyclic ligands are mostly used for these types of switches (see below). Gokel *et al.*[8] prepared several ferrocene containing cryptands and the electrochemical behaviour of these complexes indicate that they act as redox-switchable ligands for several metal cations. The oxidation state of the ferrocene/ferrocenium redox couple will influence the behaviour of the macrocycle directly. In the neutral form, the ferrocene containing macrocycle will complex cations. However, when it is oxidised [Fe(II) → Fe(III)], a repulsive positive charge is placed in close proximity to the macrocyclic-bound positively charged cation. This situation is an unfavourable one, due to the presence of two cations, and will destabilise the complex,[9] and afford the release of the cation. An illustration of this cycle is given below.[10]



Another way of controlling the complexation, or decomplexation, is the difference in the complexation abilities between the cyclic (coronand) and the acyclic (podand) forms of a macrocycle. This method appears to be better than the reduction and oxidation of macrocyclic compounds, because one destroys the entire macrocyclic ligand and thus one creates a big difference in the complexation abilities between these two forms. One way of achieving this, is the use of the thiol/disulphide couple.[11] This is shown below. The coronand macrocycle exhibits a high selectivity for Cs^+, while the podand hardly bind any metal cations.[11] Here, decomplexation occurs, not due to the close proximity of another cation, but due to the difference in the complexation ability between the cyclic (i.e. coronand) *vs.* the acyclic (i.e. podand) form of the complexing ligand.



coronand
log $K(Cs^+) = 2.51$

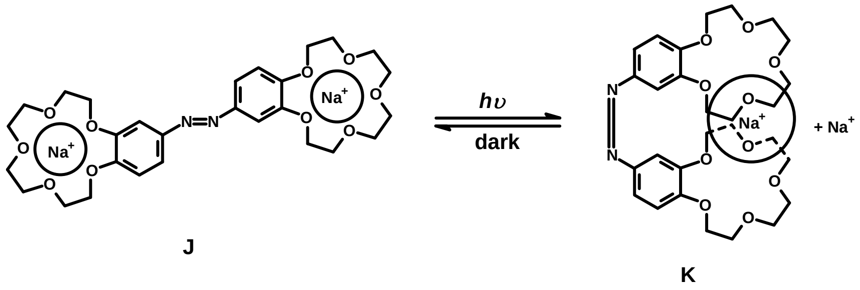
podand
log $K(Cs^+) < 0.1$

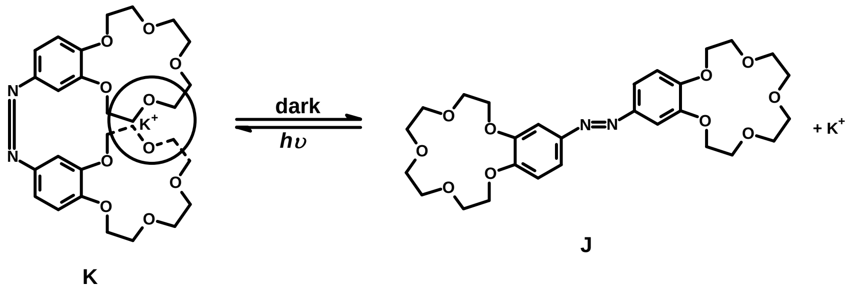
Photoresponsive systems are widely seen in nature in processes such as photosynthesis, vision, phototropism and phototaxis. In these systems light is used as a trigger to cause subsequent events, such as a change in conformation of molecules. A photo antenna to capture a light photon is utilised in conjunction with a functional group to mediate a subsequent event.[12] Chemical substances that exhibit photo-induced structural change can also be used to change the complexation ability of crown type compounds. Azobenzene derivatives of these macrocycles, which exhibit photo-induced reversible *cis*-*trans* isomerism, can be very useful in the release of cations. One reason for this, is the large geometrical change that occurs during the conversion from the *cis*- to the *trans*-isomer, and this process is also reversible.[13] The photo-induced properties of azobenzene can be used as a tool:[14]

1. to change the cation extraction capability of the macrocycle;
2. to enforce a conformational change of macromolecules in solution;
3. and to monitor the rate of the conformational changes of crown ethers and polymers.

Shinkai *et al.*[12] attempted to utilise these properties to bind and release cations via a butterfly-like motion in response to photo-irradiation. The process is shown below. The *trans*-isomer, **J,** can complex two sodium cations due to the fact that this compound is made up of two benzo-15-

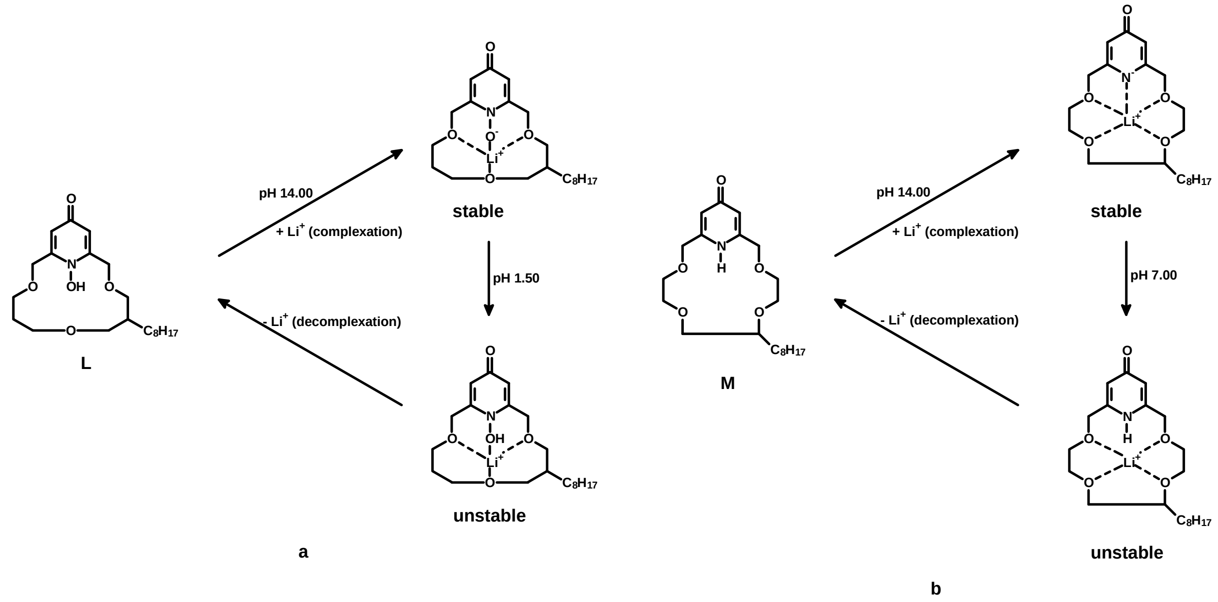
crown-5 moieties, which is selective for Na^+. When this isomer is treated with light, it switched to the *cis*-isomer, **K**. In this conformation the presence of two positive charges is unfavourable and one of the sodium cations is released. Benzo-15-crown-5 is normally not selective towards potassium cations, but, when two benzo-15-crown-5 moieties are nearby, they produce a cavity that is suitable to complex one K^+. Thus the photo-isomerised *cis*-isomer **K** exhibits greater binding abilities for larger alkali metal cations than the *trans*-isomer **J**.





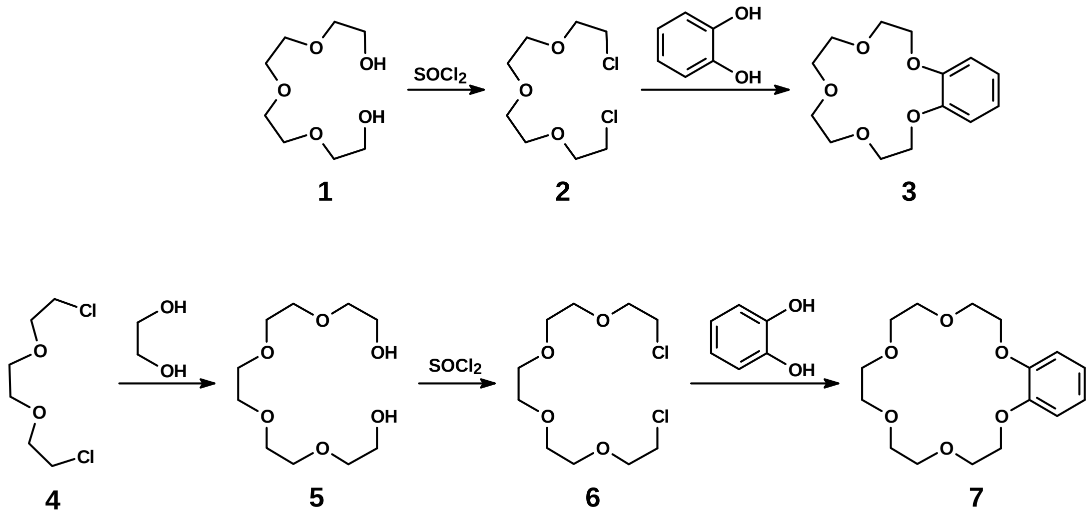
To accomplish pH switching, the macro ring must preferably contain a proton ionisable group[15]. Izatt *et al.*[16] designed proton-ionisable macrocycles containing the ionisable site at the donor atoms of the macrocyclic ring. This functional group allows the control of whether H^+ or M^+ are bound. Here, no co-anion is present due to the fact that the negative group is also associated with the complexed cation.[16] They found that at pH levels ~14 the transport of metal ions, such as Li^+, was increased. The best cation transports occurred when the source phase pH was 14, indicating that ionisation of the macrocycle was a necessary part of the transport process. The transport process is illustrated below for two different examples.

This study was aimed at designing a system containing a 15-crown-5 macrocyclic ligand in order to remove Na^+ from waste water in a cyclic way. Na^+ release from the macrocycle was achieved by means of pH control.



3.1 The synthesis of crown ethers

For the purpose of this study, 15-crown-5 and 18-crown-6 derivatives are important as the former selectively binds (or complex or trap) sodium in its core, while the second is especially selective towards potassium and calcium ions.[17] We developed a technology enabling industry to remove sodium and calcium ions from waste water utilising 15-crown-5 and 18-crown-6 derivatives. Ordinary 15-crown-5 and 18-crown-6 are difficult to functionalise to allow anchoring on a suitable polymer, but benzo-crown derivatives may be functionalised at the phenyl ring utilising organic chemistry techniques. However, both these derivatives, benzo-15-crown-5, **3**, and benzo-18-crown-6, **7**, are expensive (in excess of R250/g). We therefor set out to develop techniques to synthesise these compounds as shown in **Scheme 1**.



Scheme 1: Synthesis of benzo-15-crown-5, **3**, and benzo-18-crown-6, **7.**

Regarding benzo-18-crown-6 synthesis, conversion of the dihalide **4** to pentaethylene glycol, **5**, followed by chlorination is much cheaper than purchasing either **5** or **6**. We can now synthesise benzo-15-crown-5 and benzo-18-crown-6 in 30 g batches at less than R10/g and R15/g each.

3.2 The pH dependence of sodium extraction by benzo-15-crown-5 into chloroform

A pH profile of sodium cation extraction with benzo-15-crown-5 has been determined. As can be seen in **Figure 5**, sodium co-ordination and extraction from water into chloroform by an extraction is 30% or more successful at pH's larger than 9 and only 10% or less successful at pH's below 5. These results apply to a single extraction from water containing 8.699 mmol dm^{-3} sodium chloride (that is 200 ppm sodium cations) utilising an equal volume of a 4.350 mmol dm^{-3} benzo-15-crown-5 solution.

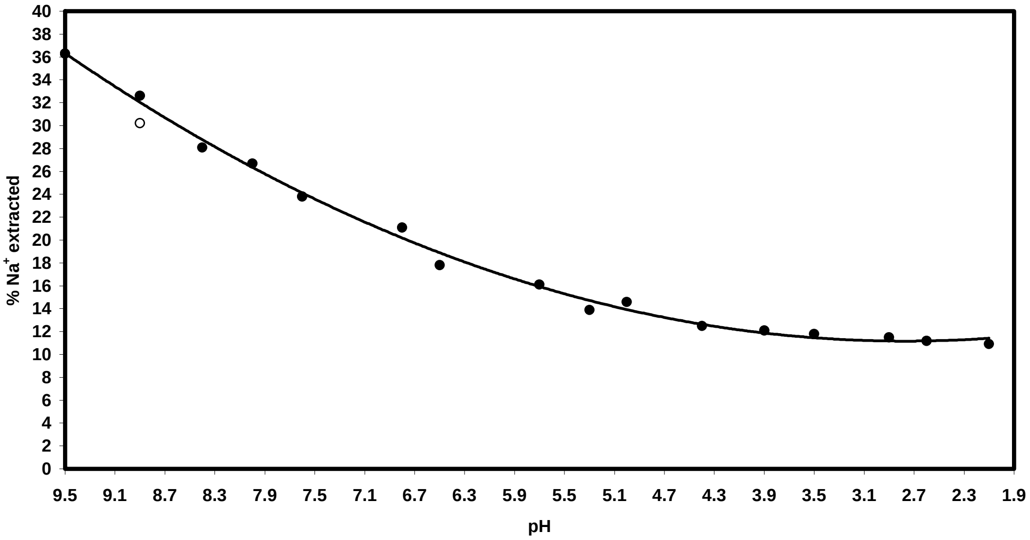
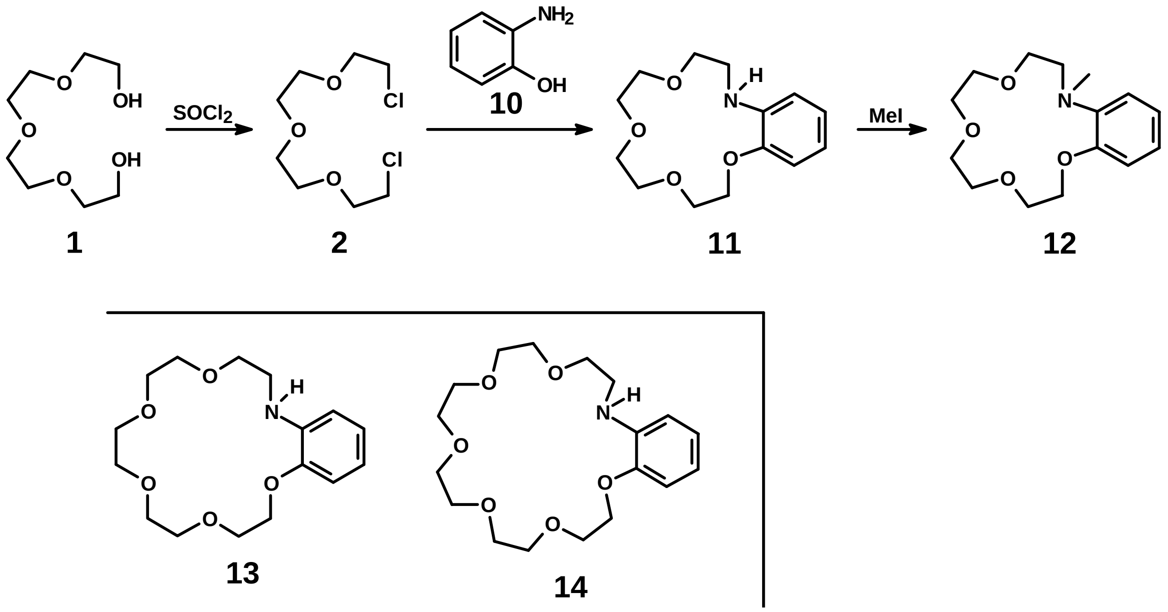


Figure 5: pH dependence of sodium extraction by benzo-15-crown-5 into chloroform from water. [NaCl] = 8.699 mmol dm^{-3} = 200 ppm Na^+, [benzo-15-crown-5] = 4.350 mmol dm^{-3}.

The same extraction-pH profile was obtained regardless of whether the extraction was performed at room temperature or at 50 °C, or for short (15 seconds) or long (5 minute) periods of time. Especially the last result relating to time was important, as it indicated that the kinetics of complexation is fast.

