A NEW METHOD TO REMOVE AND RECOVER CONTAMINATING SODIUM SALTS FROM INDUSTRIAL WASTEWATER UTILISING POLYMER-BOUND CROWN ETHERS

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TO LINDA AND HANRÉ

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ABBREVIATIONS

The following abbreviations for solvents and reagents were used throughout this thesis:

A	acetone
ADP	adenosine diphosphate
AMP	adenosine monophosphate
ATP	adenosine triphosphate
B	benzene
cm^{-1}	wave number
DMF	*N,N*-dimethylformamide
DN	donor number
EtOH	ethanol
H	hexane
HCl	hydrochloric acid
HTPB	hydroxy terminated polybutadiene
IR	infrared
m.p.	melting point
MeCN	acetonitrile
MeOH	methanol
NMe	nitromethane
NMR	nuclear magnetic resonance
THF	tetrahydrofuran
X	halogen

alcohol, carboxylic acid, amide and amine functionalised benzo-15-crown-5, benzo-15-crown-5, hydroxy terminated polybutadiene (HTPB), polyaspartamide, polyepichlorohydrin

ABSTRACT

The aim of this study was to develop a new technique to clean the total ***factory*** generated wastewater as seen in the light of the background given in Chapter 1. It was decided to develop a material that would enable an industry to complex sodium cations from a contaminated source, and to release the complexed sodium cations, under controlled conditions, at a previously determined site, or receiving reservoir, in a cyclic manner.

For this reason, 32 different functionalised crown ether derivatives were synthesised to produce a series of 17 new crown ether derivatives, including 4 carboxylic acid, 4 amide, 4 alcohol and 4 amine crown ether derivatives, with spacers ranging from one to four carbon atoms in the side chain that separate the functional group from the crown ether moiety. Selected crown ether functionalised derivatives was anchored on polymeric supports and their sodium cation complexation ability was determined.

Twenty (20) polymeric carriers were also synthesised. These include the synthesis of 12 new water-soluble polyaspartamide derivatives as well as 5 new polyepichlorohydrin water-insoluble derivatives. The experimental procedures for the synthesis of the water-soluble polymers could be tuned to achieve exact ratios between polymer anchored crown ethers and several other polymer side chains containing functional groups. The carboxylic acid derivatives could be anchored to the water-soluble polymer and this reaction could be tuned to achieve 100 % coupling, with the use of the coupling reagent *O*-benzotriazolyl-*N,N,N',N'*-tetramethyluronium hexafluorophosphate.

An elastomeric solid support was also synthesised by the curing of hydroxy terminated polybutadiene with isophorone diisocyanate. It was also demonstrated that crown ether derivatives and/or polymeric carriers could be anchored onto this elastomeric solid support, with or without the use of a spacer between the elastomeric solid support and the crown ether. Several new elastomeric solid supports containing crown ethers were synthesised.

Complexation studies of Na^+ dissolved in an aqueous phase by crown ether functionalised elastomeric solid supports were demonstrated, and it was found that 1.28 g Na^+ / m^2 surface area of the sodium cation scavenging device could be removed. Acid media was used to accomplish the release of the Na^+ from this elastomeric solid support, and it was found that 0.65 g Na^+ / m^2 surface area of the sodium cation scavenging device could be released.

OPSOMMING

Die doel van hierdie studie was om 'n nuwe tegniek te onwikkel om die totale ***fabrieks*** afval water te suiwer, soos gesien teen die agterdrond gegee in Hoofstuk 1. Daar is besluit om 'n materiaal te ontwikkel wat 'n industrie in staat sou stel om natrium katione op 'n sikliese manier vanuit 'n gekontamineerde bron te verwyder, en om die gekomplekseerde natrium katione weer vry te stel, onder gekontrolleerde kondisies, op 'n voorafbepaalde plek.

Vir hierdie doel is 32 verskillende gefunksionaliseerde kroon eter derivate gesintetiseer, om 'n reeks van 17 nuwe kroon eter derivate te gee, wat insluit 4 karbosiel suur, 4 amied, 4 alkohol en 4 amien kroon eter derivate, met tussen een en vier koolstof atome in die sy-ketting tussen die funksionele groep en die kroon eter fragment. Geselekteerde kroon eter gefunksionaliseerde derivate is op polimere geanker en hulle natrium katioon kompleksering vermoeë is bepaal.

Twintig (20) polimeriese draers is ook gesintetiseer. Dit sluit in die sintese van 12 nuwe wateroplosbare poliaspartamied derivate, asook die sintese van 5 nuwe poliepichlorohydrien wateronoplosbare derivate. Die eksperimentele prosedures tydens die sintese van die wateroplosbare polimere kon so ontwikkel word om eksakte verhoudings tussen die kroon eters en ander funksionele groepe op die polimere te verskaf. Die karboksiel suur derivate kon aan die wateroplosbare polymeer geanker word, en hierdie reaksie is ontwikkel om 100 % koppeling te verkry, deur gebruik te maak van die koppelings reagens O-bensotriasolyl-*N,N,N',N'*-tetrametieluronium heksafluorofosfaat.

'n Elastomeriese vaste ondersteuningspolimeer is gesintetiseer deur die kuring van hidroksie getermineerde polibutadieen met isoforoon diisosianaat. Hier is ook gedemonstreer dat kroon eter derivate en/of polimeriese draers aan hierdie elastomeriese vaste ondersteuning geanker kan word, met of sonder die gebruik van koppelstukke tussen die elastomeries vaste ondersteuningspolimeer en die

kroon eters. Verskeie nuwe elastomeriese vaste ondersteuningspolimere wat kroon eters bevat is gesintetiseer.

Die Na^+ verwyderings vermoeë van hierdie gesintetiseerde elastomeriese vaste ondersteuningspolimere is ook ondersoek. Daar is gevind dat 1.28 g Na^+ / m^2 natrium-katioon-verwyderingstoestel uit 'n waterige fase verwyder kon word. 'n Suur medium is gebruik om die gekomplekseerde Na^+ vanuit die elastomeriese vaste ondersteuningspolimeer vry te stel. Daar is gevind dat 0.65 g Na^+ / m^2 natrium-katioon-verwyderingspolimeer vry gestel kon word.

CHAPTER 1

INTRODUCTION

Whenever one sees a photo of the earth from outerspace, one gets the impression that this planet has lots of water. This image could mislead us into believing that we can never run out of fresh, usable water and that the pollution of some of earth's rivers, including those in our own country, has no significant detrimental impact on life. This view is wrong. The opposite is in fact true. Although it may appear that our planet contains enough fresh water to sustain life indefinitely, this is in fact not a true assumption. According to the United Nations Educational, Scientific and Cultural Organisation (UNESCO),[1] the demand for fresh water is soaring, while the supply of natural fresh water is diminishing. Between 1900 and 1995, the world's demand for water increased more than six-fold compared with the three-fold increase in the world population. This ratio may appear to be small enough to imply that there is enough water to sustain our growing population. But, according to UNESCO[1] an estimated 460 million people (8 % of the world's population) experience a shortage of drinkable water, and another quarter (more than 1.5 billion people) of the planet's inhabitants are quickly heading to the same fate. Experts predict that if nothing is done to change the current trends, two-thirds of humanity will suffer from a moderate to severe lack of water by the year 2025.

The fact is that 97.5 % of the planet's water is salty and that most of the world's fresh water supply – the remaining 2.5 % – is unusable. The reality is that 70 % of our fresh water supply is frozen in the ice-caps of Antarctica and Greenland and almost all the rest exists in the form of soil humidity or in water tables that are too deep to be tapped. In all, barely 1 % of the total fresh water supply – 0.007 % of the world's total water – is easily accessible and usable to sustain life.

UNESCO[1] also stated that the world's water quality is declining. In some areas, contamination levels are so high that water can no longer be used, not even for industrial purposes. The reasons for this decline in fresh water quality include *inter alia* untreated sewage, chemical waste, fuel leakage, dumped garbage, and the contamination of soil by chemicals used by farmers.

Table 1. 1 indicates the relative time for the complete renewal of the earth's water resources. The term renewal implies that the polluted water has to be purified by natural means, which includes excessive dilution, evaporation of the water under the influence of the sun and reprecipitation in terms of rain. This Table indicates how long it will take for the various water resources to be regenerated naturally after it is contaminated with industrial or another form of contaminated wastewater to the point where they cannot sustain life.

Table 1. 1. Periods of complete renewal of the earth's water resources.[1]

Kinds of water	Period of renewal by natural processes
Biological Water*	several hours
Atmospheric Water	8 days
Water in River Channels	16 days
Soil Moisture	1 year
Water in Swamps	5 years
Water in Storage Lakes	17 years
Groundwater	1 400 years
Mountain Glaciers	1 600 years
World Ocean	2 500 years
Polar Ice Floes	9 700 years

The problem of increasing water supply has long been seen as a technical one, calling for technical solutions such as building more dams and desalination plants, but today, technical solutions are reaching their limits. Economic and socio-ecological arguments are very important to consider when the design and building of a new dam is planned. These arguments may even prevent the final approval for construction of the proposed dam. This may happen because dams are costing more and more due to the fact that the best and easily accessible sites are already used, and the new sites may take millions of people out of their environment and upset ecosystems.

Existing methods that are employed for the purification of industrial wastewater, such as ion exchange, evaporation and reverse osmosis, are not very cost effective and it does not remove contaminants from the total volume of factory-generated wastewater effluents. These traditional purification processes operate by concentrating the contaminants from the bulk of the polluted water into

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* Biological water refers to the water in a living object, such as plants, animals, microorganisms, etc.

a fraction of the original ***factory*** effluents, thereby creating a concentrated solution of salts, or a 'brine', which are notoriously difficult to handle. The chief contaminants in these brines are simple salts containing *inter alia* Na^+, Ca^{2+}, Mg^{2+}, Cl^-, SO_4^{2-} and PO_4^{3-} ions. Typically, these brines are stored in large sludge dams, but this protocol creates new unforeseen problems. As the total volume of these brines become larger, the need to clean them also becomes more essential. If, for any reason, the sludge dams holding these brines leaks into underground water storage sites, the consequences will be catastrophic. The brines will eventually contaminate the underground water storage sites, thus rendering it unfit for supporting life. As seen in Table 1. 1, p. 3, it will take about 1 400 years for the contaminated under groundwater to completely renew itself by natural processes.

To circumvent this undesirable and tragic state of affairs, a hereto-unknown method of cleaning up brines, i.e. achieving purification of the total volume of industrial wastewater effluents generated by industrial processes, is needed. This study attempts to address this problem.