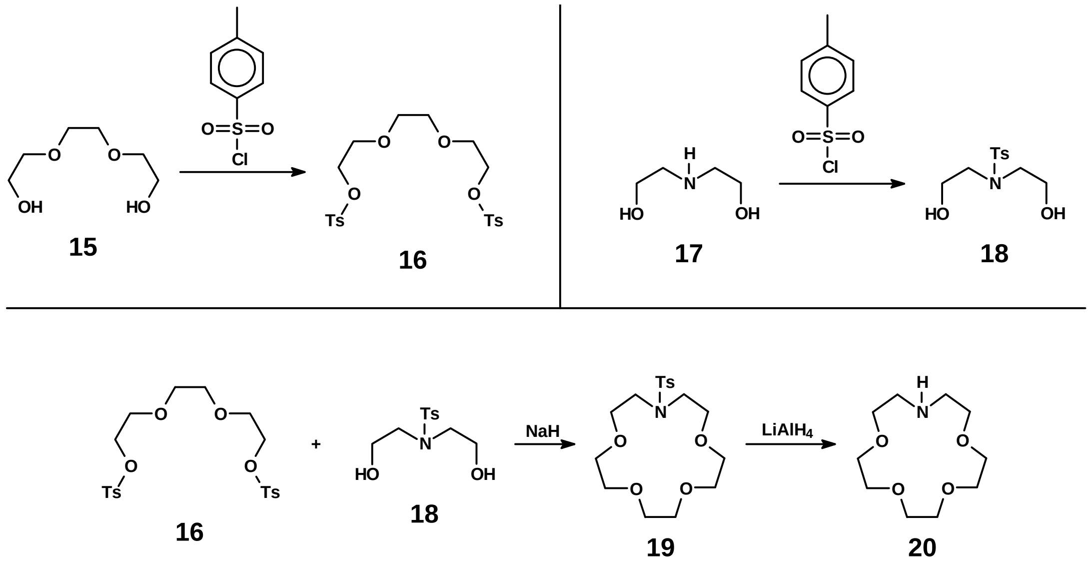
4 Aza derivatives of benzo-15-crown-5

Aza derivatives of benzo-15-crown-5 are of interest as we demonstrated that 1-aza-benzo-15-crown-5 show an enhanced pH effect in the binding and release of lithium cations. We have synthesised 1-aza-benzo-15-crown-5, **11**, and the methylated derivative **12** according to **Scheme 2**. Compound **11** was found to be more selective towards lithium chelation than sodium chelation. It removed 27 % Li^+ cations from a 200 ppm Li^+ solution while only 15 % of Na^+ cations was removed (at pH 9) by this compound. The methylated derivative **12** removed 32 % Li^+ cations from a sample of a 200 ppm Li^+ stock solution. We also synthesised the bigger homologues **13** and **14**. These compounds are, however, more suitable for transition metal complexation, and were not investigated any further.



Scheme 2: Strategy to synthesise aza-containing benzo-crown-ether derivatives **11-14**.

Since the benzo moiety on aza crown ethers are not necessary to functionalize aza crown ethers to have, for example, an alcohol side chain (see compound **12**, **Scheme 2**), we have also synthesised 1-aza-15-crown-5, **20**, as shown in **Scheme 3**.



Scheme 3: Synthesis of aza-15-crown-5**, 20**. Ts = toluenesulphonyl.

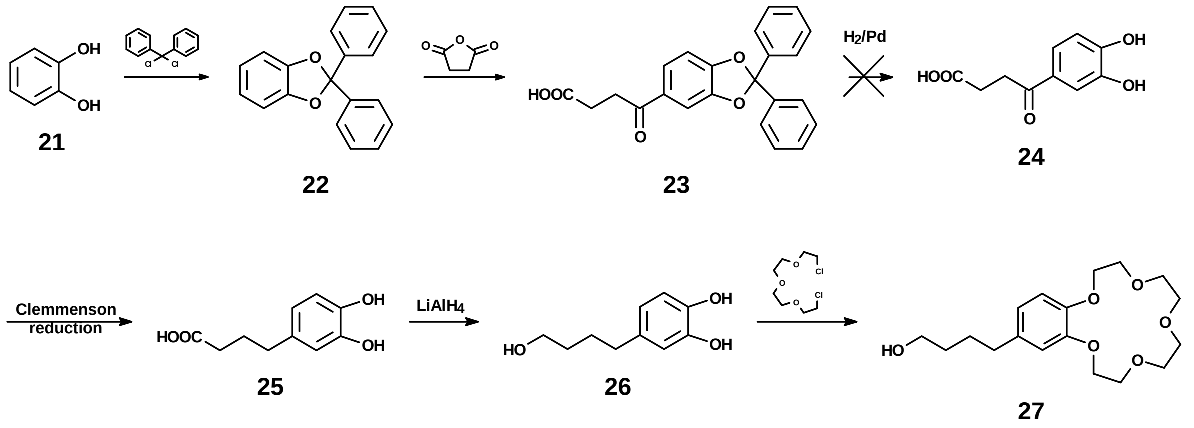
Although compound 20 can easily be functionalised to allow later anchoring later on a solid support we focussed for the remainder of this report on the functionalising and use of benzo-15-crown-5 derivatives as Na^+ scavangers.

5 The synthesis of functionalised benzo-15-crown-5 macrocyclic ethers

In order to facilitate crown ether anchoring on a solid support *via* an amide, urea or urethane bond, it is necessary to functionalise benzo-15-crown-5 to have carboxylic acid-, amine- or alcohol-containing side chains. Experience gained in the field of polymeric drug carriers also indicate that the length of these side chains should be such that the influence (sterically, electronically or otherwise) of the polymeric backbone (main chain) to which it is anchored, can be minimised.[18] The optimum side chain length, in the case of polymeric drug carriers, was found to be 3 or 4 atoms. We synthesised carboxylic acid-, amine- and alcohol-functionalised benzo-15-crown-15 ether derivatives possessing 1-4 carbon atom spacers between functional group and phenyl moiety.

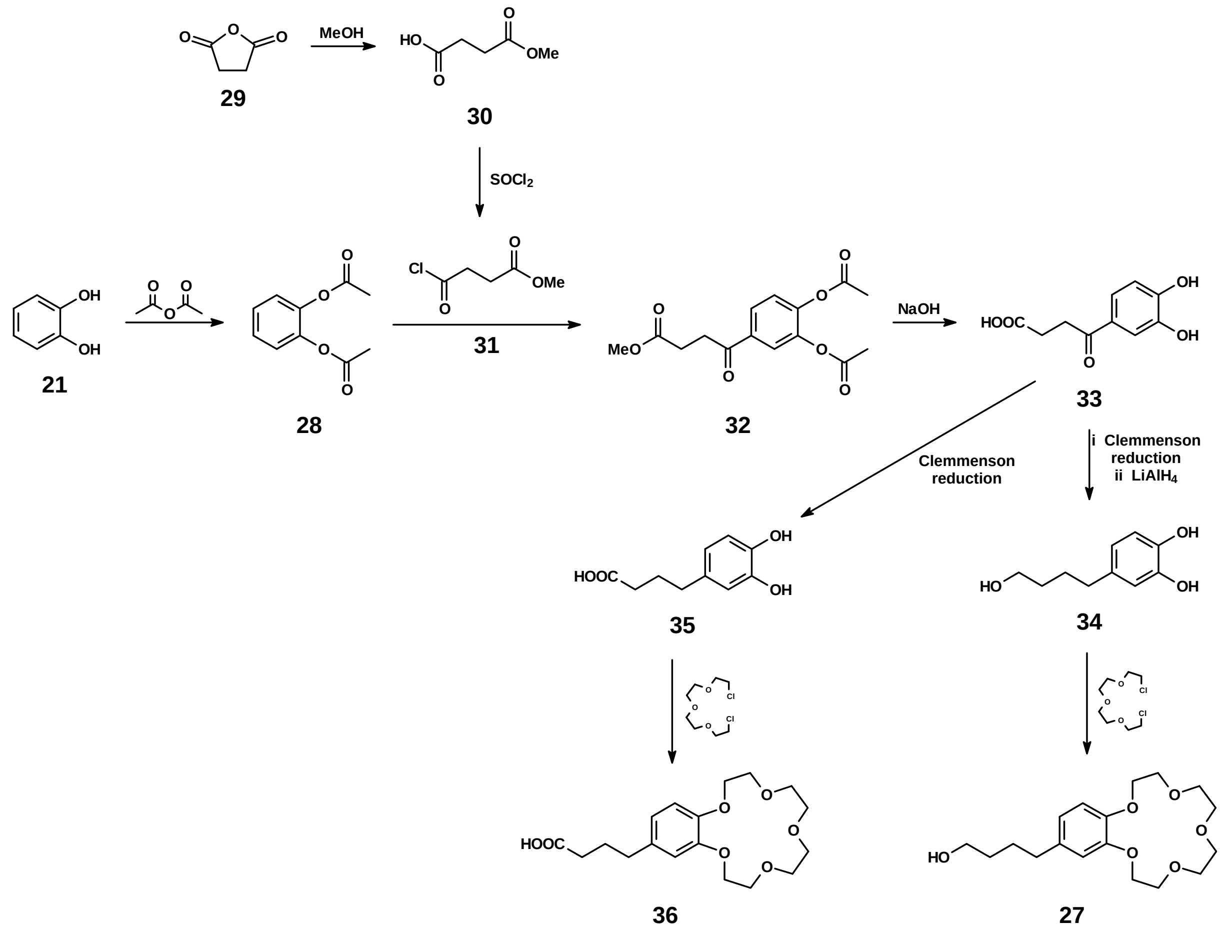
In general two methods of functionalising benso-crown-ethers of any size are possible.[19] In the first, catachol (**21**, starting material for benzo-crown-ether syntheses), may be derivatised and then the crown ether may be formed to generated the functionalised crown ether. In the second approach, benzo-crown-ethers are first formed, and then functionalised. Both approaches were tested and we found the second by far more easy and efficient for our target compounds.

In testing the first approach we attempted to synthesise the butanoic acid derivative **27** as shown in **Schemes 4** and **5**. In **Scheme 4**, catachol, **21**, was first protected utilising dibenzodichloromethane[20] to give **22**. Succinoylation of **22** to give **23** was successful, but deprotection of **23** to liberate the free catachol derivative **24** did not proceed as expected. Hence, this failure implied the target crown ether **27** was not conveniently attainable utilising the reaction sequence depicted in **Scheme 4**.



Scheme 4: The attempted syntheses of crown ether **27** failed due to the inability to deprotect the protected catachol **23**.

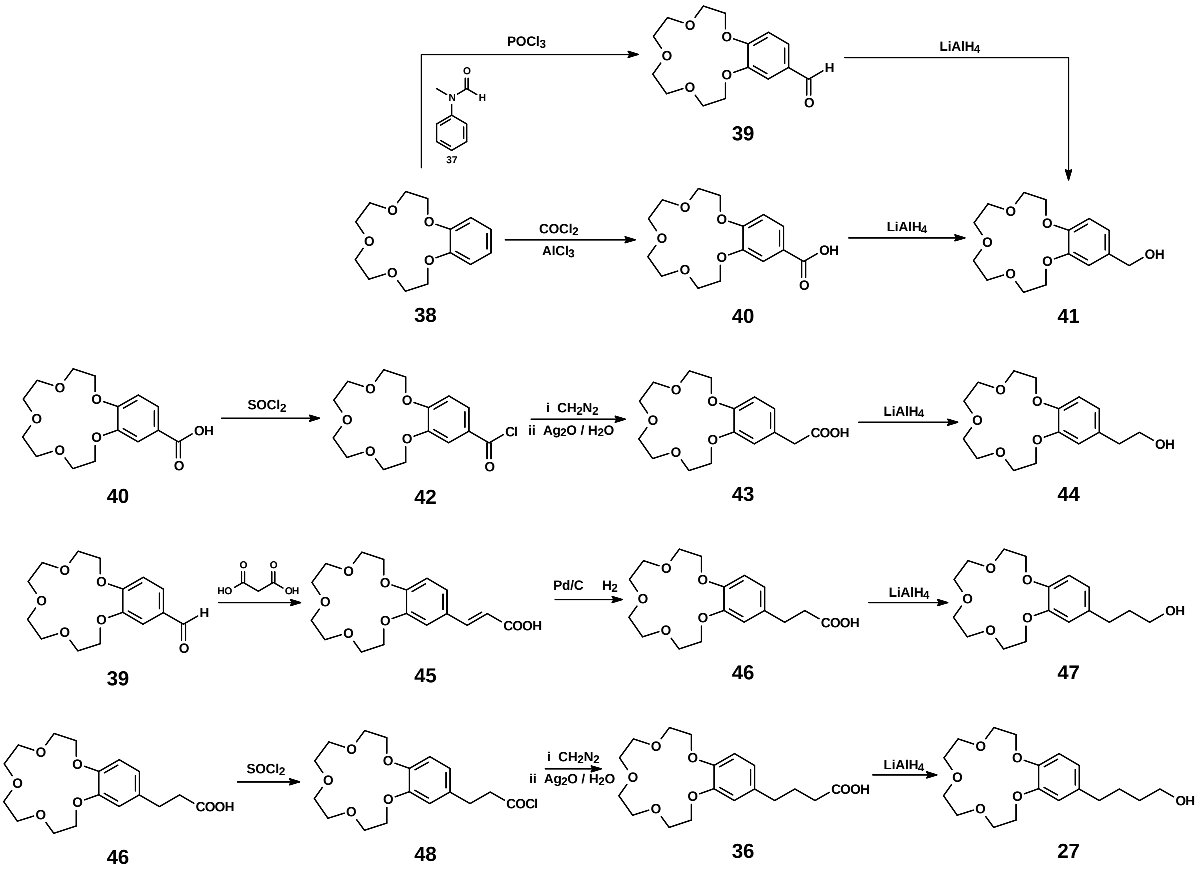
An alternative approach to the synthesis of **27** is shown in **Scheme 5**. In this approach, the OH functionalities of catachol, **21**, is protected as an acetate. Succinoylation was achieved by the mixed acid chloride/methyl ester of succinic acid,[21] compound **31**. Deprotection of all functional groups in **32** was achieved by prolonged reflux in the presence of sodium hydroxide, but yields of the functionalised catachol **33** remained low. This meant the synthesis of the functionalised crown ethers **27** and **36** are very uneconomic processes. Hence we came to the conclusion that it should probably be better to first synthesise benzo-15-crown-5 and then derivatise it.



Scheme 5: Proposed synthesis of crown ethers **36** and **37** *via* the derivatised catachol derivative **33**. Compound **33** is obtained from the ester-protected compound **32**.

Although our best efforts failed to give the desired compounds **27** and **36** economically, following the routes of **Schemes 4** and **5**, both compounds were successfully and economically obtained following the general guidelines of **Scheme 6**. With respect to target compounds of this research program it appears that the second approach to derivatised crown ethers, that of first synthesising the normal benzo-crown-ether and then functionalise the macrocycle, is the best. Within the context of this research program, the success of this second approach hinges on the easy and high yield synthesis[22] of especially 4'-carboxaldehyde benzo-15-crown-5, **39** and the commercial availability of 4'-carboxybenzo-15-crown-5, **40**.

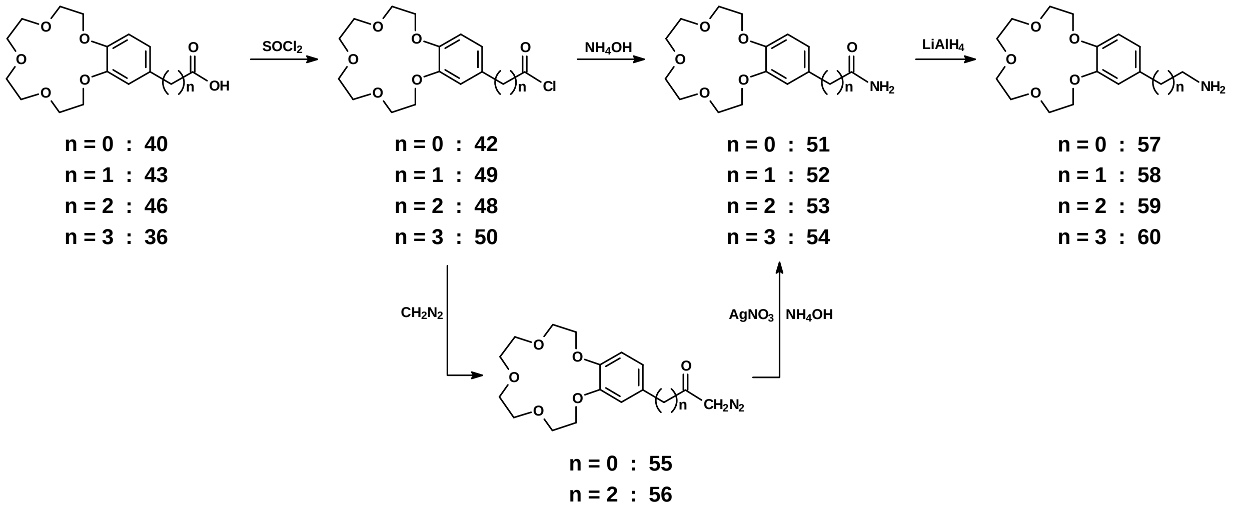
Armed with the knowledge that carboxylic acid derivatives of benzo-15-crown-5 are easily attainable *via* functionalisation of the mother compound, a series of acids, alcohols and amines were synthesised possessing different carbon atom spacer lengths between the functional group and the benzo-crown-ether moiety. The best synthetic route towards the most simple alcohol, the methanol derivative (i.e. an alcohol with one CH_2 spacer group between alcohol and crown ether, compound **41**), is *via* the aldehyde **39** as demonstrated in **Scheme 6**. The reaction sequences towards the acids **40, 43, 46** and **36**, as well as the other alcohols **44, 47** and **27** can also be found in **Scheme 6**, while the amine synthesis are shown in **Scheme 7**.



Scheme 6: Synthetic pathway towards acids **40, 43, 46** and **36** as well as the alcohols **41, 44, 47** and **27**.

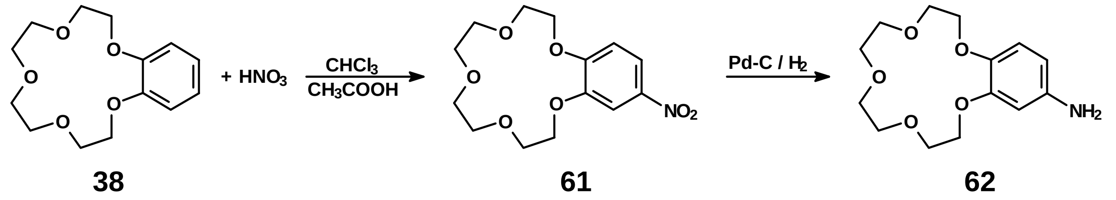
The aldehyde **39**, acid **40** and alcohol **41** are known derivatives[22] of **38**, but all the other compounds shown in **Schemes 6** and **7** are new, and we had to develop chemistry to synthesise them. The new compounds include the acid chlorides **42** and **48**, conveniently obtained by the action of thionyl chloride on the precursor acids **40** (a known acid) and **46** (a new compound). To obtain the acid **46**, a malonic acid condensation (Michael addition reaction) on the known aldehyde **39** was performed. The resulting new alkenoic acid derivative **45** was hydrogenated to the new alkanoic acid derivative **46**. Lengthening of the alkane chain length from acid **40** to **43** and **46** to **36** was conveniently performed by the action of diazomethane on the precursor acid chlorides followed by migration of the crown-containing moieties of the intermediate thus obtained under the influence of silver oxide and water. Conversion of all the acids in **Scheme 6** to alcohols was achieved by $LiAlH_4$ reduction.

The syntheses of amines **57-60** according to scheme **7** were facilitated by $LiAlH_4$ reduction of amides **51-54**. The amides **52** and **54** were obtained by reacting the acid chlorides **49** and **50** with aqueous ammonia. Amides **51** and **53** were obtained by reacting the acid chlorides **42** and **48** first with diazomethane to yield the intermediate diazoketones **55** and **56** before the interaction with ammonia and silver nitrate liberated the indicated amides.



Scheme 7: Synthesis of various amino derivatised crown ethers.

Synthesis of the simplest amine-containing benzo-15-crown-5 derivative, 4'-aminobenzo-15-crown-5, **62** was achieved by first nitrating benzo-15-crown-5 followed by hydrogenation of nitrated intermediate **61**.

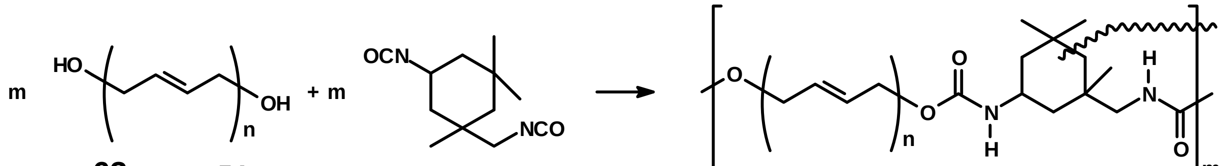


Scheme 8: Synthesis of 4'-aminobenzo-15-crown-5, **62**, *via* hydrogenation of 4'-nitrobenzo-15-crown-5, **61**

The material required to make a device as demonstrated in **Figure 1** suggests the availability of an elastomeric solid support and a sodium cation scavenging ligand. The sodium cation scavenging ligand chosen for this study is functionalised derivatives of benzo-15-crown-5 and are described in the above paragraphs. The elastomeric solid support is based on step reaction polymers obtained by condensation of hydroxy-terminated polybutadiene and diisocyanates such as isophoronediisocyanate. These will now be discussed.

6 Polymerisation of low molecular mass hydroxy-terminated polybutadiene and epichlorohydrin

One of the goals of this research program is to prepare a polymeric elastomeric solid support to which crown ethers can be anchored. This device may then be used to remove salts such as sodium chloride or sodium sulphate from factory waste water as visualised in **Figure 1**. The principle elastomeric polymer support chosen for this study is a diisocyanate cured final polymer **65** of the pre-polymer hydroxy terminated polybutadiene, **63**, molecular mass = 2950 g mol^{-1}, and it may be synthesised as shown in **Scheme 9**. The curing is particularly easy and is performed at 60 °C over 2–4 days. Since the functionality of hydroxy terminated polybutadiene are not exactly 2, as indicated in **Scheme 9**, but slightly more, *ca.* 2.3, the cured polymer **65** is insoluble due to slight cross-linking. Polymers **65** is also very flexible (elastomeric). The symbol 〰 is used to demonstrate that **65** is a cross-linked polymer.



63 : n = 54

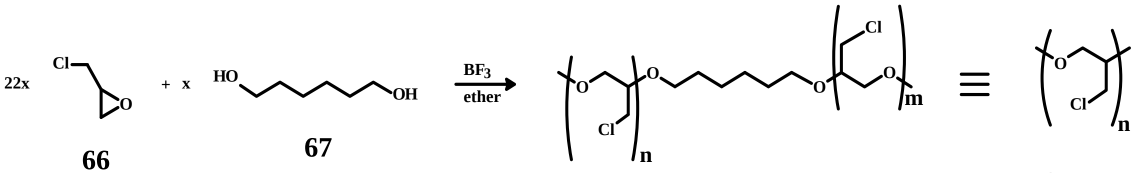
64

65

Scheme 9: Isophorone diisocyanate-induced curing of hydroxy terminated polybutadiene, **63**, leads to a slightly cross-linked, insoluble but elastomeric, solid support **65**. Cross-linking arise from the fact that the hydroxy content of **63** is not 2 as shown, but slightly higher: 2.2-2.3. The symbol 〰 will be used throughout this document to indicate the cross-linked nature of **65**.

To provide an arm to which the crown ethers may be anchored, two additional pre-polymers were synthesised. The first pre-polymer was hydroxy-terminated polyepichlorohydrin (PECH, **68**), and the synthesis of this polymer can be seen in **Scheme 10**. This pre-polymer is produced by the cationic ring opening of epichlorohydrin (**66**), as seen in **Scheme 10**. The molecular mass of polymer **68** can be predetermined by carefully controlling:

a) The molar ratio between the monomer epichlorohydrin (**66**) and the dialcohol (**67**).
b) The rate of addition of the epichlorohydrin to the reaction mixture containing the catalyst.
c) Amount of catalyst and order of reagents addition (epichlorohydrin must be added last to the reaction mixture).
d) Limiting the temperature of the reaction mixture to below 27 ^{o}C to prevent thermal runaway.



66

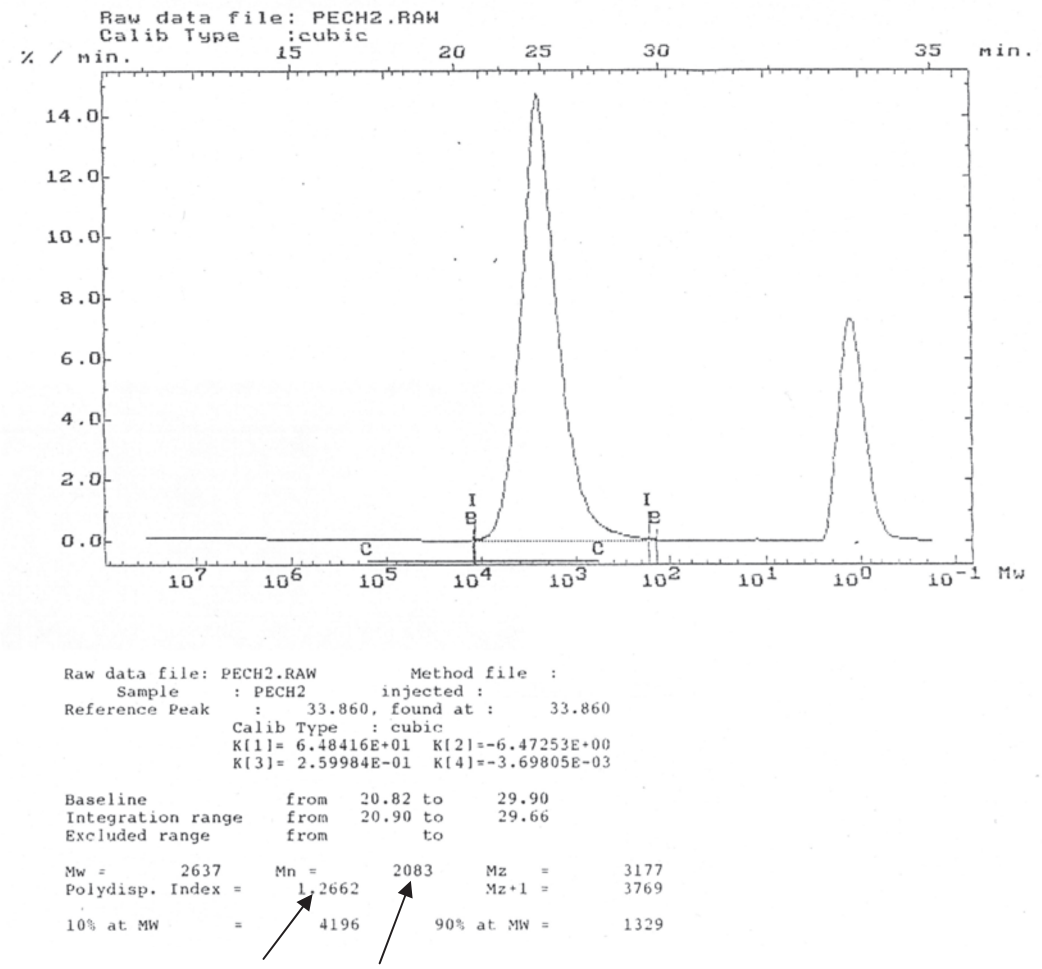
67

68a : n + m = 22

68 : n = 22

Scheme 10: The synthesis of PECH (**68**).

Note that polymers **68a** and **68** are meant to be the same, structure **68** is just a simplified presentation of **68a**. Polymer **68** was prepared in different batches having different molecular masses including 2 000, and 20 000 g mol^{-1}. **Figure 6** below shows how the obtained molecular mass differed from the target molecular mass of 2 000 g mol^{-1} for **68**. The polydispersity was determined as 1.2662, which is rather good.

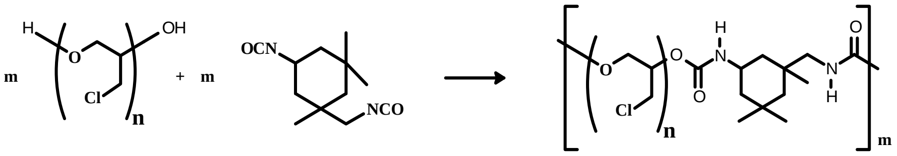


```
Raw data file: PECH2.RAW
Calib Type    :cubic
```

```
Raw data file: PECH2.RAW          Method file  :
     Sample       : PECH2       injected :
Reference Peak     :    33.860, found at :      33.860
                  Calib Type    : cubic
                  K[1]= 6.48416E+01  K[2]=-6.47253E+00
                  K[3]= 2.59984E-01  K[4]=-3.69805E-03

Baseline                 from   20.82 to      29.90
Integration range        from   20.90 to      29.66
Excluded range           from         to

Mw =          2637      Mn =          2083      Mz    =          3177
Polydisp. Index =        1.2662                 Mz+1 =          3769

10% at MW         =       4196      90% at MW =          1329
```

Figure 6: The molecular mass distribution and polydispersity of **68** in a synthesis where the target molecular mass was 2 000 g mol^{-1}.

The capacity of PECH, **68** to react or polymerise with isocyanates such as isophorone diisocyanate were investigated by polymerising **68** with **64 (Scheme 11)** and by co-polymerisation of **63**, **64** and **68 (Scheme 12)**. Good polymers were obtained in all cases.

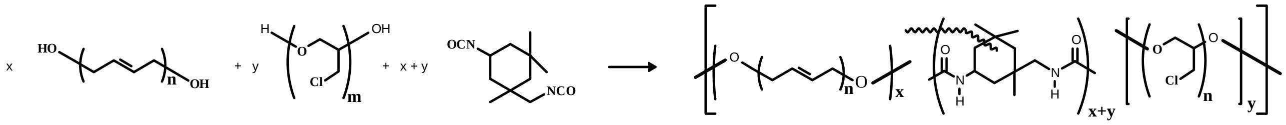


68 : n = 22

64

69

Scheme 11: The curing of PECH, **68**, with isophorone diisocyanate, **64**.



63: n = 54

68 : m = 22

64

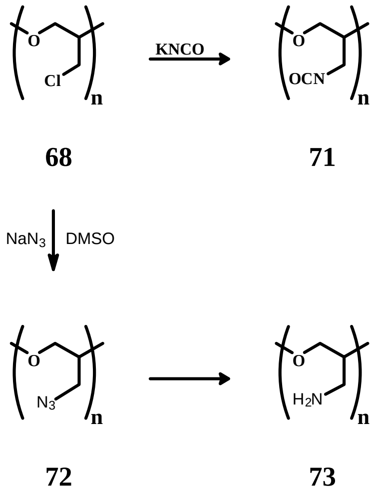
70

Scheme 12: The simultaneous curing of **63** and **68** with **64**.

7 Refunctionalisation of polyepichlorohydrin, PECH, 68

In order to easily anchor this pre-polymer onto elastomer **65**, it was decided to re-functionalise the chloride containing pre-polymer **68**, to a polymer containing isocyanate groups, **71**. This transformation is shown in **Scheme 13**. The conversion was done under seven different reaction conditions. **Table 3** shows the seven different conditions used to achieve this transformation. It was found that condition 7 produces the highest isocyanate content, *ca.* 40 % as measured by IR and NMR.

The difficulty of obtaining **71** in good yields is set into perspective when one realises that **68** is actually hydroxy terminated. The hydroxyl end groups most certainly interact with the isocyanate groups to cause some cross linking that is not shown in the idealised structure of **71** in **Scheme 13**. In contrast, the conversion to an azide-containing polymer, **72** is smooth in DMSO at 110 ^{o}C. The amine polymer, **73**, is obtained by reducing the azide polymer **72** with a suitable reducing agent, here $LiAlH_4$.

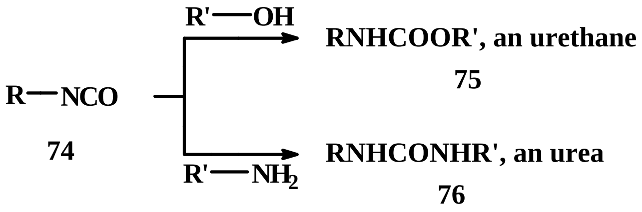


Scheme 13: The conversion of the chloride containing pre-polymer **68** to one containing isocyanates, **71**, azides, **72**, and amines, **73**

Table 3: Conditions that was utilised to convert **68** to **71**.