Ideally the removed contaminants must be recovered and recycled, in a cheap and effective way. Well documented and instructive is the use of crown ethers to transport group I and II metallic cations and common anions (Cl^-, SO_4^{2-}, NO_3^- and PO_4^{3-}) from a water phase to an organic phase. The transport of crown-ether-complexed-ions from a liquid organic phase to a water phase; the removal, or transport of these ions from a liquid into a solid matrix; and the deposit, or release of these ions from the crown ether, or other complexes to a concentrated aqueous solution, is however less known. If the latter two processes could be accomplished economically, then contaminant ions may be removed from wastewater sludge dams, or effluent brines, and be deposited, in ever increasing concentrations, in another reservoir, to eventually precipitate the unwanted ions in a crystalline form. In this way the contaminants may be recovered and recycled.

Although crown ethers are good complexing agents of ions typically found in wastewater, two deterring factors for their use as wastewater contaminant-trappers can be sited. The first is the poor solubility of common crown ether-contaminant ion complexes in water, when compared with their solubility in organic solvents, such as dichloromethane. The second relates to a practical method that must be developed to allow the cyclic use of crown ethers in scavenging wastewater contaminants from contaminated water and dumping them, in a controlled manner, at a previously determined site. One way of addressing both these problems are to synthesise a polymeric carrier compound to which the wastewater contaminant-trappers, crown ethers for this study, can be anchored. The polymer bound crown ethers can then be used to complex, or catch, the contaminants in the brine-like wastewater and to release them afterwards in another water phase – the collecting reservoir. In order to visualise this process, one may think of the crown ether as bound to the surface of a water-insoluble polymeric carrier, cast in the form of a rod or woven as a conveyor belt. Although the carrier-polymer is water-insoluble, the polymer side chains to which the crown ether is attached may be made very hydrophilic. When the conveyor belt is then run through the brine-like wastewater, the water loving side chains containing the crown ethers, will pick up a specific contaminant, e.g. sodium nitrate, *via* co-ordination and thereafter release it in a suitable reservoir, under specific conditions (Figure 1. 1). In principle, one will eventually enrich the receiving reservoir with a specific cation and anion, Na^+ and NO_3^- in this example, to the point where it will begin to precipitate in a crystalline form. The precipitate may then be reclaimed and recycled in industries where they may be required.

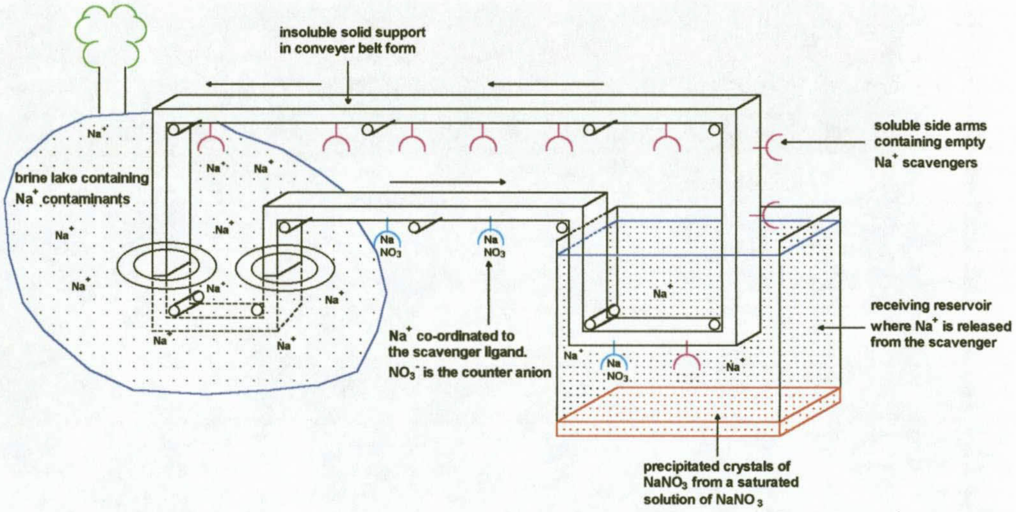


Figure 1. 1. A schematic representation of the process of transferring sodium nitrate from a brine wastewater phase to a suitable reservoir, until the latter eventually becomes saturated in $NaNO_3$ and the salt crystallises. Ideally one will want a device that is simultaneously specific for both Na^+ and NO_3^-. Drawing not to scale. The brine lake obviously is very large, while the receiving reservoir, in comparison, may have minute dimensions (5 x 5 x 5 m).

Crown ethers in particular, but also other related compounds, are attractive as the trappers of group I and II metallic cationic wastewater contaminants, due to the fact that they can be made selective towards cations of group I and II and even for certain anions. If the process depicted in Figure 1. 1, p. 5, can be made to work, it would in principle be possible to simultaneously remove a mixture contaminants, for example $NaNO_3$, NaCl and $CaSO_4$ from the brine-like contaminated water sources and to selectively recover them in separate collecting reservoirs.

In this study, the pioneering work in the design of polymeric crown ether compounds that are selective towards trapping sodium cations from wastewater is described. Towards this goal the following targets were set for this study:

1. Functionalisation of the sodium-selective crown ether, benzo-15-crown-5, for the specific purpose to ultimate anchor it onto a suitable polymeric carrier.
2. Development of suitable elastomeric polymeric carriers that may act as supports for the crown ethers of goal 1.
3. Development of suitable methods of covalently binding the crown ether derivatives of goal 1 to the polymeric carriers/supports of goal 2.
4. Development of suitable water-soluble polymers that may be used as side chains, acting as spacers, between the polymeric supports of goal 2 and the crown ethers of goal 1.
5. Investigation of the sodium scavenging properties of this polymeric sodium cation scavenging device.
6. Investigation of the methods of sodium release from this polymeric sodium cation scavenging device.

CHAPTER 2

LITERATURE SURVEY

2.1 INTRODUCTION

According to UNESCO,[1] fresh water is very important to all living organisms. Contamination of our natural waterways by industries is therefore a general problem. Several techniques exist for the removal of contaminants from industrial wastewater, such as membrane technology, distillation (energy costly), evaporation process (possibility of contaminating the underground water), and even reverse osmosis. The disadvantage of these techniques is that they all just reduce the amount of wastewater. Most of these techniques produce brines (highly contaminated and concentrated salt mixtures). These brines are stored in sludge dams and the possibility exists that these can leak into the underground waterways and render it lifeless.

The goal of this study is to clean the brines produced by the other cleaning techniques. This can be accomplished by the use of polymer-bound crown ethers. This study represents the first attempt to use polymer-bound crown ethers to remove contaminating salts from industrial wastewater. In order to achieve this goal, the following topics need to be considered:

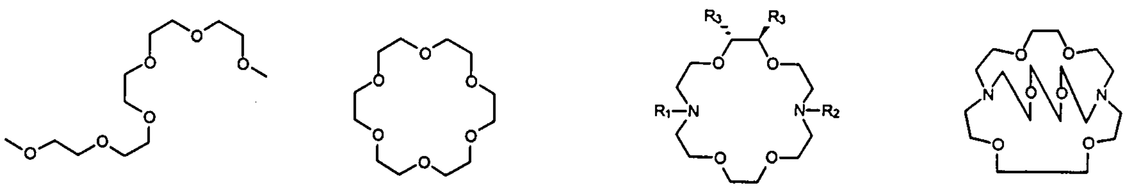
1. Crown ethers and related compounds.
2. Functionalisation of crown ethers.
3. Utilising polymers as suitable carrier agents.

In this Chapter the reader will be will be introduced to some basic knowledge on the above three topics.

2.2 CROWN ETHERS AND RELATED COMPOUNDS

Since the discovery of crown ethers by Pedersen,[2] 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[2] or coronands[3] (Figure 2. 2, p. 10) are macrocyclic ligands that only contain oxygen atoms as donor atoms. Crown ethers are known for their complexation preference for alkali and alkaline earth metal cations.[2] 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.

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 **1** (Figure 2. 1) and K^+ is 2.30, compared to 6.32 for the interaction between **6** (Figure 2. 2, p. 10), 4.80 for the interaction between **49** (Figure 2. 5, p. 13), and 10.49 for the interaction between **55** (Figure 2. 6, p. 14) 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, as can be seen by the log *K* values. 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".[4]



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

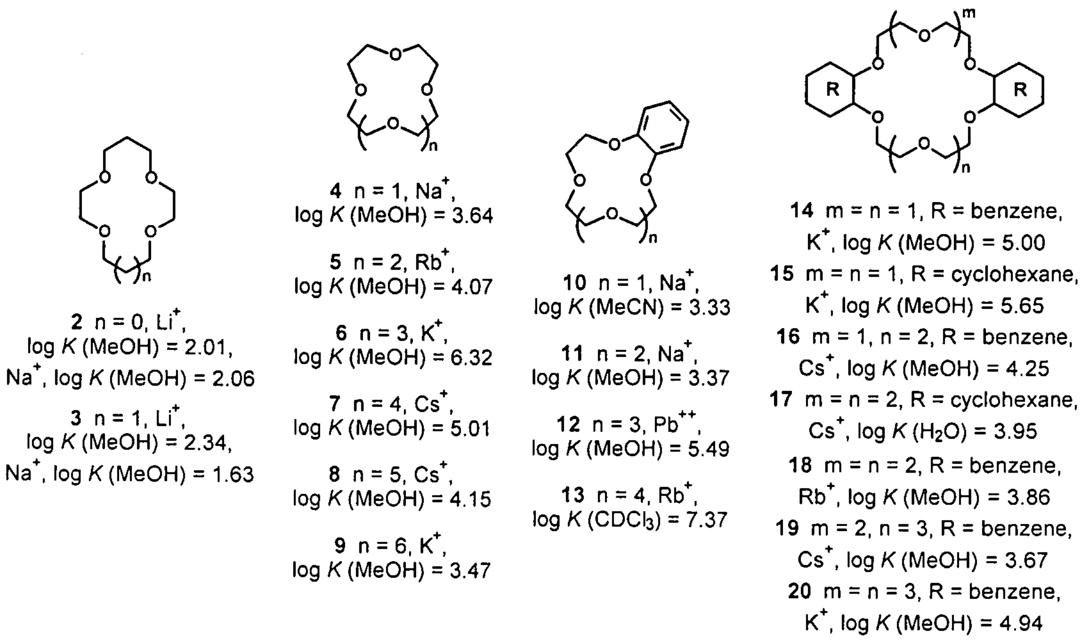
6 K^+, log *K* (MeOH) = 6.32

49 $R_1 = (CH_2CH_2O)_2CH_3$, $R_2 = CH_3$, $R_3 = H$, K^+, log *K* (MeOH) = 4.80

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

Figure 2. 1. An example of a podand (a linear equivalent of the cyclic crown ether).