Reaction number	**Reaction Condition**	**NCO-content**
1	KNCO / Benzene / 24 h / 100 °C	< 5 %
2	KNCO / DMF	< 5 %
3	KNCO / $^+N(CH_2CH_2CH_3)_4Br^-$ / K_2CO_3 / DMSO / 24 h / 120 °C	Cross-linked insoluble product
4	KNCO / $^+N(CH_2CH_2CH_3)_4Br^-$ / K_2CO_3 / DMF / 16 h / 100 °C / DMF then removed at reduced pressure	± 10 %
5	KNCO / $^+N(CH_2CH_2CH_3)_4Br^-$ / K_2CO_3 / DMF / 16 h / 100 °C / DMF extracted with hexane	10 – 20 %
6	KNCO / $^+N(CH_2CH_2CH_3)_4Br^-$ / K_2CO_3 / DMF / 2 h / 100 °C / DMF removed at reduced pressure	± 10 – 20 %
7	KNCO / $^+N(CH_2CH_2CH_3)_4Br^-$ / K_2CO_3 / DMF / 2 h / 100 °C / DMF extracted with hexane / 100 °C	30 – 50 %

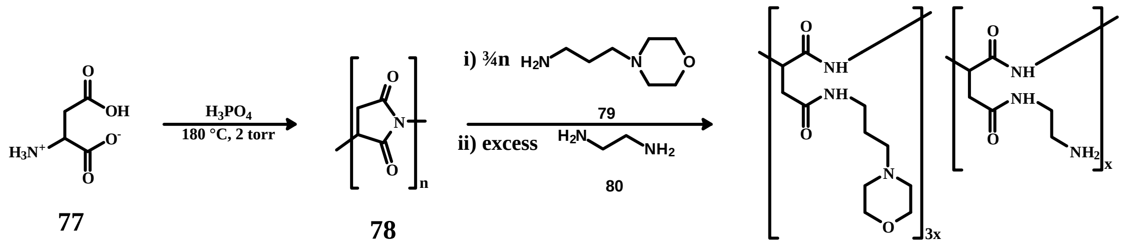
The NCO-functional group of **71** allows anchoring of this pre-polymer to elastomeric solid support **65**. It also allows anchoring of any of the OH- (**41**, **44**, **47** and **27**) or NH_2-containing crown ethers (**57** – **60**) by virtue of the following general reactions:



Scheme 14: The general reaction between a NCO-functionalised derivative and an OH- or NH_2-functionalised compound.

8 Anchoring of crown ethers on water-soluble polyaspartates or epichlorohydrin derivatives

A water-soluble polyaspartate was synthesised (**Scheme 15)** onto which carboxylic acid functionalised crown ethers could eventually be anchored.



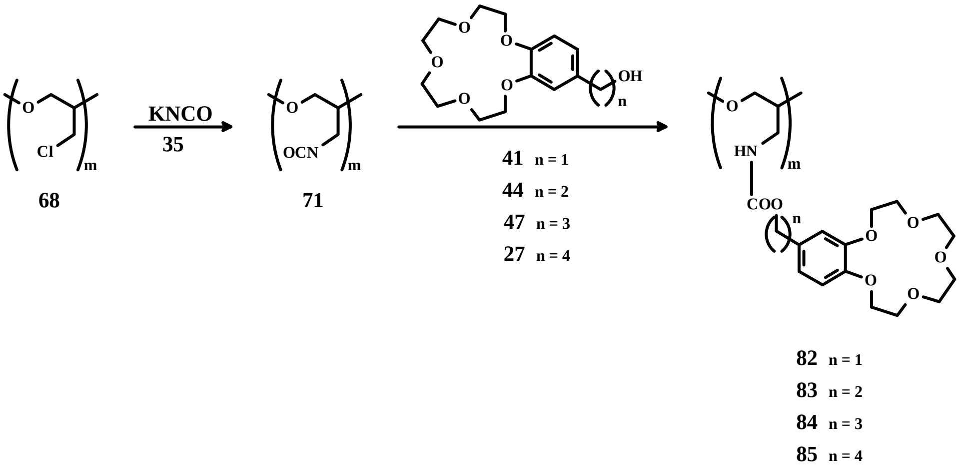
81: n = 4x

Scheme 15: Synthesis of water-soluble polymeric carrier **81**.

Polymer **81** is not a regular or block polymer as indicated in **Scheme 15**, but consists of a random distribution pattern of monomers with the average ratio between the different types of side groups 3:1. Polysuccinimide **78** were prepared by thermal polymerisation of aspartic acid **77** at low pressures. This polymer is not water-soluble, but soluble in DMF, and has an average molecular mass of *ca.* 70 000 g mol^{-1} as determined by solution phase viscometry. The water-soluble polymer **81** was obtained by controlled ring opening of polysuccinimide **78**, with amine functionalised compounds. The first compound, 3-aminopropylmorpholine, **79**, was used to make the polymer more water soluble, while the second compound, ethylenediamine **80**, was chosen to provide an anchoring position for the acid-functionalised crown ethers **40**, **43**, **46** and **36** of **Schemes 6** or **7** (see pages 15 and 16).

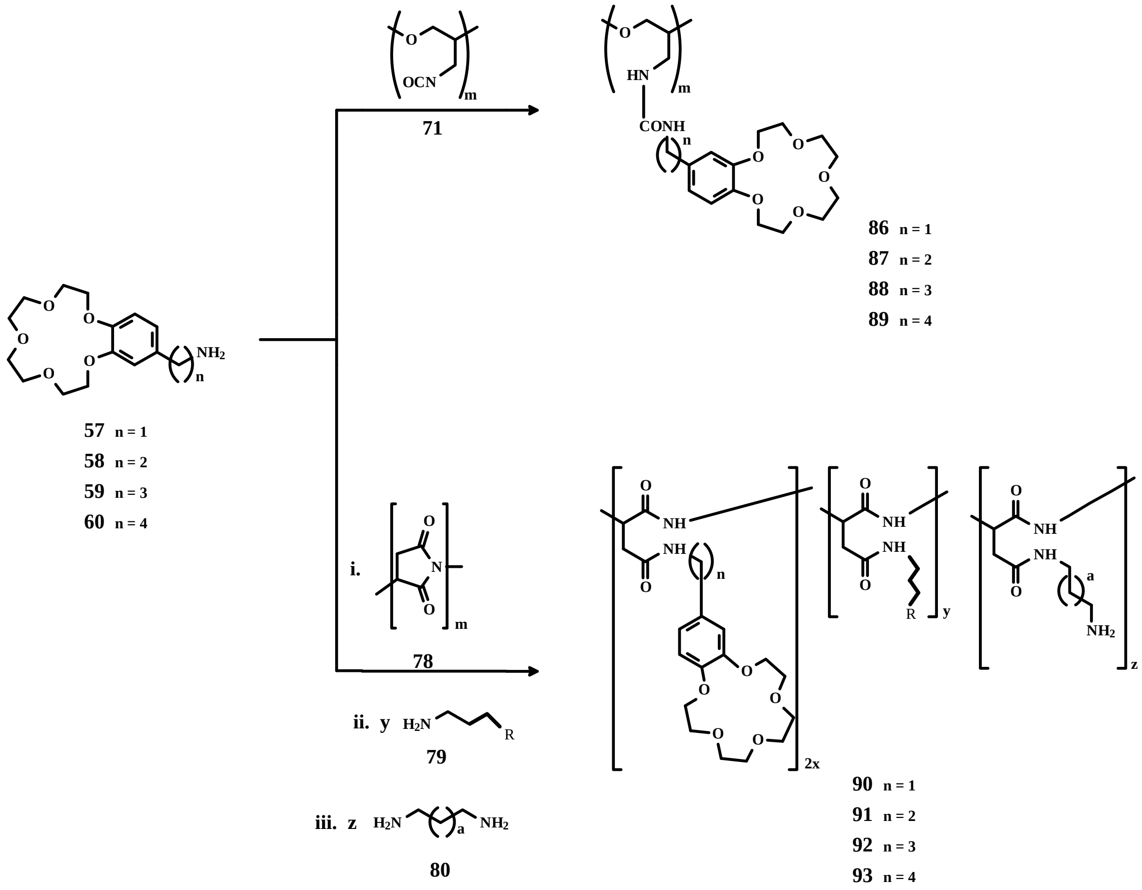
The anchoring of derivatised crown ethers onto pre-polymers **71**, **78**, **81** and others was investigated next. Although these compounds are in themselves not suitable as devices for removing Na^+ cations from polluted water, it provides a tool to later ensure a high density of crown ethers on a solid polymeric support. It also served the additional purpose of determining conditions of crown ether anchoring on polymeric devices.

Towards this end then, the alcohol-functionalised crown ethers **41, 44, 47** and **27** were anchored onto polyisocyanate **71**, as shown in **Scheme16**. The reactions were highly efficient in dichloromethane or dichloroethane solutions, but care has to be taken to prevent thermal runaway.



Scheme 16: Anchoring of alcohols **41, 44, 47** and **27** on the isocyanate-functionalised pre-polymer **71** via urethane bonds, m = 22 or 220.

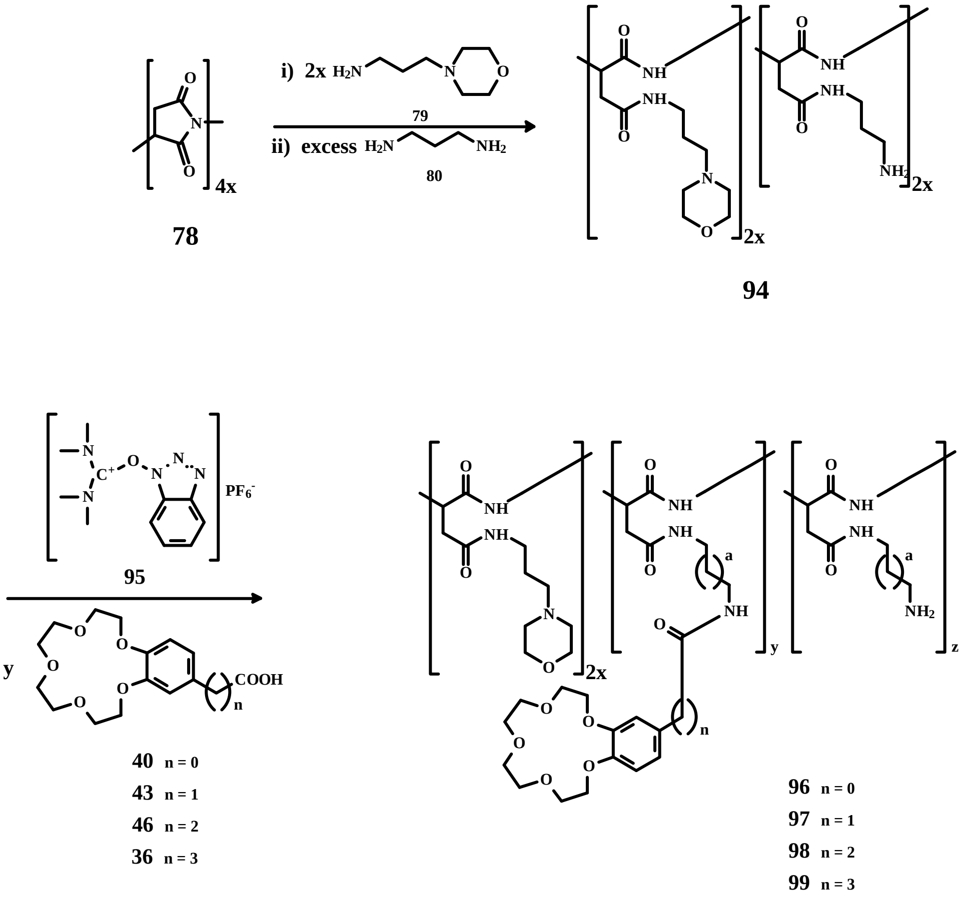
The amine-functionalised crown ethers of **57-60** were then anchored onto polyisocyanates and polysuccinimides, as shown in **Scheme 17**. The reaction between **71** and the amines of **Scheme 17** is similar to the reaction between **71** and the alcohols of **Scheme 16**; the most notable difference is the higher reactivity of the amine derivatives **57-60** as compared to the alcohols **41, 44, 47** and **27**. Also, the polymers **82-85** have urethane (-NHCOO-) bonds in the side chain while **86-89** has urea (-NHCONH-) bonds. In contrast, polymers **90-93** has amide (-NHCO-) bonds in the side chain.



Scheme 17: Anchoring of amine-containing crown ethers **57-60** via urea bonds to **71** (polyisocyanates, m = 22, 220), or via amide bonds to **78** (polysuccinimide). R = morpholino, but may also be dimethylamino or other water-loving/hydrophilic groups, y ≈ z, a = 1.

Two additional features of **90-93** includes (a) use of a water-solubilising agent, R (mostly the morpholino group) and (b) the presence of a reactive amine-containing side chain. These amine-containing side chains will later provide the handle by which **90-93** may be anchored onto a solid support.

Anchoring of the carboxylic acid crown ether derivatives **40, 43, 46** and **36** on amine-functionalised polymers is demonstrated in **Scheme 18**. Amide formation is promoted by a catalyst, here O-benzotriazolyl-N,N,N',N'-tetramethyluronium hexafluorophosphate, **95**. The reaction proceeds well at room temperature over 16 hours in dry DMF. As seen in **Scheme 18**, only half of the available amine-groups, about 1x, were used to anchor the crown ether moieties. The other 1x amine-groups was specifically left to anchor this water-soluble polymer onto elastomer **65**.



Scheme 18: The anchoring of crown ether **40, 43, 46** and **36** onto polymer **94**, with the help of the coupling reagent, **95**, y+z = 2x with y ≈ x, a = 1 but can be anything between 0-4, the water-solubilising morpholino group can be replaced with dimethylamino or any other water-loving/hydrophilic group. Note all structures are idealised and that monomers follow a random distribution.

Repetitive synthetic experiments allowed us to pot up as required functionalised polymers capable of acting as insoluble solid supports or soluble polymeric carriers to which crown ethers may be bound. The most important compounds that we concentrated on are listed in **Figure 7** below. All of them has one common property: It has a reactive site or sites at which functionalised crown ethers or other soluble polymeric support systems may be anchored.

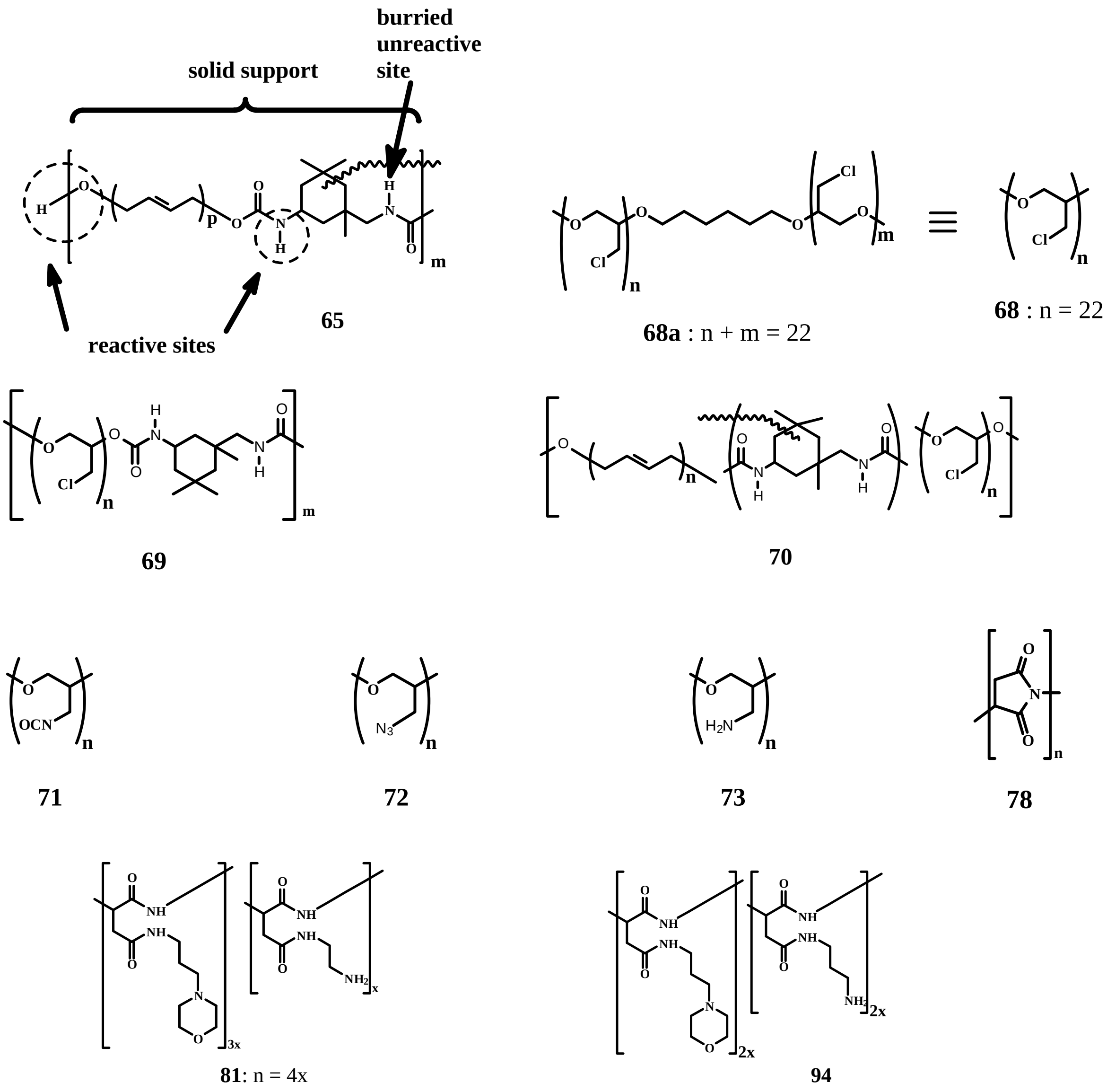
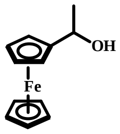


Figure 7: Polymeric precursors to which crown ethers may be anchored. Polymer **65** forms the basis of our insoluble, elastomeric, polymeric solid support. The symbol 〰 is used to demonstrate that **65** is a cross linked polymer. Cross-linking arises from the hydroxyl-content of 2.2 for HTPB (a precursor of **65**). All structures are presented in idealised form. No flaws, side chain branches or cross-linking is shown in any of the idealised structures.

9 Anchoring of the benzo-15-crown-5 derivatives onto a solid insoluble polymeric support

The polymeric elastomer **65** gave us an insoluble support onto which the crown ethers of **Schemes 6** and **7** may be anchored. In the first approach, it was deemed advisable to anchor an alcohol-derivatised crown ether onto the surface of the solid support **65** while at the same time avoid migration or trapping of the crown ethers into the interior of **65**. The surface bound crown ethers would be available for binding sodium cations. Any crown ethers that get buried in the interior of the solid elastomeric support would be unavailable for cation binding.

In order to obtain the correct experimental conditions to achieve surface anchoring while avoiding loss of material in the interior of **65**, the anchoring step was first investigated with an inexpensive and brightly orange coloured compound, 1-hydroxyethyl ferrocene, **100.**

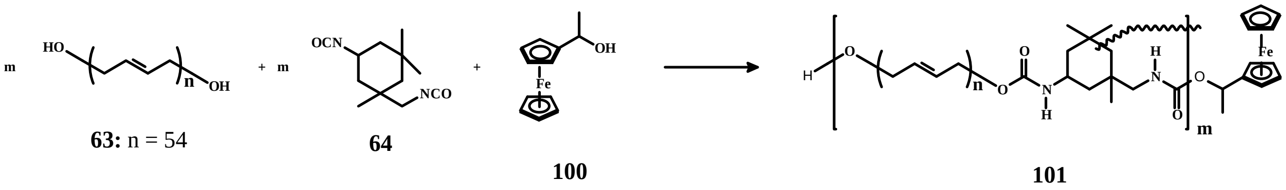


100

Figure 8: 1-Hydroxyethyl ferrocene, **100**.

Several methods were used to anchor the ferrocenyl derivative **100** to the elastomer **65**:

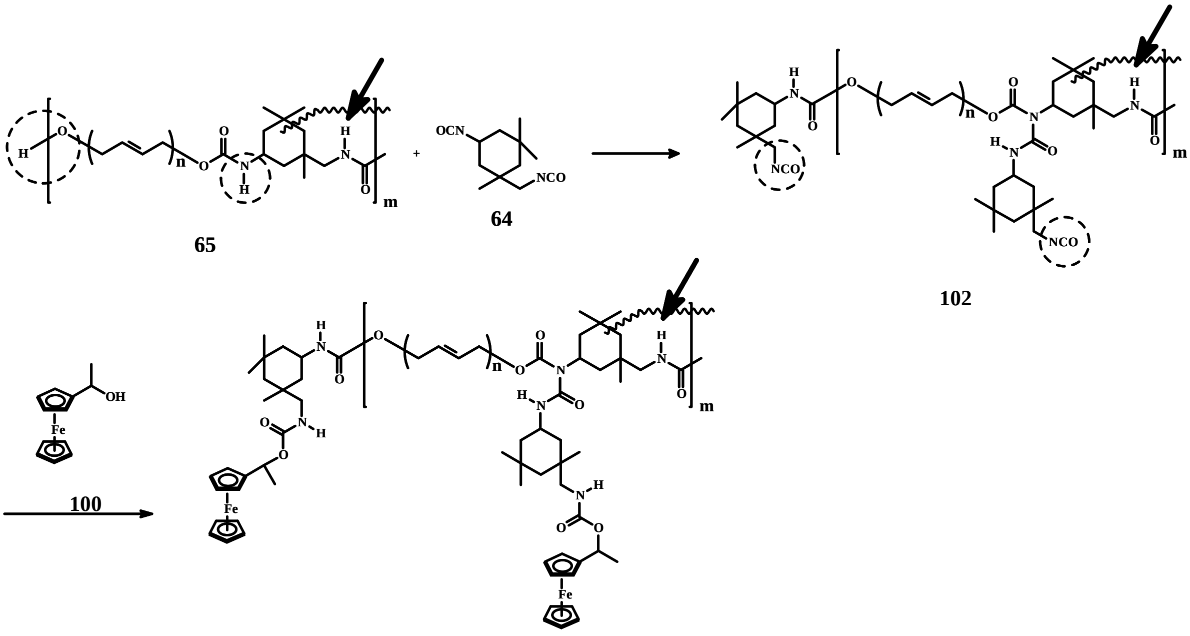
1. The ferrocene dye was added to the polymer before any curing took placed between **63** and **64**, **Scheme 19**. This produced a polymer with the dye anchored not only on the cured elastomer surface but throughout the cured polymeric matrix, including the interior. This implies a large amount of the dye is not accessible on the surface of the cured elastomer. The product can be seen in photos **88** (**Figure 9**) and **93** (**Figure 10**).



Scheme 19: Curing of **63**, **64** and **100** to produced elastomer **101**. When the reactant **100** is sprinkled on top of a mixture of **63** and **64** prior to curing, the dye **100** is found almost homogeneously distributed throughout the polymeric matrix after curing.

2. The ferrocene dye was added after the partial curing of **63** and **64** took place. The reaction is the same one as in **Scheme 19** but it was hoped that the dye would only bind to the surface of the elastomer. However, as demonstrated in photos **87** (**Figure 9**) and **94** (**Figure 10**), migration of the dye again took place into the interior of the semi (partially) cured elastomer. Hence this method was also not the method of choice for the binding of alcohols onto the surface of the elastomeric solid support.

3. After the failures of the previous two attempts, it was decided to completely cure the elastomeric carrier, compound **65** according to **Scheme 9** (page 17), and then to try and anchor the dye to the *freshly prepared,* cured elastomer. This was done by using isophorone diisocyanate, **64**, as an intermediate between the elastomer and the ferrocene dye. This is possible because the cured elastomer **65** has *some* active hydrogens on its surface. This process is highlighted in **Scheme 20**. It was expected that the diisocyanate **64** would bind at least too some of the active surface hydrogens to produce surface bound isocyanates, as shown in **Scheme 20**. These surface-bound isocyanates can be allowed to react with the alcohol dye **100** to give **103**.



103

Scheme 20: Representation of the reaction between **100**, the coupling agent **64** and the solid support **65**. It should be realised that not all of the NH groups in polymeric elastomer **65** reacts with **64**.

Several different conditions were used to achieve this desired coupling. It was found that solvents such as ether and dichloromethane produced a swelling of polymer **65**. If this swelling occurs, the dye is again not only bound on the surface of the elastomer, as seen in photo **91**, **Figure 9**. It was found that hexane did not produce excessive swelling of the elastomer. The ferrocene dye was subsequently anchored to elastomer **65** using hexane as the solvent and by dipping **65** into it. The product that was obtained in this way is shown in photos **87** and **94**, **Figure 9** and **Figure 10**.

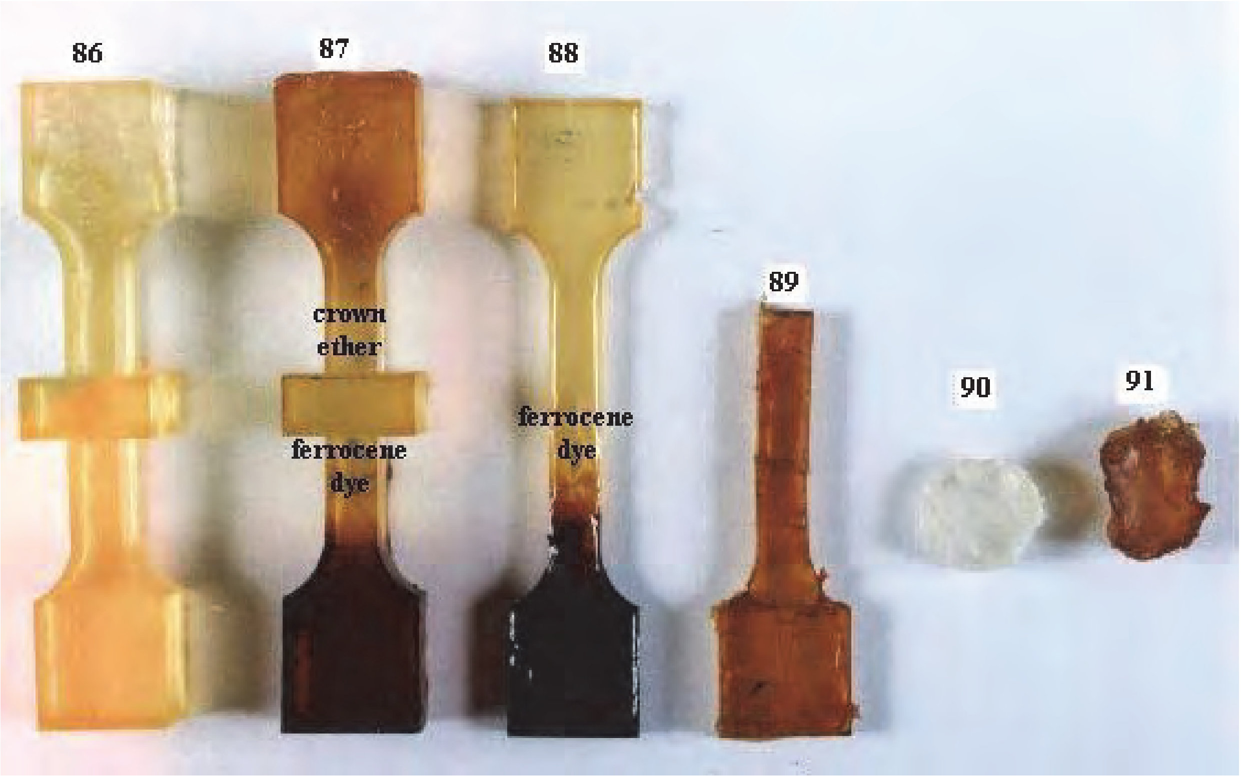


Figure 9: Photos of samples from results of different methods of anchoring the ferrocene dye **100** onto the polymeric solid support **65**. Photo **86** represent the cured elastomer **65** after casting in the absence of any dye **(Scheme 9)**; photo **87** represent elastomer **103**, **(Scheme 20)** and elastomer **104 (Scheme 21).** Photo **88** represent elastomer **101**, **(Scheme 19)** while photo **89** represents the reaction between the partially cured elastomer **65** and **100.** Photo **90** is that of the cured elastomer **65** only cast into another form compared to photo **86**. Photo **91** shows the effect that swelling (due, for example, to stirring a sample shaped as in photo **90** in dichloromethane or chloroform) has on the cured elastomer **65**.

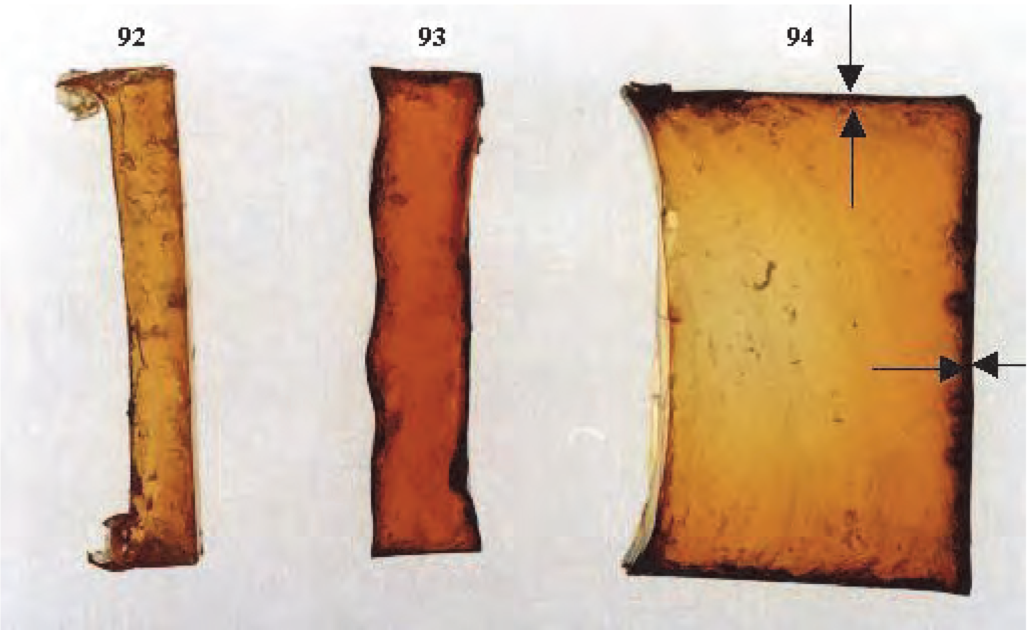


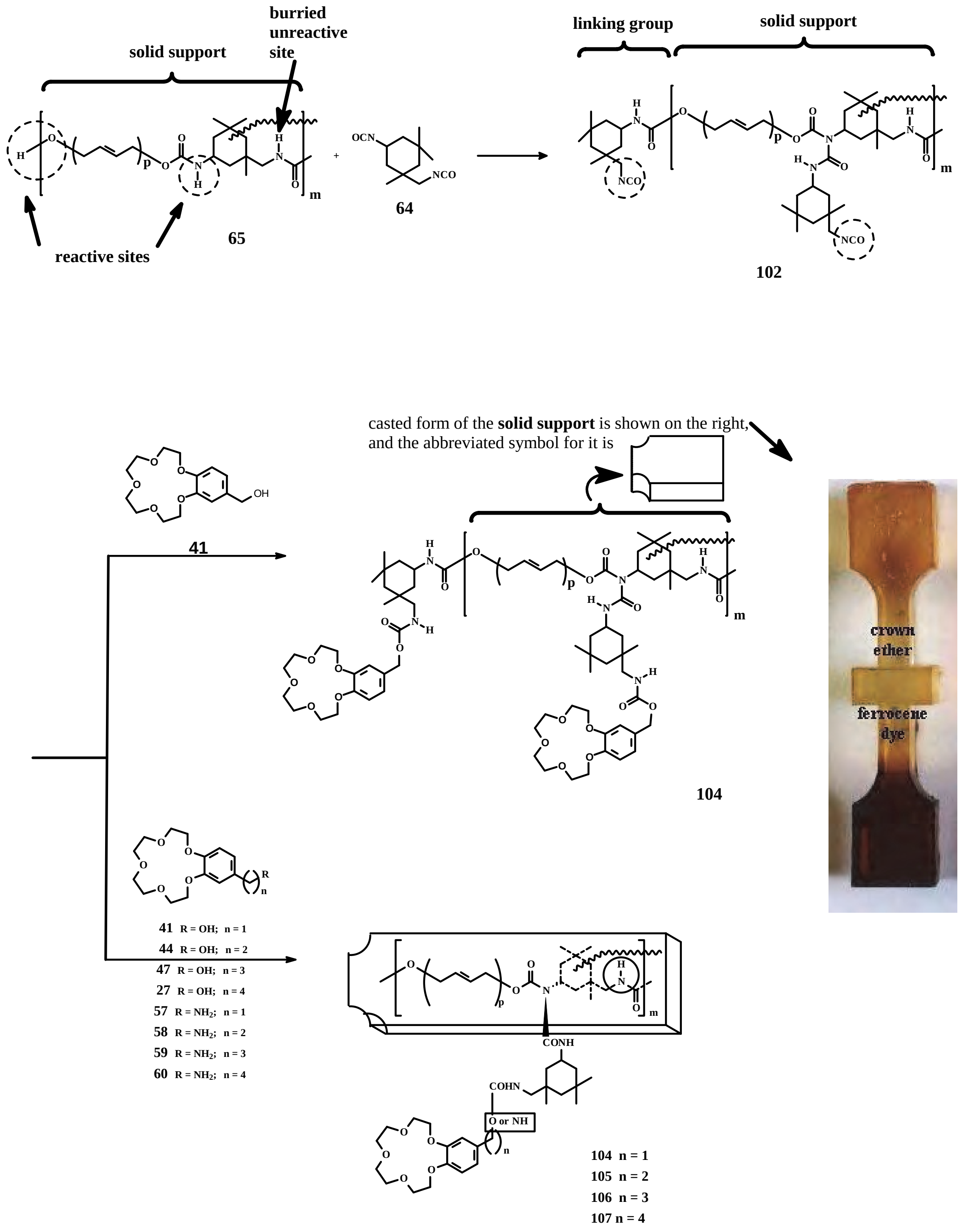
Figure 10: Photo **92** is that of a cross-section of the product of the reaction between the partially cured elastomer **65** and **100** while photo **93** shows a cross-section of the reaction depicted in **Scheme 19**. Photo **94** is that of a cross-section of elastomer **103 (Scheme 20)**.