As mentioned above it is very important to have a ring, or cyclic structure, to obtain a more stable cation-ligand complex. The next question that comes to mind is what role does the structural difference between ligands with the same amount of donor atoms have on the binding strength of these ligands? Both crown ethers **2** and **3** (Figure 2. 2, p. 10) can complex both Li^+ and Na^+, and they both contain the same amount of donor atoms, i.e. 4 oxygen donor atoms, in their macrocyclic rings. It was found that for the interaction between **2** and **3** and the metal cations, Li$^+$ and Na$^+$, different preferences were observed. For the interaction of **2** with Li$^+$ and Na$^+$ the log *K* (MeOH) = 2.01 and 2.06, respectively, while the interaction of **3** with Li$^+$ and Na$^+$ gave log *K* (MeOH) = 2.34 and 1.63, respectively.[4] So despite the same amount of donor atoms in their macrocyclic rings, i.e. 4 oxygen donor atoms, the structural difference does play a role in the complexation preference of these ligands for cations. It is evident that **3** prefer Li$^+$ above Na$^+$, while **2** do not exhibit a cation preference between Li$^+$ and Na$^+$.



2 n = 0, Li$^+$, log *K* (MeOH) = 2.01, Na$^+$, log *K* (MeOH) = 2.06

3 n = 1, Li$^+$, log *K* (MeOH) = 2.34, Na$^+$, log *K* (MeOH) = 1.63

4 n = 1, Na$^+$, log *K* (MeOH) = 3.64

5 n = 2, Rb$^+$, log *K* (MeOH) = 4.07

6 n = 3, K$^+$, log *K* (MeOH) = 6.32

7 n = 4, Cs$^+$, log *K* (MeOH) = 5.01

8 n = 5, Cs$^+$, log *K* (MeOH) = 4.15

9 n = 6, K$^+$, log *K* (MeOH) = 3.47

10 n = 1, Na$^+$, log *K* (MeCN) = 3.33

11 n = 2, Na$^+$, log *K* (MeOH) = 3.37

12 n = 3, Pb^{++}, log *K* (MeOH) = 5.49

13 n = 4, Rb$^+$, log *K* ($CDCl_3$) = 7.37

14 m = n = 1, R = benzene, K$^+$, log *K* (MeOH) = 5.00

15 m = n = 1, R = cyclohexane, K$^+$, log *K* (MeOH) = 5.65

16 m = 1, n = 2, R = benzene, Cs$^+$, log *K* (MeOH) = 4.25

17 m = n = 2, R = cyclohexane, Cs$^+$, log *K* (H_2O) = 3.95

18 m = n = 2, R = benzene, Rb$^+$, log *K* (MeOH) = 3.86

19 m = 2, n = 3, R = benzene, Cs$^+$, log *K* (MeOH) = 3.67

20 m = n = 3, R = benzene, K$^+$, log *K* (MeOH) = 4.94

Figure 2. 2. Examples of crown ethers.

From the previous discussion it is evident that it is very important to have a cyclic ligand, and it is also evident that the structural difference between macrocyclic ligands with the same amount of donor atoms is significant. 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 **14** (Figure 2. 2), rigidifies the crown ether and it also reduces the donicity of the attached oxygen atoms.[5] This can clearly be observed by comparing the interaction between **6** and **14** and the K$^+$. The log *K* (MeOH) value for the interaction between **6** and K$^+$ and between **14** and K$^+$ is 6.32 and

5.00, respectively. One can clearly see that the affinity of **14** for the K^+ has dropped by about 20 % as compared to the affinity of **6** for the same cation.

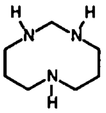
So, the complexation of cations by macrocyclic ligands is not as straightforward as one would expect. Factors such as the presence of a cyclic structure, the structural arrangement of the donor atoms and the presence of rigid groups, must all be considered to ascertain the viability of ligands as complexons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

Many of the crown ethers are known to be biologically active.[5] The LD_{50} values for crown ethers **5**, **6** and **7** were reported as 3.15 g/kg, 1.02 g/kg and 0.71 g/kg.[5] The data reported in the Merck Index for **15** place LD_{50} in mice at 300 mg/kg orally and 130 mg/kg by skin absorption. The LD_{50} reported for aspirin in mice is 1.10 g/kg, and for strychnine sulphate 5 mg/kg.[5]

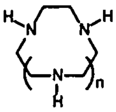
Due to the cumbersome IUPAC names of these macrocycles, e.g. 2,3-benzo-1,4,7,10,13-pentaoxacyclopentadec-2-ene for **11**, the trivial names, e.g. benzo-15-crown-5 for **11**, will be used throughout this thesis. These trivial names consist of:

i. The substituents on the macrocyclic ring, e.g. the benzo group of **11**.
ii. The number of atoms in the macrocyclic ring, e.g. 15 for **11**.
iii. The base name 'crown'.
iv. The number and type of donor atoms in the macrocyclic ring, e.g. 5 for **11**.

Azacoronands[6] (Figure 2. 3, p. 12) are macrocyclic ligands that only contain nitrogen atoms instead of oxygen atoms as the donor atoms. When nitrogen atoms substitute oxygen atoms, one generally observes a change in the preferred metal cation. The crown ethers prefer group I and II metal cations, such as Li^+, Na^+ and K^+, while the azacoronands prefer the transition metal cations, such as Cu^{2+}, Zn^{2+}, Ag^{2+} and Hg^{2+}.[4] The large polyprotonated azacoronands, such as **25** can also co-ordinate anions and can also be used as models for supramolecular catalysts, such as enzymes.[4] Only those compounds that is capable of incorporating more than three protons at neutral pH, such as **24** and **25**[7] form stable complexes with anions, such as PO_4^{3-}, AMP^{2-}, ADP^{3-} and ATP^{4-}.



21 Cu^{++},
log K (H_2O) = 16.19



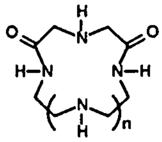
22 n = 1, Cu^{++},
log K (H_2O, 0.1 M $NaNO_3$) = 10.86

23 n = 2, Cu^{++},
log K (H_2O, 0.1 M $NaNO_3$) = 23.30

24 n = 3, Ag^{++},
log K (H_2O) = 43.60

25 n = 4, Hg^{++},
log K (H_2O, 0.2 M $NaClO_4$) = 29.10
SO_4^-, log K (H_2O, 0.05 M NaCl) = 8.58

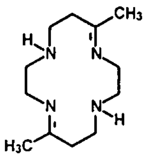
26 n = 5, Cu^{++},
log K (H_2O, 0.5 M $NaClO_4$) = 34.40



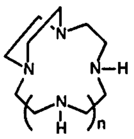
27 n = 1, Cu^{++},
log K (H_2O, 0.5 M KNO_3) = 5.51

28 n = 2, H^+,
log K (H_2O, 0.2 M $NaClO_4$) = 8.35

29 n = 3, Cu^{++},
log K (H_2O, 0.2 M $NaClO_4$) = 10.56



30 Zn^{++}, log K (H_2O,
0.1 M $NaClO_4$, pH 9.5 - 11) = 15.00



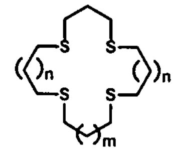
31 n = 1, Cu^{++},
log K (H_2O, 0.1 M $NaNO_3$) = 21.50

32 n = 2, Cu^{++},
log K (H_2O, 0.1 M $NaNO_3$) = 15.10

Figure 2. 3. Examples of azacoronands.

Thiacoronands[8] (Figure 2. 4, p. 13) are macrocyclic ligands that only contain sulphur atoms as the donor atoms instead of oxygen atoms as the donor atoms. When sulphur atoms substitute oxygen atoms, one generally observes a change in the preferred metal cation. The crown ethers prefer group I and II metal cations, such as Li^+, Na^+ and K^+, while the thiacoronands prefer the transition metal cations, such as Cu^{2+} and Hg^{2+}.[9]

Lariat ethers[10] (Figure 2. 5, p. 13) are modified azacoronand or coronand compounds with pendant side arms and were first synthesised by Gokel and his co-workers. Lariat ethers were synthesised to fill the gap between crown ethers, which was dynamic but lacked sufficient binding strength, and cryptands, which form stable complexes but lacked dynamics. This was discussed on page 9.

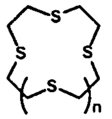


33 n = m = 0, Cu^+, log *K* (H_2O, 0.1 M ClO_4^-) = 14.80

34 n = 0, m = 1, Hg^{++}, log *K* (MeCN, 0.1 M Bu_4NClO_4) = 9.82

35 n = 1, m = 0, Cu^+, log *K* (H_2O, 0.1 M ClO_4^-) = 13.00

36 n = m = 1, H^+, log *K* (H_2O, 0.2 M $NaClO_4$) = 10.04



37 n = 1, Cu^+, log *K* (H_2O, 0.1 M ClO_4^-) = 15.60

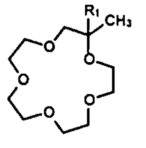
38 n = 2, Cu^+, log *K* (H_2O, 0.1 M ClO_4^-) = 15.00

Figure 2. 4. Examples of thiacoronands.

Two types of lariat ethers are known:

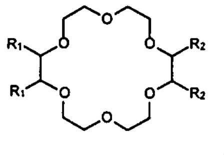
(i) When the side arm is attached to a carbon atom of the macrocyclic ligand, the *C*-pivot lariat ethers, e.g. **39**, are produced.

(ii) When the side arm is attached to a donor atom in the ring, usually a nitrogen donor atom, the *N*-pivot lariat ethers, e.g. **43** are produced.



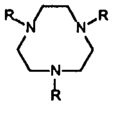
39 $R_1 = CH_2OCH_2CH_2OH$, Na^+, log *K* (MeOH) = 3.88

40 $R_1 = CH_2(OCH_2CH_2)_2OH$, Na^+, log *K* (MeOH) = 3.88



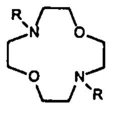
41 R_1 = H, R_2 = COOH, Tl^+, log *K* (H_2O, 0.05 M Me_4NCl) = 9.30

42 $R_1 = R_2$ = COOH, K^+, log *K* (H_2O, 0.05 M Me_4NCl) = 12.60



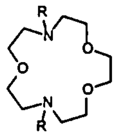
43 R = CH_2COOH, Cu^{++}, log *K* (H_2O, 0.1 M $NaNO_3$) = 21.97

44 R = $CH_2CON(CH_3)_2$, H^+, log *K* (H_2O, 0.1 M Me_4NNO_3) = 10.30



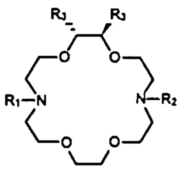
45 R = CH_2COOH, Ca^{++}, log *K* (MeOH-H_2O (9:1), 0.1 M Me_4NBr) = 6.90

46 R = CH_2CH_2OH, H^+, log *K* (H_2O, 0.1 M Me_4NNO_3) = 9.56



47 R = CH_2CH_2OH, Ba^{++}, log *K* (H_2O, 0.1 M Me_4NBr) = 3.30

48 R = $(CH_2)_3NH_2$, K^+, log *K* (Me_2CO) = 4.20



49 $R_1 = (CH_2CH_2O)_2CH_3$, $R_2 = CH_3$, R_3 = H, K^+, log *K* (MeOH) = 4.80

50 $R_1 = R_2 = CH_2CH_2OH$, R_3 = H, Cd^{++}, log *K* (H_2O, 0.1 M Me_4NBr) = 7.10