To determine whether the surface-bound ferrocenyl groups remained redox active, it was attempted to oxidise the surfaced-coated ferrocene-containing polymer **103** with benzoquinone. The oxidation was successful as the orange surface turned blue-black as the ferricenium species was generated, and it was thus concluded that no dramatic loss in chemical activity of the ferrocene occurred if surface-bound onto the solid support. This result is important because it implied that the envisaged surface-bound crown ethers may also still be capable of complexing cations when anchored onto the surface of the solid polymer support (**65**). The successful synthesis of **103** led to the anchoring of 4'-hydroxymethylbenzo-15-crown-5 (**41**) onto elastomer **65**, as illustrated in **Scheme 21**.

To obtain a new cation-scavenging device for use in removing cations from water, and more particularly, for use in the purification of industrial waste water, either the small-molecular crown ether derivatives of **Schemes 6** and **7** or polymer-bound crown ether derivatives, including inter alia those of **Schemes 16**, **17** and **18,** should be immobilised on a solid support. The solid support developed for this study is **65**. Two prerequisites for the solid support are that it be insoluble in water or organic solvents and that it have active sites to which the crown ether derivatives of the invention can be covalently anchored. Examples of such anchoring reactions are shown in **Schemes 21-26**.

Scheme 21 (next page) shows the anchoring of alcohols **41**, **44**, **47** and **27** as well as the amines **57-60** onto the elastomeric solid support **65** via a diisocyanate linking molecule, such as, for example, isophoronediisocyanate **64** or hexamethylenediisocyanate (not shown). The solid polymeric support **65** incorporates polybutadiene fragments and is cross-linked in a spacial network to induce insolubility.

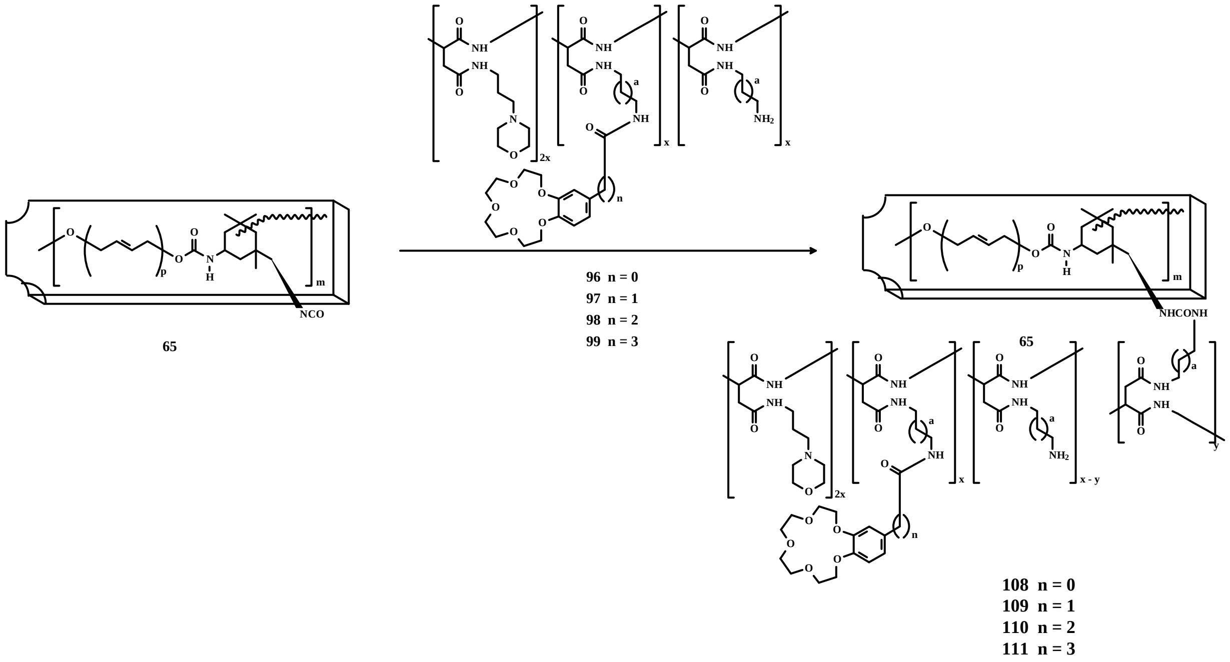
Polymers **104-107**, with active surface area 0.00125 m^2, were tested to determine the amount of sodium cations it can remove from 10 cm^3 of a 200 ppm sodium chloride source solution. These devices were successful in removing 0.021 - 0.044 g Na$^+$ cations per m^2 active elastomer surface area. This represents 1 and 3% of the available sodium cations (**Table 4**, page 38). Tests also showed that the complexation process is fast because no difference in ectraction results could be detected in experiments where the time of extraction was 2, 5 or 10 minutes The urethane (-NHCOO-) bound crown ether-containing devices hinted of performing marginally better than the urea (-NHCONH-) bound crown ether-containing devices. This is probably due to the higher reactivity of amines towards isocyanates than alcohols, inter alia to generate side products that lower the crown ether content on the solid support.



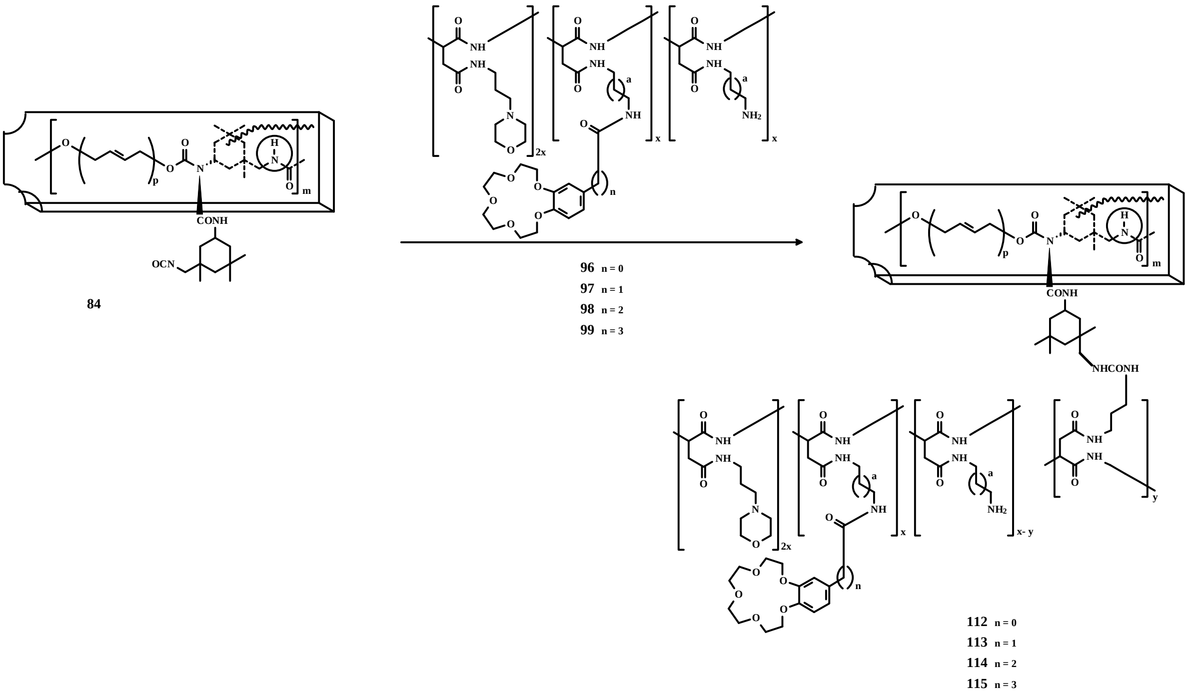
Scheme 21: The grafting of crown ether derivatives **41, 44, 47, 27** and **57-60** onto the solid polymeric support **65** utilising a diisocyanate linking group, here shown to be isophorone-diisocyanate **64**. The symbol 〰 is used to demonstrate that **65** is a crosslinked polymer. Cross-linking arises from the hydroxyl-content of 2.2 for HTPB (a precursor of **65**). ***Note:*** *The final structure of* ***104*** *(middle reaction line) serves as an example of how it ideally should look. However, throughout this report the abbreviated structure as in the bottom reaction line will be shown. It should also be noted that the indicated structures are idealised as no cross-linking or any other side reactions are shown. The amount of crown ethers anchored is also not necessary "1" for each "m" repeating unit. On average it may be much less. It depends on the effectiveness of the anchoring reactions. A measure of the effectiveness is found in the amount of* Na^+ *cations each device can scavenge from aqueous solutions.*

Also, the length of the side chain separating crown ether moieties with functional groups, either OH or NH_2 in **41, 44, 47, 27** and **57-60**, that is $(CH_2)_n$ with n = 1, 2, 3 or 4, did not noticeably influence the Na^+ scavenging capabilities of **104-107**. This was unexpected, as it is known that chain length influence the reactivity of amide formation in the reaction between polyamines and carboxylic acids. It also effects the effectivity of polymer-bound chemotherapeutic drugs. The reason for this unexpected result is probably traceable to the fast kinetics of Na^+ co-ordination by crown ethers, and the relative high reactivity of the isocyanate functional group which leads to effective anchoring reactions.

Scheme 22 shows the immobilisation of crown ether-containing pre-polymers **96-99** via their amine-containing polyaspartate side chains on the isocyanate endgroups of solid support **65**, while in **Scheme 23**, anchoring is achieved via a diisocyanate linking unit between solid support and crown-ether-containing pre-polymer. Devices **108-111** and **112-115** are obtained. **Scheme 23** highlights the use of isophoronediisocyanate but any diisocyanate can be used.



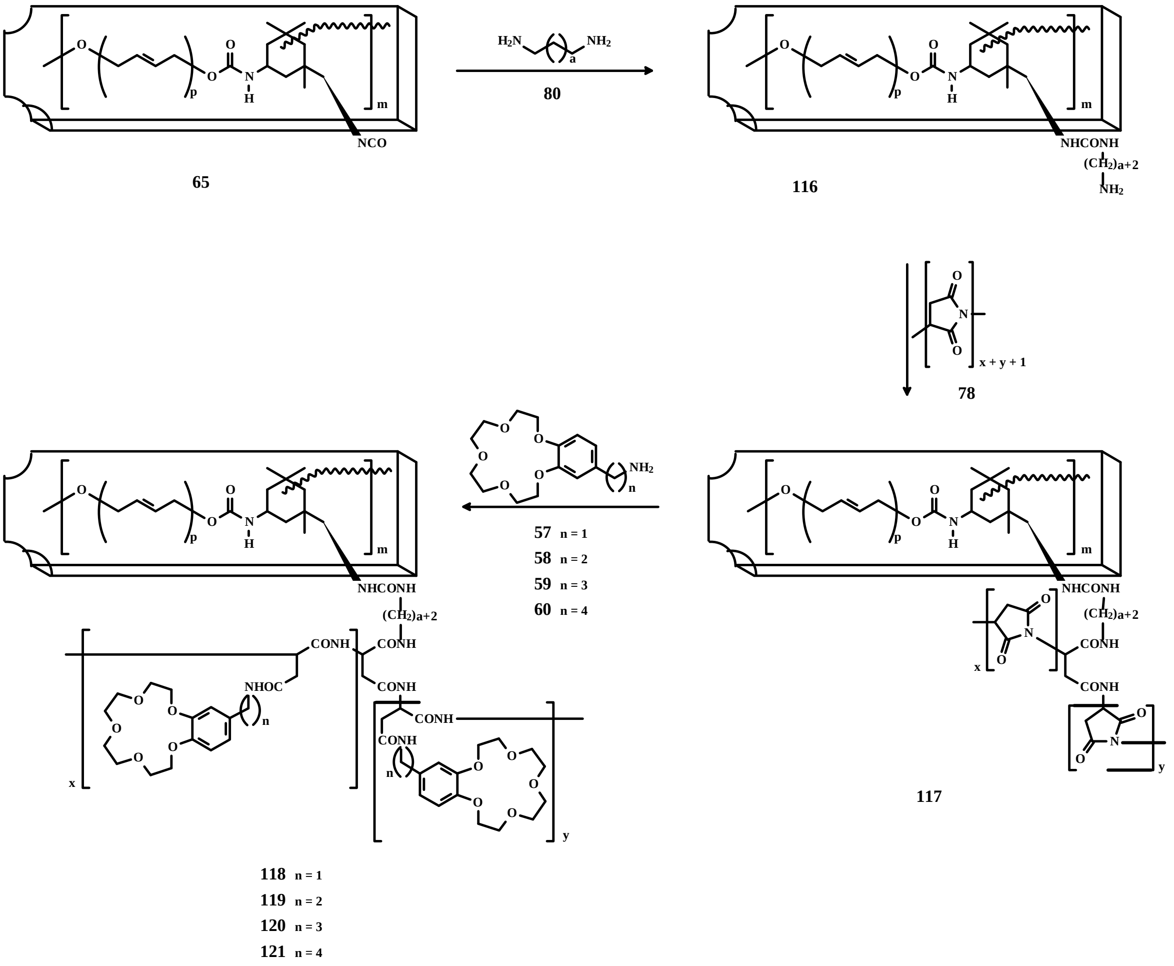
Scheme 22: Anchoring of crown ether-containing water-soluble polymers **96-99** on solid support **65** via-amine functionalised polymer side chains. a = 1. Structures are idealised as per the ***Note*** in the subscript of **Scheme 21.** Also, not all NCO endgroups in **65** are at the surface of the casted polymer. A significant amount, probably even most, should be in the interior of the casted polymer **65**.