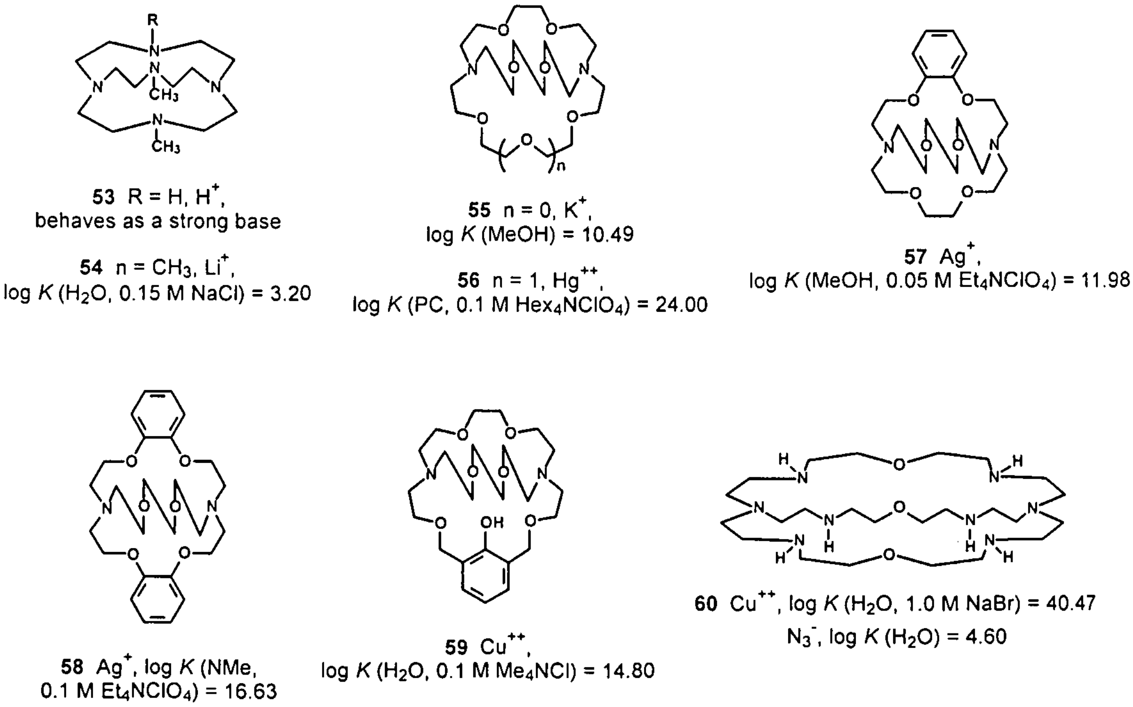
51 $R_1 = R_2 = CH_2CH_2COOH$, R_3 = H, Pb^{++}, log *K* (H_2O, 0.1 M Me_4NCl) = 9.20

52 $R_1 = R_2 = CH_2COOH$, R_3 = COOH, K^+, log *K* (H_2O, 0.1 M Me_4NNO_3) = 12.70

Figure 2. 5. Examples of lariat ethers.

The *C*-pivot lariat ethers are generally poor cation binders, compared to the *N*-pivot lariat ethers, but the addition of a quaternary methyl group at the pivot atom apparently favours the binding conformation.[5] Gokel and his co-workers[11] attributed this, in part, to the geometrical requirements for cation binding. In the *N*-pivot compounds, the cation binding by the macroring involves the nitrogen lone electron pair and this force the side arm into a more or less perpendicular position. This position is appropriate for a secondary interaction of the donor group with the ring-bound cation.

Cryptands[12] (Figure 2. 6) are macrobicyclic ligands and were first synthesised by Lehn. These macrobicyclic ligands complex a wide variety of metal cations, which include group I and II and also transition metal cations. The most stable complex is formed when the ionic radii of the metal cation best match the cavity radius of the cryptand. Due to its more rigid structure, the correspondence between the cavity size and stability is more pronounced in cryptands than in coronands (crown ethers). This stability can be ascribed to the more preorganised nature of the cryptands compared to the coronands and podands as discussed on page 9.



53 R = H, H^+, behaves as a strong base

54 n = CH_3, Li^+, log *K* (H_2O, 0.15 M NaCl) = 3.20

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

56 n = 1, Hg^{++}, log *K* (PC, 0.1 M Hex_4NClO_4) = 24.00

57 Ag^+, log *K* (MeOH, 0.05 M Et_4NClO_4) = 11.98

58 Ag^+, log *K* (NMe, 0.1 M Et_4NClO_4) = 16.63

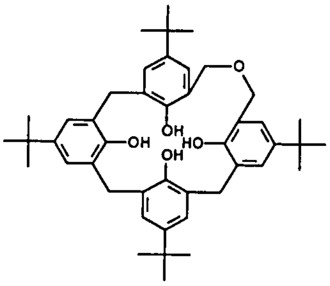
59 Cu^{++}, log *K* (H_2O, 0.1 M Me_4NCl) = 14.80

60 Cu^{++}, log *K* (H_2O, 1.0 M NaBr) = 40.47
N_3^-, log *K* (H_2O) = 4.60

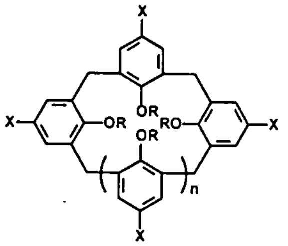
Figure 2. 6. Examples of cryptands.

Lehn[13] found that the protonated form of cryptand **60** was also selective towards the azide (N_3^-) anion.

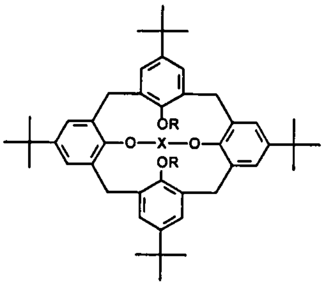
Calixarenes[14] (Figure 2. 7) are cavity-shaped cyclic oligomers made up of phenol units and was first synthesised by Zinke and Ziegler, but made public by the efforts of Gutsche and his co-workers. Calixarenes are mainly ligands for small neutral molecules, but they also interact with cations if the solutions are sufficiently basic to permit deprotonation of the phenolic groups.[15]



61 $t\text{-}C_4H_9NH_3^+$,
log K (MeCN) = 4.23



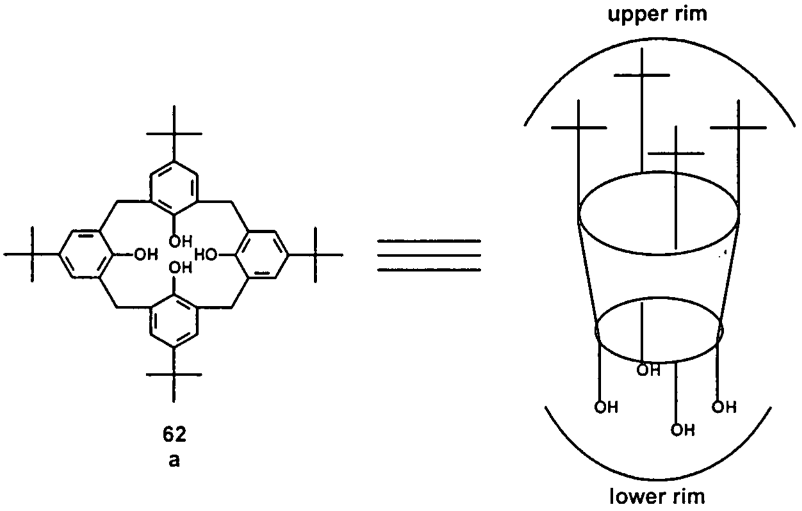
62 n = 1, R = H, X = $t\text{-}C_4H_9$,
$t\text{-}C_4H_9NH_3^+$, log K (MeCN) = 4.68
63 n = 1, R = H, X = SO_3Na,
H^+, log K (H_2O) = 4.00
64 n = 2, R = H, X = SO_3Na,
UO_2^{++}, log K (H_2O) = 18.90
65 n = 2, R = CH_2COOH, X = SO_3Na,
UO_2^{++}, log K (H_2O) = 18.40
66 n = 3, R = H, X = SO_3Na,
UO_2^{++}, log K (H_2O) = 19.20
67 n = 3, R = CH_3, X = SO_3Na,
$t\text{-}C_4H_9NH_3^+$, log K (MeCN) = 5.90
68 n = 5, R = H, X = SO_3Na,
$(CH_3)_3N^+Ph$, log K (D_2O) = 3.72
69 n = 5, R = $CH_2COOC_2H_5$,
X = $t\text{-}C_4H_9$, K^+, log K (THF) = 3.11



70 R = CH_3, X = $CH_2CH_2(OCH_2CH_2)_3$,
K^+, log K (H_2O) = 8.48
71 R = $CH_2C_6H_5$, X = $CH_2CH_2(OCH_2CH_2)_3$,
K^+, log K (H_2O) = 6.08
72 R = CH_3, X = $CH_2CH_2(OCH_2CH_2)_4$,
Cs^+, log K (H_2O) = 6.51

Figure 2. 7. Examples of calixarenes.

Calixarenes can easily be functionalised on both the "lower" and "upper" rims (Figure 2. 8, p. 16) by attaching a wide variety of ligating groups, as seen by the examples in Figure 2. 7. The pK_a of calixarenes are very important for the complexation of cations.[16] The dissociation of the first proton of **63** occurs at a very low pH.[17] The pK_a for the dissociation of this first "super acidic" proton occurs in a very acidic region < 1.[17] The pK_a for the dissociation of the first proton of **62** occurs at about 4.11[18]. It is worthwhile to notice that the pK_a of **62** is not as low as that observed for **63**.[18] This is probably due to the more electron-donating group, the *t*-C_4H_9 group, of **62**, compared to the more electron-withdrawing group, the SO_3Na group, of **63**.

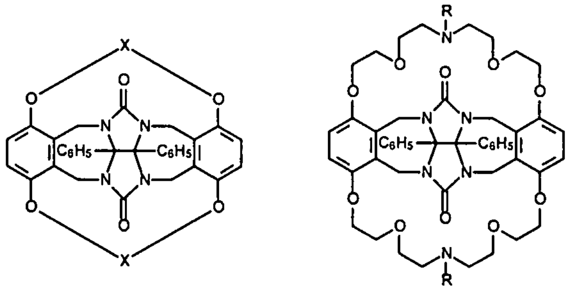


62
a

b

Figure 2. 8. The 'lower' and 'upper' rims of calixarenes can be represented as a vase like structure b, with the hydroxy groups forming the 'lower' rim and the *t*-butane units forming the 'upper' rim.

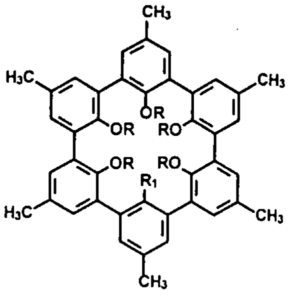
Suitcase-shaped compounds[19] (Figure 2. 9) and spherands[20] (Figure 2. 10, p. 17) are fully preorganised macrocyclic ligands. See page 9 for the explanation of preorganised ligands.



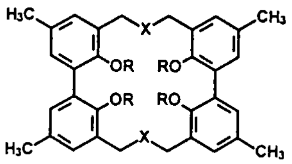
73 X = $(CH_2CH_2O)_2CH_2CH_2$, Na^+, log *K* (H_2O) = 5.81
74 X = $(CH_2CH_2O)_3CH_2CH_2$, K^+, log *K* (H_2O) = 8.62
75 X = $(CH_2CH_2O)_4CH_2CH_2$, K^+, log *K* (H_2O) = 6.97

76 R = H, NH_4^+, log *K* (H_2O) = 7.57
77 R = $CH_2C_6H_5$, K^+, log *K* (H_2O) = 6.28
78 R = $CH_2CH_2OCH_2CH_2OH$, NH_4^+, log *K* (H_2O) = 6.98

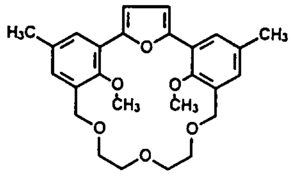
Figure 2. 9. Examples of suitcase-shaped macrocycles.



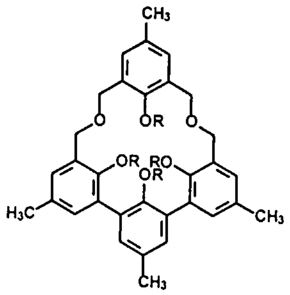
79 R = CH_3, R_1 = OCH_3,
Na^+, log *K* (D_2O) = 14.15
80 R = CH_3, R_1 = OH,
Li^+, log *K* (D_2O) = 9.04



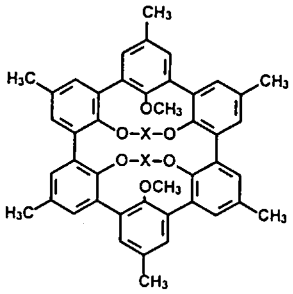
81 R = CH_3, X = O,
Na^+, log *K* ($CDCl_3$) = 3.79
82 R = CH_3, X = S,
K^+, log *K* ($CDCl_3$) = 3.28



83 K^+,
log *K* (D_2O) = 6.74



84 R = CH_3, Na^+,
log *K* ($CDCl_3$) = 5.69



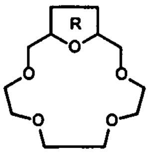
85 X = $(CH_3)_3$,
Li^+, log *K* (D_2O) = 12.30
86 X = $CH_2CH_2OCH_2CH_2$,
Na^+, log *K* (D_2O) = 13.73

Figure 2. 10. Examples of spherands.

In some cases a donor atom can also be part of another hetero-aromatic compound[21] (Figure 2. 11, p. 18). The subheterocyclic units often used, include the following groups: the furano (**87**), THF (**88**), pyridino (**89**) and triazolo groups (**93**). They are good examples of subheterocyclic units.

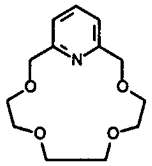
The incorporation of the furane unit does not significantly alter the complexation strength, even though oxygen is part of an aromatic heterocycle. This is due, in part, to the fact that oxygen is still properly positioned within the macroring for effective binding.[5] The incorporation of pyridine as a subheterocyclic unit makes the crown ether more basic and also more rigid.[5]

Macrocycles also exists with donor atoms other than O, N, and S, and examples of these other donor atoms include atoms such as phosphor[3] and tin[22] (Figure 2. 12, p. 18).

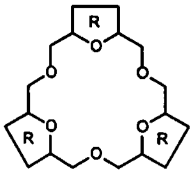


87 R = Furan, K^+,
log *K* ($CDCl_3$) = 5.40

88 R = THF, t-$C_4H_9NH_3^+$,
log *K* ($CDCl_3$) = 4.26

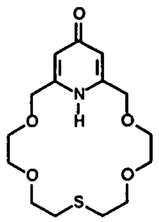


89 Ba^{++}, log *K* (MeOH,
0.1 M Et_4NCl) = 5.05

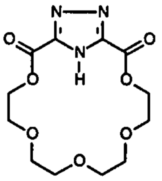


90 R = Furan, t-$C_4H_9NH_3^+$,
log *K* ($CDCl_3$) = 4.04

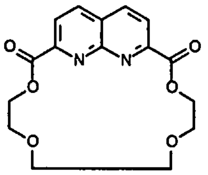
91 R = THF, t-$C_4H_9NH_3^+$,
log *K* ($CDCl_3$) = 7.52



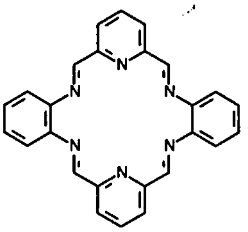
92 Ag^+, log *K* (H_2O,
0.1 M HNO_3) = 5.36



93 H^+,
log *K* (H_2O) = 8.40

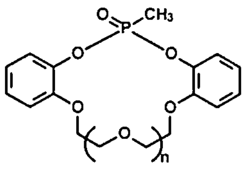


94 Ca^{++},
log *K* ($CDCl_3$) = 7.59



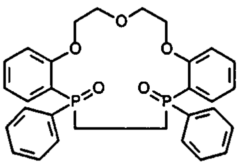
95 K^+,
log *K* (Me_2SO-d_6) = 4.10

Figure 2. 11. Crown compounds with donor atoms as part of another hetero-aromatic compound.

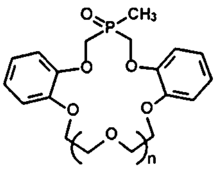


96 n = 1, Ca^{++},
log *K* (MeCN-CH_2Cl_2 (2:98)) = 3.99

97 n = 2, Na^+,
log *K* (MeCN-CH_2Cl_2 (2:98)) = 4.50

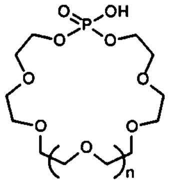


98 $CuCl^+$,
log *K* (Me_2CO) = 4.42



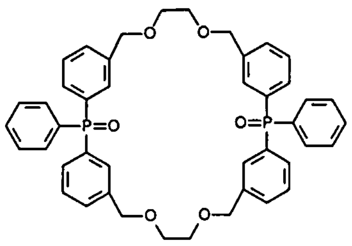
99 n = 0, Ca^{++},
log *K* (MeCN) = 3.02

100 n = 1, Ca^{++},
log *K* (MeCN) = 2.61

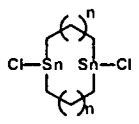


101 n = 0, Ni^{++},
log *K* (H_2O) = 2.44

102 n = 1, H^+,
log *K* (H_2O) = 1.00



103 Na^+,
log *K* ($CDCl_3$) = 5.01

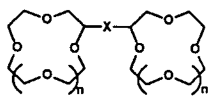


104 n = 6, Cl^-,
log *K* (MeCN) = 2.91

105 n = 8, Cl^-,
log *K* (MeCN) = 2.94

Figure 2. 12. Crown compounds with donor groups other than O, N and S.

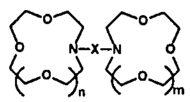
Macrocycles may also exist as bis- or poly(macrocycles) (Figure 2. 13), i.e. two or more macrocycles joined in one molecule. The use of these macrocycles can be tailored to complex a specific cation, such as K^+, and a specific anion, such as $H_2PO_4^-$.[23] This tailoring can be very useful in the purification of wastewater, because one can then selectively complex only one salt from a mixture of salts in a reservoir, such as KH_2PO_4, with **115**.



106 n = 1, X = $CH_2CO_2CO_2CH_2$, K^+, log *K* (MeOH) = 1.72

107 n = 2, X = $CH_2OC(O)C(CH_3)(C_{12}H_{25})C(O)OCH_2$, K^+, log *K* (MeOH-H_2O (95:5)) = 5.06

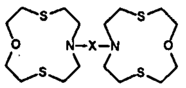
108 n = 3, X = $CH_2OC(O)C(CH_3)(C_{12}H_{25})C(O)OCH_2$, log *K* (MeOH-$H_2O$ (95:5)) = 4.00



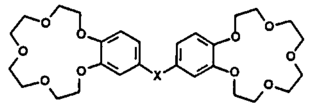
109 n = m = 1, X = $CH_2CH(OH)CH_2$, Na^+, log *K* (99 % MeOH, 0.01 M Me_4NOH) = 3.77

110 n = 1, m = 2, X = $CH_2CH(OH)CH_2$, Na^+, log *K* (99 % MeOH, 0.01 M Me_4NOH) = 4.44

111 n = 1, m = 3, X = $CH_2CH(OH)CH_2$, Na^+, log *K* (99 % MeOH, 0.01 M Me_4NOH) = 4.84

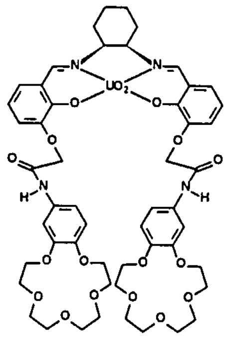


112 X = CH_2-[1,4-C_6H_4]CH_2, Cu^{++}, log *K* (H_2O, 0.1 M $LiNO_3$) = 9.20

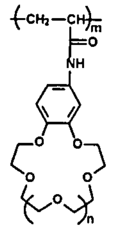


113 X = CH_3, K^+, log *K* (MeOH-H_2O (8:2)) = 2.92

114 X = $(CH_2)_5$, K^+, log *K* (MeOH-H_2O (8:2)) = 4.36



115 K^+, log *K* ($CHCl_3$) = 5.30, $H_2PO_4^-$, log *K* (DMSO) = 3.11



116 n = 0, Na^+, log *K* ($CHCl_3$) = 6.22

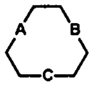
117 n = 1, K^+, log *K* ($CHCl_3$) = 10.30

118 n = 2, Ba^{++}, log *K* ($CHCl_3$) = 10.90

Figure 2. 13. Examples of bis- and poly(macrocycles).

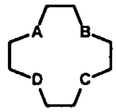
Other macrocycles exist where O, N, and S are donor atoms in the same macrocyclic ligand (Figure 2. 14, p. 20).

Anion selective ligands are very rare compared to those ligands that are selective for cations. This may be due, in part, to the large ionic radii of anions and the high free energy of solvation.[24] Enzymes almost exclusively act on negative charged substrates or cofactors, so the synthesise and complexation behaviour of synthetic ligands for anions should provide interesting comparisons with substrate binding to enzyme pockets and to cell wall receptors. Some examples of these anion selective ligands can be seen in Figure 2. 15, p. 21.