Scheme 23: Anchoring of crown ether-containing water-soluble polymers **96-99** on solid support **84** via amine-functionalised polymer side chains. a = 1. Structures are idealised as per the ***Note*** in the subscript of **Scheme 21**

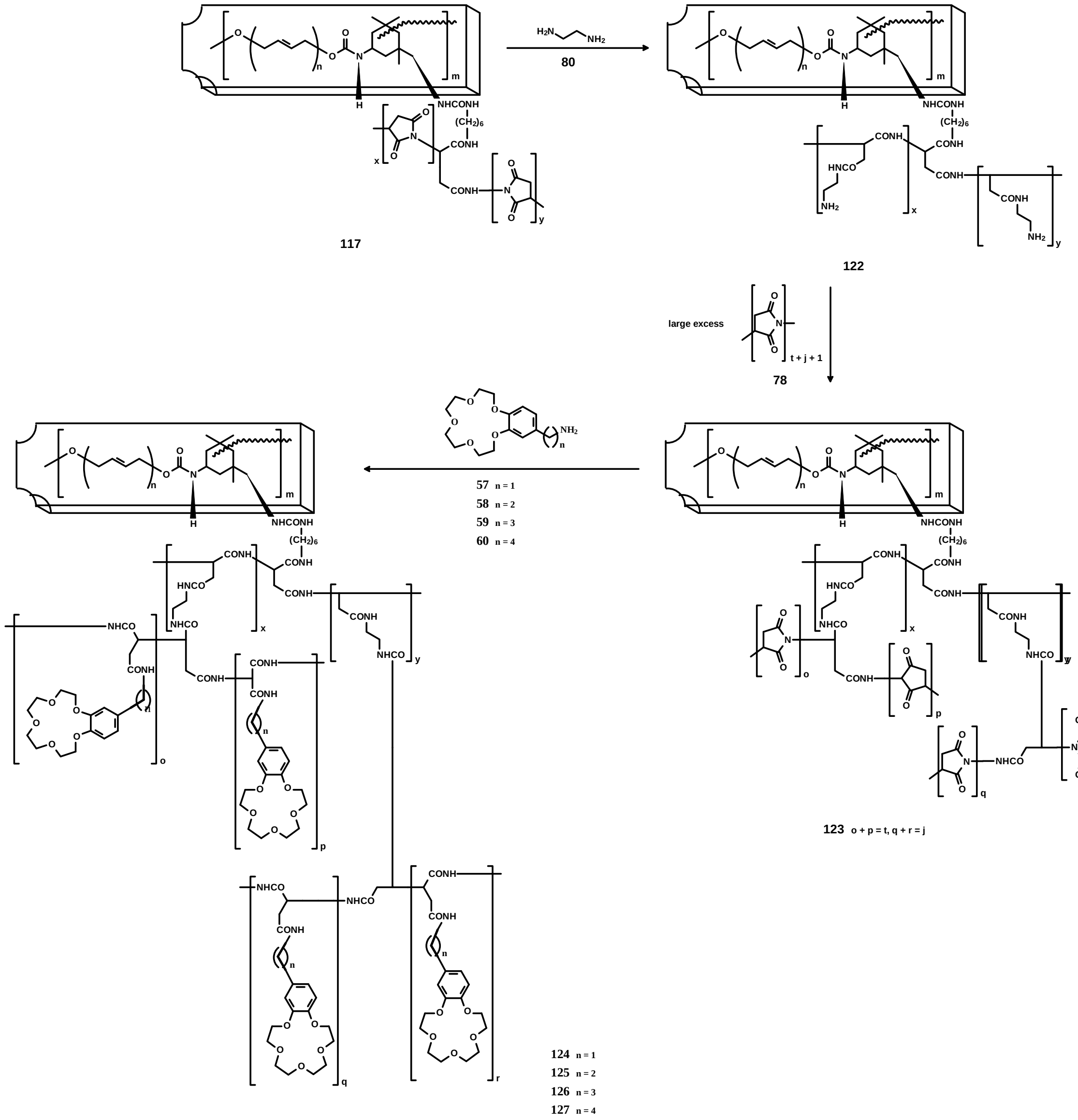
The effectiveness of sodium cation removal from water by the devices **108-111** of **Scheme 22** did not exceed 0.06 g Na$^+$/m^2 of the surface area of the sodium cation scavenging device, while devices **112-115** of **Scheme 23** removed Na$^+$ in quantities of up to 0.07 g Na$^+$/m^2 of the surface area of the solid support from a 200 ppm Na$^+$ solution. These values correspond to approximately 3.5% (devices **108-111**) and 4.5% (devices **112-115**) of the available dissolved Na$^+$ cations (**Table 4**, page 38). The extraction times (i.e. exposure times of solution to cation scavenging device) was 1, 2,5 and 10 minutes, and the extraction results remained unchanged.

By first anchoring to **65** a diamine derivative, such as for example hexamethylenediamine, **80**, (see **Scheme 24**), and thereafter allowing a polysuccinimide, **78**, to react with the intermediate **116** so-formed, followed by ring opening of the polysuccinimide ring by amine-derivatised crown ethers **57-60** (i.e. by reversing the order of polysuccinimide ring opening reactions), polymers **118-121** were obtained as examples of this class of Na$^+$ cation scavengers. The derivatives **118 - 121** of **Scheme 24** removed 0.06-0.07 g Na$^+$ per square meter of the surface of solid support from a 50 ppm aqueous solutions of Na$^+$ cations. This translates to sequestering of between 16 and 18% of the available Na$^+$ cations in 10 cm^3 of a 50 ppm Na$^+$ solution by a device having an active surface area of 0.00125 m^2 (See **Table 4**, page 38 for a summary of all results).



Scheme 24: A further example of immobilisation of crown ether derivatives on a solid support utilising polyaspartates as linking group. a = 4, x+y ≈ 600. Structures **118-121** is again an idealised visualisation of the product obtained as it does not show any cross-linking that may occur between succinimide moieties upon its addition to the multiple amine-containing device **116**.

Now, to further improve the sodium cation scavenging properties of **118-121**, it is clear that more crown ether moieties must be anchored onto the solid support. This implies the addition of more polysuccinimide moieties to the surface of elastomer **65**. To achieve this, the device **117** from **Scheme 24** was swamped with a large excess of ethylenediamine (**80**) to obtain the highly aminated surface **122** in **Scheme 25**.



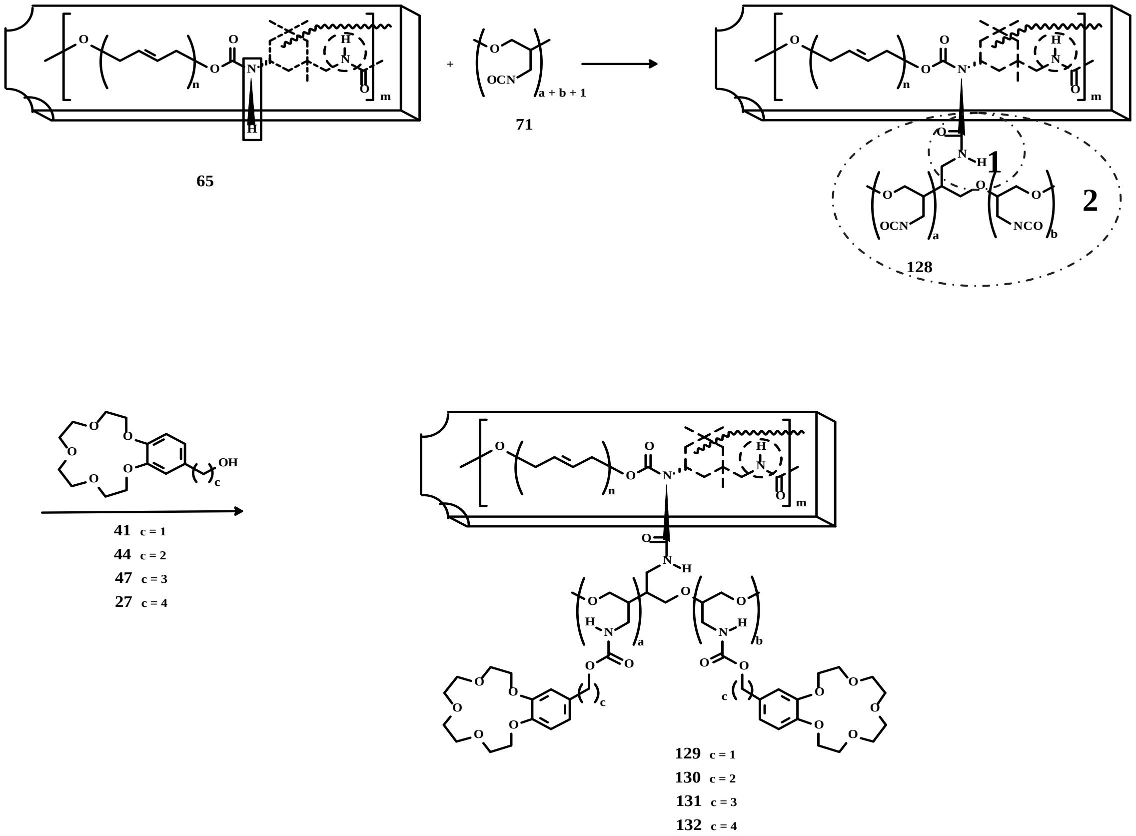
Scheme 25: The synthesis of elastomers **124-127**. The structures shown are idealised presentations as per the ***Note*** in the subscript of **Scheme 21**.

The device **122** was then thoroughly washed and treated with a large excess of polysuccinimide, **78**, to liberate elastomer **123**. It was anticipated that this procedure should result in the solid support being much heavier laden with succinimide moieties than device **117.** The nucleophilic attachment of amine-containing benzo-15-crown-5 derivatives **57-60** onto elastomer **123** then resulted in the idealised presentation of elastomers **124-127**. Structures **122, 123** and **124-127** is again an idealised visualisation of the product obtained as it does not show any cross-linking that may occur between succinimide moieties upon the addition of a diamine. However, the use of a large excess of ethylenediamine, **80**, should have minimised this unwanted side reaction.

The effectiveness of the sodium cation scavenging devices **124-127** to remove Na^+ from a standard sodium chloride solution (50 ppm) was then determined. It was found that elastomer **124** could remove only about 0.10 g Na^+ / m^2 surface area of the sodium cation scavenging device. Although this corresponds to removal of approximately 21-25% of available Na^+ cations from solution (**Table 4,** page 38), it was concluded that polysuccinimide derivatised sodium cation scavengers are inherently not efficient enough to warrant further research on these complexes. Anchoring of aminated crown ether derivatives onto polysuccinimide-containing derivative **123** appears not to be a highly efficient reaction inter alia because of excessive cross-linking reactions that may occur upon converting **122** to **123**. Attention was then focussed on more reactive polymeric side chains that could be used to anchor crown ethers more effectively on them.

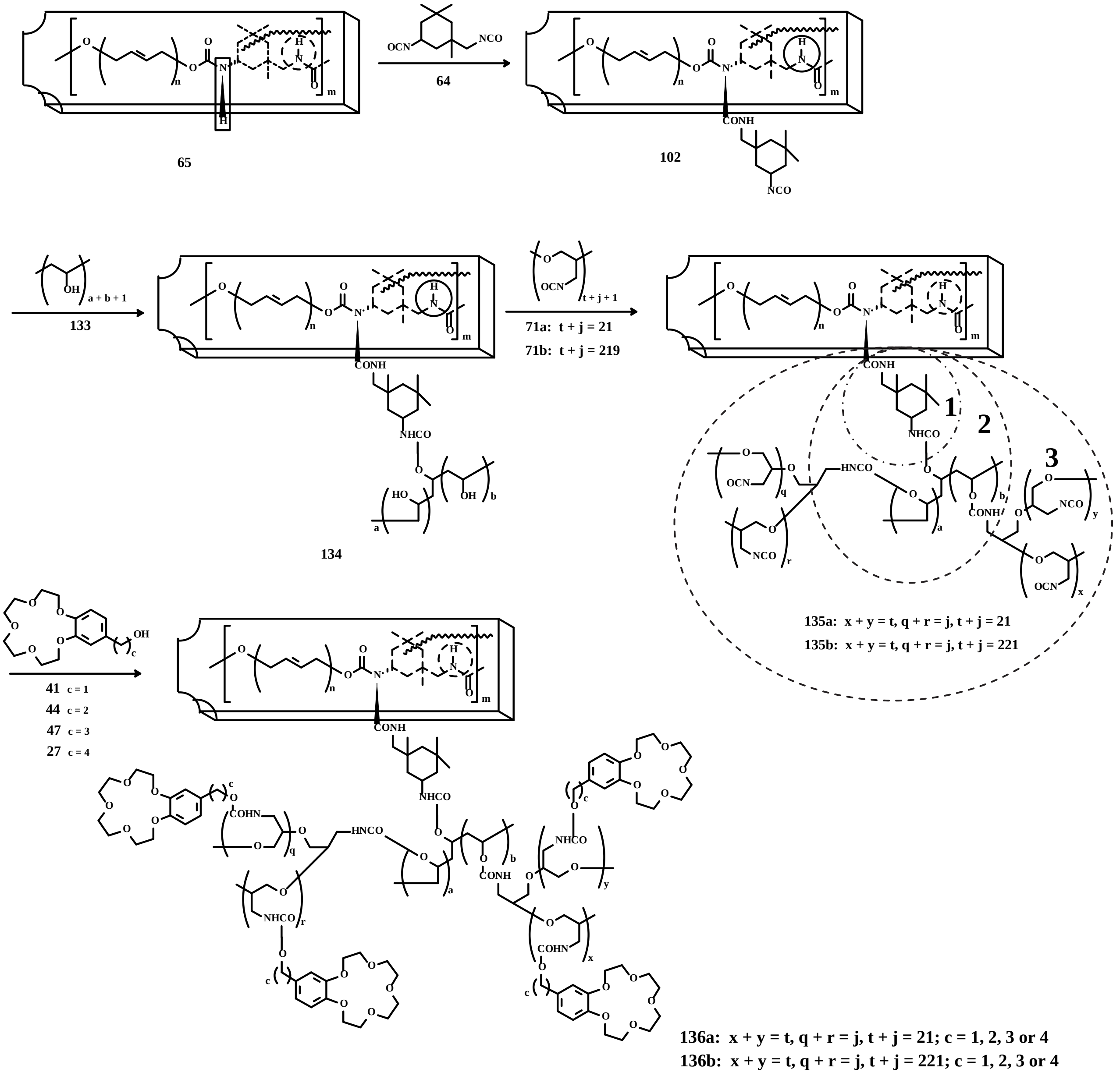
Hence our attention again focussed on the isocyanate-containing pre-polymers **71**. First, the isocyanate-containing pre-polymers **71** were anchored onto the cured elastomer **65**. Thereafter, the alcohol-containing crown ether derivatives **41, 44, 47** and **27** were anchored onto the so-obtained intermediate polymer conjugate **128**. The reaction is shown in **Scheme 26**. This procedure resulted in the intermediate **128** having a much larger NCO content than device **102** (**Scheme 21**, page 30). It follows that devices **129-132**, obtained by reacting **128** with the alcohols **41, 44, 47** and **27**, also should have a larger crown ether content than the corresponding devices **104-107** (**Scheme 21**) because devices **129-132** are second generation starburst molecules (our term for a polymeric dendrimer). The systems **104-107** described in **Scheme 21** are first generation starburst molecules. The second generation starburst devices **129-132** were found to be much more successful in scavenging Na^+ cations than ***any*** of the previously described devices. The amount of sodium which the cation elastomeric scavenging device **129-132** could remove from a 200 ppm Na^+ solution was determined to be around 0.27 g Na^+ per m^2 elastomer surface area (**Table 4**, page 38). This corresponds to the removal of approximately 17% of the available Na^+ cations in 10 cm^3 of a 200 ppm Na^+ solution by a device having an active surface area of 0.00125 m^2 (**Table 4**, page 38).

It was also found that uptake of the sodium cations by the crown ether devices occurred faster than 30 seconds, as all samples of elastomer **104** were allowed to be in contact with the Na^+ stock solution for periods of 30 seconds till 10 minutes. No significant differences in the amount of Na^+ that the Na^+ scavenging device **129** could remove were detected for the 30 second, 2 minute and 10 minute experiments.



Scheme 26: Anchoring of crown ether derivatives on support system number **128**. a + b = 21. The numbers **1** and **2** identifies the first and second generation of the starburst structure. ***Note**: the scheme only illustrates the reaction for OH-functionalised crown ethers on a solid support via polyisocyanate derivatives of **30** as binding intermediates. If the crown ethers are amine functionalised (e.g. **57-60, Scheme 20**), the linking group will be a urea unit, -NHCONH-, and not the urethane functional group, -NHCOO-, as in polymers **129-132**.*

To further improve the effectiveness of Na^+ removal from water by a crown ether-containing solid support, a protocol that would provide a solid support covered very heavily with crown ethers was developed. In essence it meant synthesising third generation starburst molecules. To this end, elastomer **102** was first treated with polyvinyl alcohol **133** of high molecular mass (72 000 g mol^{-1}) at 78 °C for 24 h, and also at room temperature for 72 h, to increase the number of alcohol groups on the surface of the elastomer (**Scheme 27**). The poly-isocyanate derivatives **71a** (M_r = 2000) and **71b** (M_r = 20000) were then reacted with separate samples of the intermediate **134** at 78 °C and at room temperature to give **135a** and **135b**. This served to increase the number of NCO groups on the surface of the solid support significantly by comparison with previous devices described in this report. Finally, the alcohol derivatised crown ethers **41, 44, 47** and **27** and the devices **135** were reacted at 78 °C and at room temperature to give the Na^+ scavenging devices **136a** and **136b**. The devices **136a**, which used the smaller molecular mass of **71** (i.e. polyisocyanate **71a)** removed 0.6-0.7 g Na^+ per m^2 surface area elastomer. This corresponds to the removal of between 38 and 48% of the available Na^+ cations in 10 cm^3 of a 200 ppm Na^+ solution by a device having an active surface area of 0.00125 m^2 (**Table 4**, page 38). Devices **135b**, which used the higher molecular mass derivative of **71**, that is polyisocyanate **71b**) removed 1.22-1.48 g Na^+ per m^2 surface area elastomer. This corresponds to the removal of between 76 and 92% of the available Na^+ cations in 10 cm^3 of a 200 ppm Na^+ solution by a device having the same active surface area as before. (**Table 4**, page 38).