119 A = B = NH, C = O, Cu^{++},
log *K* (H_2O, 0.1 M $NaNO_3$) = 10.86

120 A = B = NH, C = S, Cu^{++},
log *K* (H_2O, 0.1 M $NaNO_3$) = 12.42

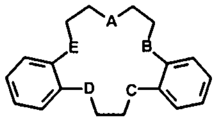


121 A = C = S, B = D = O, Ag^+,
log *K* (MeOH, 0.05 M Et_4NClO_4) = 7.56

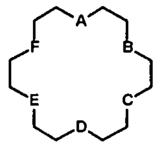
122 A = O, B = D = S, C = $NCH_2C_6H_5$,
H^+, log *K* (H_2O, 0.1 M $LiNO_3$) = 7.00

123 A = B = NH, C = D = S, Cu^{++},
log *K* (H_2O, 0.5 M KNO_3) = 14.21

124 A = B = C = NH, D = S, Hg^{++},
log *K* (H_2O, 0.2 M $NaClO_4$) = 24.32



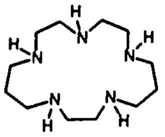
125 A = S, B = E = NH,
C = D = O, Ag^+, log *K* (DCE) = 4.85
126 A = C = D = S,
B = E = NH, Hg^{++}, log *K* (DCE) = 5.70



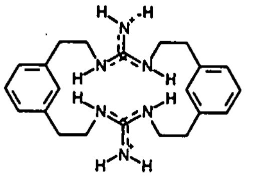
127 A = S, B = C = D = E = F = O,
$(C_2H_5)Tl^{+++}$, log *K* (MeCN-d_6) > 3
128 A = D = S, B = C = E = F = O,
Pd^{++}, log *K* (H_2O, 0.5 M HNO_3) = 21.10
129 A = D = NH, B = C = O,
E = F = S, Ag^+, log *K* (MeOH) = 11.50
130 A = B = C = S, D = E = F = O,
$(CH_3)_2Tl^{+++}$, log *K* (MeCN-d_6) = 2.09
131 A = D = NH, B = C = E = F = S,
Ag^+, log *K* (MeOH) = 13.70
132 A = D = SO, B = C = E = F = O,
Au^{+++}, 4 Cl^-, log *K* (H_2O, pH 2 (HCl)) = 7.77

Figure 2. 14. Examples of macrocycles with mixed donor atoms in the macrocyclic ring.

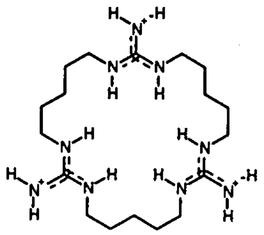
Lehn and his co-workers[25] found that **134**, **135** and **136** complexate the PO_4^{3-} ion and that the log *K* (MeOH-H_2O (9:1)) values observed was 3.10, 4.30 and 3.40, respectively.[22] According to Schmidtchen[26] **141** is able to complex the Br^-, and the log *K* (95 % MeOH) value was determined to be 2.70[26].



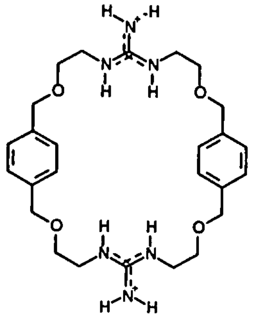
133 CO_3^{-}, log *K* (H_2O, pH 7.0 - 8.2) = 4.28



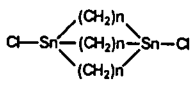
134 PO_4^{-}, log *K* (MeOH-H_2O (9:1)) = 3.10



135 PO_4^{-}, log *K* (MeOH-H_2O (9:1)) = 4.30



136 PO_4^{-}, log *K* (MeOH-H_2O (9:1)) = 3.40

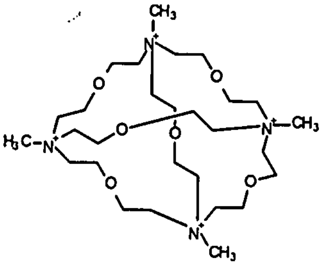


137 n = 6, F^-, log *K* ($CDCl_3$) = 2.30

138 n = 8, Cl^-, log *K* (CDCl3) = 1.65

139: n = 10, Cl^-, log *K* (CDCl3) = 1.98

140 n = 12, Cl^-, log *K* (CH_2Cl_2 with 10 % C_6D_6) = 2.06



141 Br^-, log *K* (95 % MeOH) = 2.70

Figure 2. 15. Examples of anion selective ligands.

2.3 SOLUBILITY AND POLARITY OF CROWN ETHERS

According to Hansch's series of lipophilia,[27] 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.[8] 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 2. 16, p. 22). 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 2. 16 a, p. 22). 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 2. 16 b, p. 22). In the latter case, a hydrophilic and electronegative cavity is produced, and this cavity is suitable for inclusion (Figure 2. 16 c), e.g. complexations of cations, such as K^+.

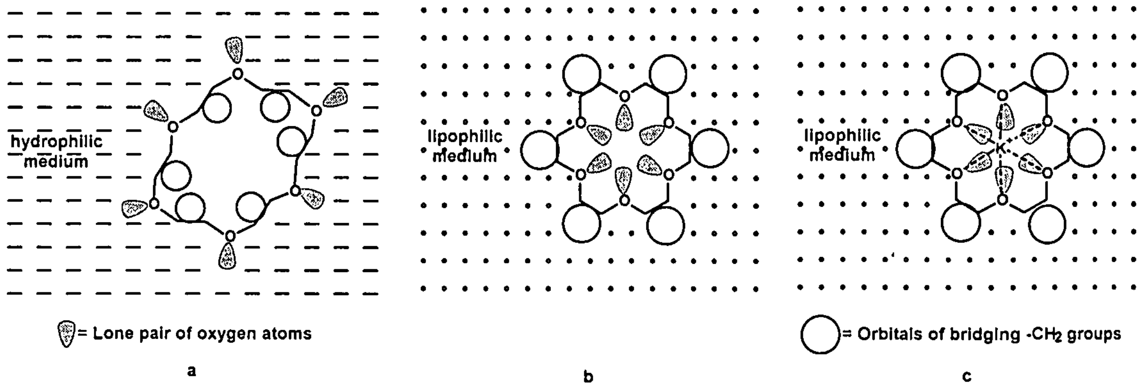


Figure 2. 16. The influence of both lipophilic and hydrophilic media on the orientation of the 18-crown-6 macroring in both hydrophilic (a) and lipophilic (b) media, and the subsequent formation of a hydrophilic cavity that is suitable for the inclusion of cations (c), such as K^+.

2.4 CATION-MACROCYCLE INTERACTION

The main aim in designing macrocyclic compounds is to synthesise macrocycles that are able to discriminate among different cations in complexation reactions. Many factors have been determined that influence the selectiveness of macrocycles for specific cations and may be divided into several groups including macrocycle cavity dimensions, shape and topology, substituent effects, conformational flexibility/ rigidity, and donor atom type, number and arrangement.

The cation radii of selected cations can be seen in Table 2. 1, p. 23, while Table 2. 2, p. 23, represent the general class of macrocycles containing either 14-, 15-, 18- or 21-members in the macroring, meaning that all the crown ethers that contain 14-members in their macrocyclic ring contain cavities with dimensions between 1.20 – 1.50 Å, see Table 2. 2, p. 23. If one have a need to bind K^+, one needs to find a crown ether with a cavity size comparable to that of the cation, being 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. 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 2. 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. 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

Pedersen and Frensdorff[28] reported that the picrate anion extraction constants exhibited a correlation between the cation's radius and the cavity diameter of the molecular host. Although this concept did not conclusively explain the selectiveness of crown ethers, this concept still led to the design and synthesis of a variety of cation and molecular hosts. Several research groups set out to explain this selectiveness thermodynamically. The thermodynamic and kinetic data these researchers obtained provided a quantitative base for understanding the effect of the macrocycle and guest parameters on the stabilities of the resulting complexes.

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 are assumed to consist 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 **6** 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.[5]

The process of ion-macrocycle association depends on several factors relating to the characteristic properties of the ligand, reacting ion and solvent. The multistep Eigen-Winkler[22] mechanism (eq. 1) explains the complexation of a metal cation by a macrocyclic ligand; with M^+ = solvated metal cation, L = free macrocyclic ligand, $M^+{\circ\circ\circ}L$ = solvent-separated metal-macrocyclic ligand pair, M^+L = contact pair, $(ML)^+$ = final complex with the metal cation embedded in the macrocyclic cavity.

$$M^+ + L \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} M^+ \circ\circ\circ L \underset{k_{-2}}{\overset{k_2}{\rightleftarrows}} M^+L \underset{k_{-3}}{\overset{k_3}{\rightleftarrows}} (ML)^+ \qquad 1$$

The Eigen-Winkler mechanism consists of a series of steps, where, for the same metal cations, both solvent and macrocycle may influence the activation energy profile of the process. The first step, after the outer-sphere complex is formed, involves the partial rearrangement of the macrocyclic ligand and the partial cation desolvation. The second step leads to the encirclement, or encapsulation, of the metal cation and more complete desolvation. The rate determining step for the last process is desolvation (in H_2O) or ligand rearrangement (e.g. in DMF or methanol) depending on the relative energy of desolvation *vs.* that for ligand rearrangement.

To understand the selectivities of crown ethers towards alkali metal cations in non-aqueous media, two hypothetical mechanisms should be considered. The first that follows the models based on the Eigen-Winkler reaction mechanism, is a *dissociative* (unimolecular) mechanism, with dissociation and recombination steps as given in eq. 2 and eq. 3, respectively:

$$(M:L) \underset{k_1}{\overset{k_{-1}}{\rightleftarrows}} M^+ + L \qquad 2$$

$$M^{+*} + L \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} (M^*:L)^+ \qquad 3$$

The second is an *associative* exchange (bimolecular) mechanism as given by eq. 4:

$$(M:L)^+ + M^{+*} \underset{k_{-2}}{\overset{k_2}{\rightleftarrows}} (M^+ \bullet\bullet\bullet L \bullet\bullet\bullet M^{+*}) \underset{k_{-3}}{\overset{k_3}{\rightleftarrows}} (M^*:L)^+ + M^+ \qquad 4$$

The nature of the solvent affects the competition between these two mechanisms. The solvent plays an important role in the unimolecular mechanism. This mechanism is favoured in solvents with a high donicity, despite a higher activation enthalpy, which is compensated by higher activation entropy. The bimolecular mechanism is mainly controlled by conformational rearrangements of the ligand and the free energy for the decomplexation process is solvent independent. The kinetics of dissociation of **6** + Na^+, BPh_4^- in propylene carbonate, acetonitrile, pyridine and acetone have been determined.[22] In the first three solvents, i.e. propylene carbonate, acetonitrile and pyridine, the bimolecular and unimolecular mechanisms compete against each other. In the case of acetone, the unimolecular mechanism has been exclusively observed. The activation enthalpy, $\Delta H^\ddagger$ (unimolecular), follows the trend acetonitrile < acetone < pyridine ≈ propylene carbonate. The bimolecular mechanism was predominant for **11** + Na^+, BPh_4^- in nitromethane with the following activation parameters: $\Delta H^\ddagger$ = 28 kJ/mol, $\Delta S^\ddagger$ = -57 J/K·mol and $\Delta G^\ddagger$ = 45 kJ/mol.[22]

Popov[29] studied the influence of anions on the kinetics of decomplexation of **6** + Na^+ in THF and found that with BPh_4^- as the counteranion, the unimolecular mechanism was predominant, but with SCN^- the predominant mechanism was a bimolecular one.

As said earlier, the nature of the solvent effect will dominate. There is an inverse relationship between the stabilities of complexes and the Gutmann donicity of the solvents.[30] The stabilities of all 1:1 complexes of alkali metal cations with **20** decrease in the order 1,2-dichloroethane (log K = 5.96) (most stable) > nitromethane (log K = 5.37) > acetonitrile (log K = 4.63) > acetone (log K = 4.39) > DMF (log K = 3.13) (least stable) for the interaction of **20** with K^+. In solvents with lower donicity, cation desolvation is less pronounced and the enhancement of stability is primarily an enthalpic effect, while the reaction entropies oppose the stability enhancement.[4] Thus, the maximum stability for a given metal cation complex results from a balance between the binding and the solvation energies.

The metal interchange in the complex between **11** and Na^+ in a solvent of low donor number (DN),[30] such as nitromethane (DN = 2.70), proceeds *via* the bimolecular pathway, while in acetonitrile (DN = 14.10) the unimolecular pathway is preferred.[4] In mixtures of these two solvents, as the acetonitrile content increases, a gradual change from the bimolecular to the unimolecular pathway is observed.[4] According to Izatt *et al.*[4] the overall dissociative process is the result of a series of stepwise sodium-oxygen bond raptures, followed by sodium-solvent bond formation.

The nature of the solvent is not the only factor influencing the mechanism used, but also the temperature. At lower temperatures, the bimolecular process is dominant, whereas at higher temperatures, the unimolecular mechanism becomes more competitive.[4] The bimolecular exchange is mainly controlled by conformational changes of the macrocycle during the concerted partial decomplexation of the one cation and the partial complexation of a second one, while the solvation of the complexed cation plays a major role in the unimolecular mechanism.[4]

Alkaline earth metal complexes with **6** in several non-aqueous solutions exhibit similar mechanisms and correlations. Izatt *et al.*[4] observed a correlation between the donor number of the solvents and the decomplexation rate (k_d) and activation parameters. For the interaction of **6** with Mg^{2+} in nitromethane (DN = 2.70) and acetonitrile (DN = 14.10) the $k_d = 2.6 \times 10^3$ and 1.8×10^3 s^{-1};

$\Delta H^{\ddagger}$ = 11.7 and 14.2 kJ/mol; and $\Delta S^{\ddagger}$ = -141 and -135 J/K·mol, respectively, were found[4]. The activation energy for the release of **6** from its complexes increases with increasing donicity of the solvent. They also observed that, except for Ba^{2+}, the k_d values in a given solvent decreases with increasing ionic size.[4] This decrease reflects the increase in the kinetic stability of this complex with ionic size, e.g. $k_d = 2.6 \times 10^3$, 2.4×10^3 and 5.5×10^2 s^{-1} for the interaction of **6** with Mg^{2+}, Ca^{2+} and Sr^{2+}, respectively, in nitromethane.[4]

Cram and co-workers[20] synthesised a variety of preorganised molecules (Figure 2. 9, p. 16) and found that these molecules are very selective towards the cation that they complexed. The reason for this is the fact that the log *K* for the host-guest complex formation is increased significantly if the host and the guest are organised for binding and have low solvation prior to complexation. These high negative values for the free energy of complexation can be attributed to three factors.

1. Due to the rigid molecular framework, the host does not undergo conformational changes upon complexation. These conformational changes usually lower the stabilities of the complexes of flexible hosts.
2. The repulsive forces between electronegative binding sites cannot be minimised by conformational changes in the non-complexed host, as a consequence of the preorganisation of the rigid host. Upon complexation of an electron-deficient guest, these repulsive forces are converted into attractive forces.
3. The methoxy groups, see for example **79** (Figure 2. 10, p. 17), prevent solvent molecules from entering the cavity, and therefore the binding sites do not have to be desolvated during complexation.

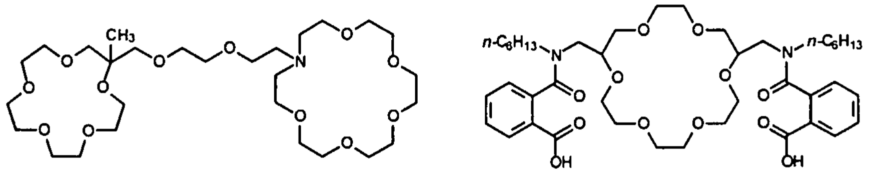
The arrangement of the hosts in decreasing order of their degree of preorganisation results in the same order as that observed when the same hosts are arrange in decreasing order of their $\Delta G°$ values for their complexation reactions with cations. The binding strength of these ligands decreases in the order spherands (strongest binding) > cryptospherands > cryptands >

hemispherands > coronands ≈ crown ethers > podands > solvent (weakest binding).[22]

2.5 CATION RELEASE

Owing to the increasing environmental concerns about wastewater remediation, the principal effort in this study is towards the design of new materials that can effectively remove, or recover, toxic or an excessive amount of metal cations from aqueous solutions. The removal of these toxic or excessive cations can possibly be accomplished by anchoring crown ethers onto a solid support. The unique ability of these macrocycles can then be exploited to selectively remove the desired metal cation from a complex solution of cations. However to facilitate a cyclic process, it is necessary to control the release of the cations from the scavenging crown ether device. Nature already solved this problem. An example that comes to mind is the enzyme Na^+-K^+ ATPase,[31] which transports Na^+ and K^+ actively, and in opposite directions, across a biological membrane.

As far as synthetic (man-made) compounds are concerned, Nakatsuji *et al.*[32] recently succeeded in the synthesis of a Na^+-K^+ ATPase model, which consists of a monoaza-18-crown-6 and a 15-crown-5 ring (**142**, Figure 2. 17). Ionophore **142** concentrate Na^+ in a basic media, while it concentrates K^+ in an acidic media. Nakatsuji *et al.*[32] also achieved the double uphill transport of K^+ and Ca^{2+}, in opposite directions, by using 18-crown-6 dicarboxylic acid derivative **143** (Figure 2. 17).



142

143

Figure 2. 17. Compounds that can be used to facilitate the double uphill transport of cations, such as Na^+, K^+ and Ca^{2+}.

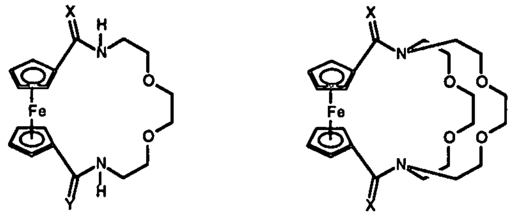
To selectively transport cations from a source phase to a receiving phase, one must design a molecule that will selectively complex a cation in the source phase, change its complexation ability for the complexed cation, and release the complexed cation in the receiving phase. A few examples (see paragraphs 2.5.1 – 2.5.3) of chemical subspecies that can be utilised as molecular switches to obtain the desired release from the macrocyclic ligands are: ferrocene (neutral → cation redox switch), nitrobenzene and anthraquinone (neutral → anion redox switch), the azo group (photochemical switch), and phenolic groups (pH switch).[33]

As the release of cations from the transport system is crucial to the success of the approach developed in this study, it was deemed important to discuss some of the techniques available to facilitate cation release.

2.5.1 Redox-active and electrochemical switching

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.*[34] 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.[35] Ferrocene substituted macrocyclic ligands are mostly used for these types of switches (Figure 2. 18, p. 30). Gokel *et al.*[33] prepared ferrocene containing cryptands **146** and **147** (Figure 2. 18, p. 30) and the electrochemical behaviour of **146** indicates that this cryptand acts as a redox-switchable ligand 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,[32] and afford the release of the cation. An illustration of this cycle can be seen in Scheme 2. 1[36] with macrocycle **146** and Ag^+ as the cation.



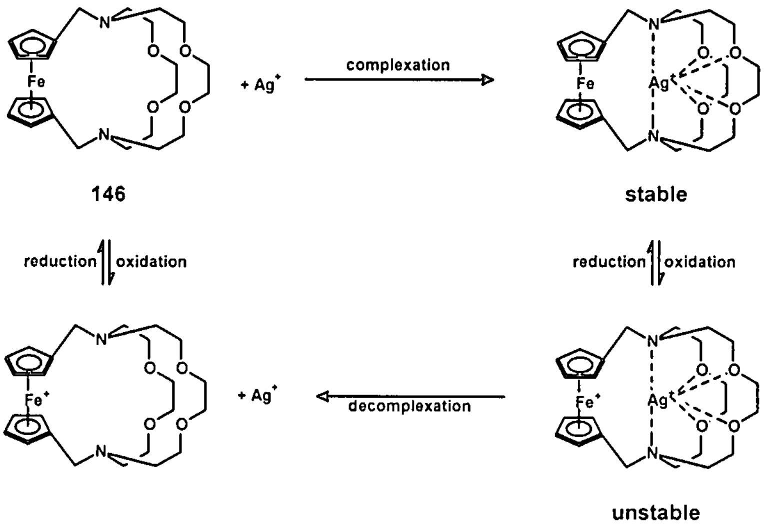
144 X = Y = O, Mg^{++},
log *K* (MeCN) = 6.60

145 X = O, Y = S, Ca^{++},
log *K* ($MeCN\text{-}CHCl_3$ (1:1)) = 6.90

146 X = 2 H, Ag^+,
log *K* (MeCN) = 8.35

147 X = O, Ba^{++},
log *K* (MeCN) = 4.50

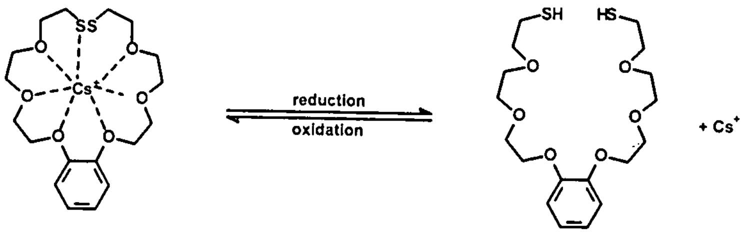
Figure 2. 18. Examples of redox-active compounds usually containing ferrocene substituted macrocycles.