Scheme 27: Synthesis of a Na^+ scavenging devices heavily coated with crown ether moieties. The numbers **1, 2** and **3** identifies the first, second and third generation of the starburst (= polymeric dendrimer) structure. Structures are idealised as per the **Note** in the subscript of **Scheme 21**.

Table 4. Effectiveness of sodium cation scavenging devices of this study in the removal of Na^+ from 10 cm^3 of a solution containing the indicated amount of Na^+ cations. Active surface area of devices = 0.00125 m^2

Device	**Na^+ complexation capability expressed as g Na^+ / m^2 surface area of the sodium cation scavenging device**	**[Na^+] (ppm) in water that was used to test the capabilities of each device**	**Percentage of Na^+ cations removed from 10cm^3 of Na^+ solutions**
From Scheme 21	NHCOO NHCONH Bonds Bonds		NHCOO NHCONH Bonds Bonds
104	0.044, 0.026	200	2.7 1.6
105	0.021, -	200	1.3 -
106	0.038, 0.032	200	2.4 2.0
107	0.028, 0.022	200	1.8 1.4
From Scheme 22			
108	? 0.7	20% Na_2SO_4	No meaningful calculation possible
108	0.062	200	3.8
109	0.058	200	3.6
110	0.052	200	3.2
111	0.052	200	3.2
From Scheme 23			
112	0.065	200	4.0
113	0.068	200	4.3
114	0.051	200	3.2
115	0.068	200	4.3
From Scheme 24			
118	0.068	50	17
119	-	50	-
120	0.071	50	18
121	0.065	50	16
From Scheme 25			
124	0.087	50	22
125	-	50	-
126	0.095	50	24
127	0.098	50	25
From Scheme 26			
129	0.264	200	17
130	0.279	200	18
131	0.260	200	16
132	0.273	200	17
From Scheme 27			
136a, n = 1	0.76	200	48
136a, n = 2	0.60	200	38
136a, n = 3	0.69	200	43
136a, n = 4	0.73	200	46
136b, n = 1	1.28	200	80
136b, n = 2	1.22	200	76
136b, n = 3	1.44	200	90
136b, n = 4	1.48	200	92

It should be noted that during the course of this study, we have improved the effectiveness of our sodium cation scavenging devices from removing 0.03 g Na^+ to 1.48 g Na^+ from a standard 200 ppm sodium (Na^+) solution solution. This represents a ca. 4700% improvement in performance. The improvement was obtained by utilising reactive groups (here the NCO group) in coupling reactions and by developing a starburst (polymeric dendrimer) device of the third order. For device **136** the first order (or layer) is obtained with the aid of the isophoronediisocyanate **64** fragment, the second comes from the polyvinyl alcohol (**133**) fragments, while the third order segment comes from the polyisocyanate (**71**) layer. It stands to reason that further improvements in Na^+ cation scavenging capability may be achieved by moving into fourth and fifth generation starburst molecules.

10 Removal of the Na^+ cation from the crown ether-containing devices

In order to determine whether a polymeric device as described above could release the trapped sodium cations from its surface, experiments were performed to show how many Na^+ cations are released as a function of acid strength, concentration, time and temperature. Results are summarised in **Figure 11** and **Table 5**. **Figure 1** shows that cation release is optimum at 70 °C or higher, and that device **108** lost no effectiveness even after ten cycles of sodium cation binding and subsequent sodium cation release.

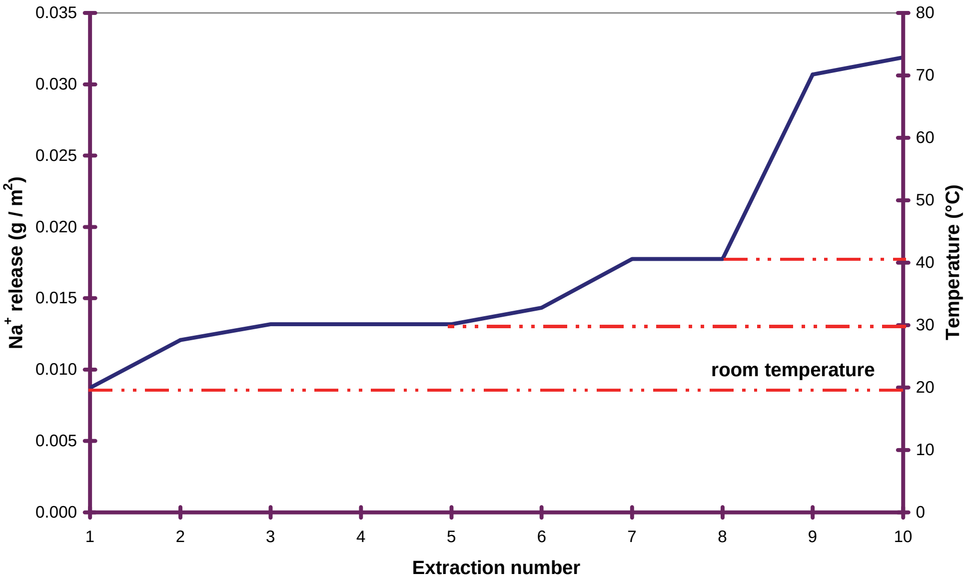


Figure 11: Sodium cation release from device **108** is most effective at temperatures warmer than 70 °C. Device **108** does not loose any effectiveness after 10 cycles of Na^+ binding and subsequent release.

In terms of acid strength, it was found that at both 1 mol dm^{-3} and 6 mol dm^{-3} (i.e. pH < 1) equal amounts of Na$^+$ is released from the devices **104, 108, 121, 124, 129, 136a** and **136b**. However, an acid strength of 0.5 mol dm^{-3} caused **108** to release only 0.008 g. Acid strengths of 0.1 mol dm^{-3} induces no release whatsoever. It was also found that device **108** was more effective in removing Na$^+$ from concentrated solutions than from diluted solutions. In particular, when **108** was allowed to co-ordinate Na$^+$ cations from a 20% solution of Na_2SO_4, it was found to set free 0.35 g / m^2 surface area of cation scavenging device. In each case, as per **Table 5**, approximately half the amount of Na$^+$ originally trapped is released upon treatment with acid. This implies that device **108** in all probability co-ordinated 0.7 g / m^2 surface area of cation scavenging device after it was allowed to scavenge Na$^+$ from a 20% Na_2SO_4 sollution. It was also found that the devices of **Table 5** released the same amount of Na$^+$ after 2 minute or 10 minute exposures to 1 mol dm^{-3} HCl solutions.

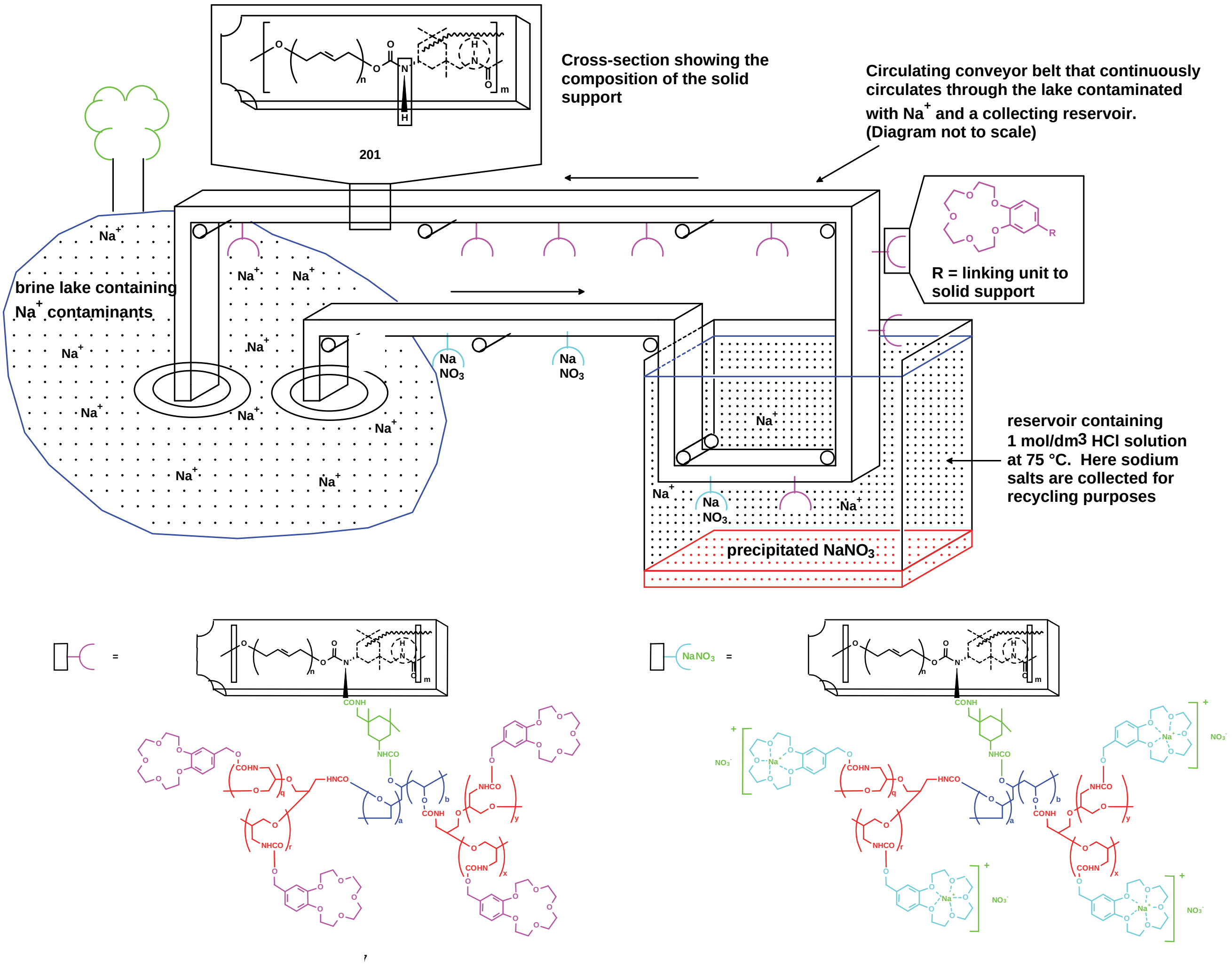
Table 5: Na$^+$ released from the indicated sodium cation scavenging devices at 70 °C in 1 mol/dm^3 HCl solution.

Device, Scheme number	**Na$^+$ released from the surface of the indicated device expressed as g Na$^+$ / m^2 surface area of the sodium cation scavenging device**	**Mass of Na$^+$ that was originally trapped on the surface of the indicated sodium cation scavenging devices expressed as g Na$^+$ / surface area of the sodium cation scavenging device**
104, Scheme 21	0.023	0.044
108, Scheme 22	0.032	0.062
120, Scheme 24	0.033	0.065
124, Scheme 25	0.050	0.098
129, Scheme 26	0.136	0.264
136a, c=1, Scheme 27	0.391	0.760
136b, c=1, Scheme 27	0.658	1.280

The author believes that the novel Na$^+$ scavenging devices developed during the course of this research program provides the scientific foundation for an effective method of removing sodium cations from wastewater. It is acknowledged, however, that a removal efficiency of 1.4 g Na$^+$ /m^2 surface area of Na$^+$ scavenging device is not a large enough quantity to allow immediate industrial applications. Once a value of 10g/m^2 is obtained, this process may become economical. To achieve this, starburst side chains of the 4th, 5th or higher generations of starburst molecules may be required.

11 Conclusions

During the period 2000 –2002 we have set ourselves the goal of developing the science required to develop a new means of cleaning factory wastewater. This new process is distinctly different from current state of the art ion exchange or membrane technology. We have developed procedures to synthesise an elastomeric polymer support, synthesise Na^+ scavenging devices in the form of crown ether derivatives, and we developed the science required to very heavily coat the surface of the solid support with the crown ether Na^+ scavenging molecules. In particular we used dendrimer technology adapted to polymer systems and we called these starburst molecules. The design of our device is again provided in schematic form below, this time providing details of the system. **Figure 12** below should be compared with **Figure 1** on page 1.


Cross-section showing the composition of the solid support

Circulating conveyor belt that continuously circulates through the lake contaminated with Na^+ and a collecting reservoir. (Diagram not to scale)

reservoir containing 1 mol/dm3 HCl solution at 75 °C. Here sodium salts are collected for recycling purposes

Cross-section showing how sodium cation scavengers (here crown ethers) may be bound to the surface of the solid support. On the left the crown ethers are empty, while on the right, the cavity is filled with Na^+.

Figure 12. **A schematic representation of the process of transferring Na^+ from a sodium aqueous phase to a suitable reservoir.** The above device, having an active surface area of 0.00125 m^2, could remove 76-92% of the available Na^+ cations in 10 cm^3 of a 200 ppm Na^+ solution.

12 Recommendations

Although this research program succeeded to develop the science required to manufacture a device that is capable of transferring 76-92% of the available Na^+ cations from a 200 ppm Na^+ solution, and release half of this amount again in a previously determined reservoir in a single cycle, the density of Na^+ cations on the solid support is still low: only about 1.5 g / m^2. Also, the present technology only supports Na^+ removal from water. To improve the loading capacity, and to expand the technology to also include other cations including heavy metals, it is recommended that

1) Funding be made available to develop the technology to increase the density of Na^+ loading by expanding the order of the existing starburst structure from 3 to 6.
2) Devices be developed that can remove (and selectively recover) other metals from aqueous solution including magnesium (pollutant), lead (poison), platinum and silver (precious metals), copper and cobalt (economically important but scarce metals in South Africa) cations.
3) The present technology be expanded to include inputs from engineering institutions to test and develop this new technology on pilot plant scale and beyond.

13 Products emanating from research

The most important product from this research is the development of the technology to manufacture a device that is capable of transferring Na^+ from a sodium aqueous phase to a suitable reservoir. This device could remove 76-92% of the available Na^+ cations from a 200 ppm Na^+ solution, and release half of this amount again in a previously determined reservoir in a single cycle. This technology, through many cycles, will be able to clean up brine wastewater left overs after inter alia membrane technology purified the bulk of polluted industrial wastewater. It can replace the need for evaporation dams to do the final cleaning of industrial waste water.

In total 23 new (i.e. previously unknown) crown ether compounds were made. Of these, 4 were carboxylic acids, 4 were acid chlorides, 4 were diazoketones, 4 were amides, 4 were amines and

3 were alcohols. In terms of polymeric devices more than 50 new polymers were also synthesised.

Possible applications from this research include

1) the removal of sodium cations from water with both high and low sodium cation content;
2) the purification of waste water brines after other technologies (e.g. membrane technology) concentrated the pollutants in a large body of water into a smaller volume fraction containing a higher concentration of salts;
3) adaptation of the present technology to also allow selective retrieval of heavy metal pollutants in water and the retrieval of scarce or valuable metals.

Further, in terms of products emanating from this research, this project contributed to the development of scientific knowledge, specifically in methods of synthesising new crown ether derivatives, polymer derivatives, solid supports and to the training and developing of synthetic and analytical skills of the twelve (12) students. Of these, 7 are from the previously disadvantaged community. One PhD and one MSc student graduated from this project, 10 3rd year Chemistry students and Hons. BSc students performed project studies on this program.

A student seminar on this research entitled

Synthesis of crown ether derivatives for the purification of waste water

was given. This seminar was given both to Bloemfontein students and staff as well as to students and staff at Rhodes University in Grahamstown.

A patent on this work was filed in October 2002 via the patent attorneys Adams and Adams of Pretoria. Details are

Title: Crown ether derivatives
Date of Submission: 10 October 2002
Patent Number: 2002/8176
Inventor: Johannes Christiaan Swarts

14 References

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