Scheme 2. 1. The cycle of Ag^+ complexation and decomplexation of a macrocycle containing a ferrocene moiety (146).

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 remove the whole cyclic 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[37] (Scheme 2. 2, p. 31).

Macrocycle **148** exhibit a high selectivity for Cs^+, while **149** hardly bind any metal cations.[37] The 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.

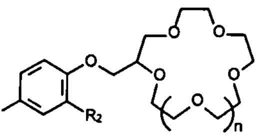


148 a coronand, Cs^+, log *K* (PC) = 2.51

149 a podand, Cs^+, log *K* (PC) < 0.1

Scheme 2. 2. The interconversion of the thiol/disulphide redox couple.

Electrochemical switching can be distinguished from redox switching as follows: electrochemical switching occurs on the side chain of lariat ethers, while redox switching occurs in or near the cavity, usually with a ferrocene moiety present. Gokel *et al.*[38] synthesised one-armed carbon- and nitrogen-pivot lariat ethers containing a terminal phenyl substituent, which contained a nitro group (Figure 2. 19).

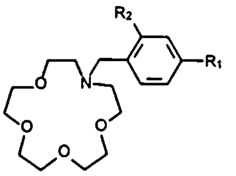


150 n = 1, R_1 = H, R_2 = NO_2, Na^+, log *K* (MeOH) = 2.83

151 n = 1, R_1 = NO_2, R_2 = H, Na^+, log *K* (MeOH) = 2.72

152 n = 2, R_1 = H, R_2 = NO_2 Na^+, log *K* (MeOH) = 3.82

153 n = 2, R_1 = NO_2, R_2 = H, Na^+, log *K* (MeOH) = 3.67

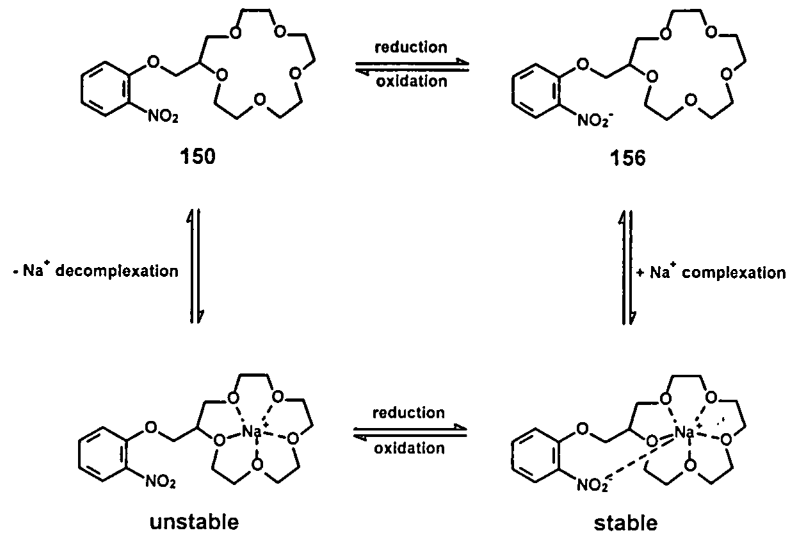


154 R_1 = H, R_2 = NO_2, Na^+, log *K* (MeOH) = 2.40

155 R_1 = NO_2, R_2 = H, Na^+, log *K* (MeOH) = 2.30

Figure 2. 19. Examples of electrochemical switchable lariat ethers.

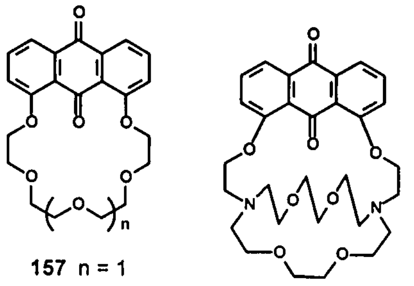
Upon reduction, the nitro group of these macrocycles is reduced to the corresponding anion radical (Scheme 2. 3, p. 32), which forms a more stable complex with the Na^+ than the neutral compound.



Scheme 2. 3. The cycle of Na$^+$ complexation and decomplexation of a macrocycle containing a nitro group (150).

The anionic macrocycle **156** exhibit a much higher affinity for metal cations than does the corresponding neutral macrocycle **150**. This is clearly demonstrated by the comparison of the log *K* (MeOH) values for the interaction of the neutral compound (**150**) and the anionic compound (**156**) with Na$^+$. The log *K* (MeOH) value for the neutral compound (**150**) and the anionic compound (**156**) is 2.83 and 7.59, respectively.[38] This reduction process is reversible and it is therefore possible to switch these ligands between their neutral (**150**) and anionic (**156**) forms to control the cation binding ability of these ligands on demand.

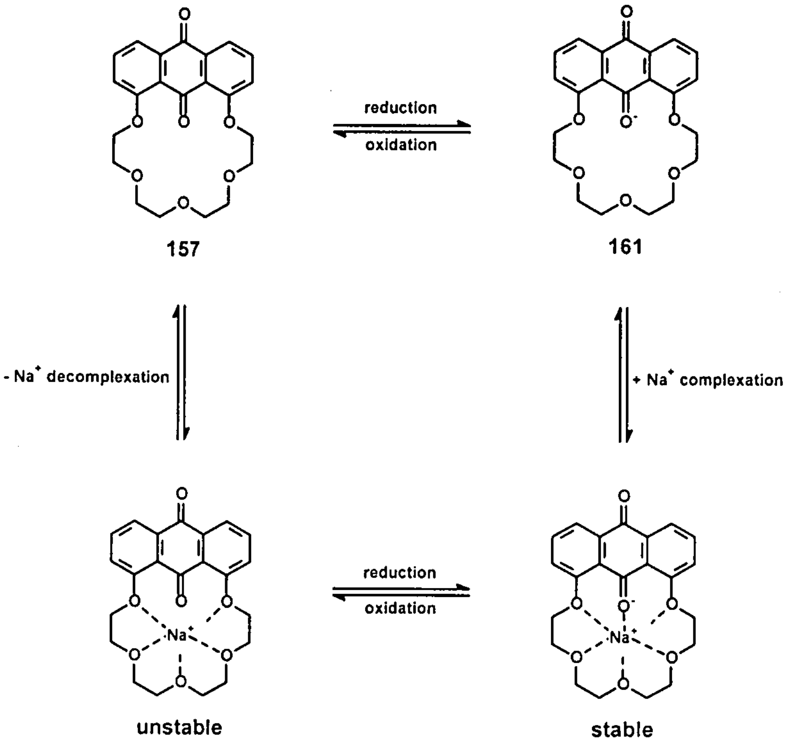
Gokel *et al.*[39] also synthesised a series of macrocycles containing the anthraquinone moiety (**157**, **158**, **159**, and **160**, Figure 2. 20, p. 33). The electrochemical reduction of these macrocycles leads to an excess negative charge, which in turn enhances the binding of cations (Scheme 2. 4, p. 33). This reduction process is reversible and it is therefore possible to switch these ligands between their neutral (**157**) and anionic (**161**) forms to control the cation binding ability of these ligands on demand. According to Gokel and his co-workers[39] the major problem that they encountered was the lack of cation binding selectivity of these ligands once they were reduced.



157 n = 1
158 n = 2
159 n = 3

160

Figure 2. 20. Examples of electrochemical switchable compounds containing the anthraquinone moiety.



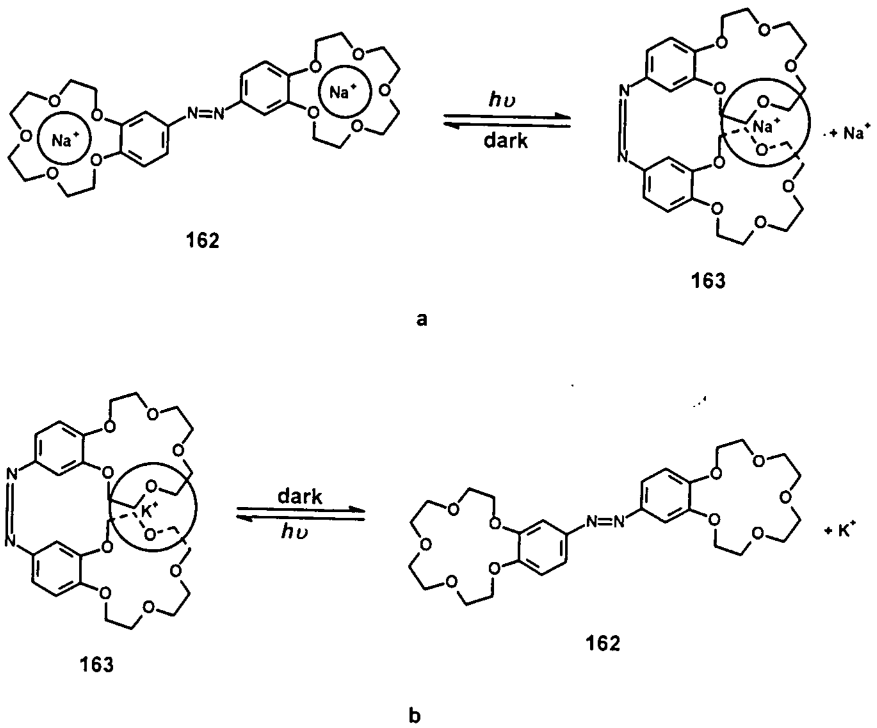
Scheme 2. 4. The cycle of Na$^+$ complexation and decomplexation of a macrocycle containing an anthraquinone moiety (157).

2.5.2 Photochemical switching

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.[40] 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.[41] The photo-induced properties of azobenzene can be used as a tool:[42]

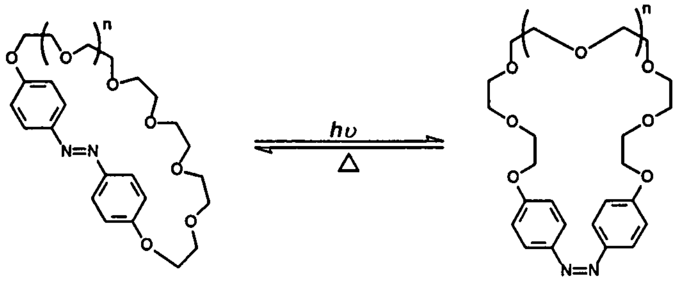
1. to change the cation extraction capability of the macrocycle;
2. to enforce a conformational change of macromolecules in solution;
3. and to monitor the rate of the conformational changes of crown ethers and polymers.

Shinkai *et al.*[40] used these properties to synthesise a bis(crown ether) (**162**) that exhibit a butterfly-like motion in response to photo-irradiation (Scheme 2. 5, p. 35). The *trans*-isomer (**162**) 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 (**163**). In this conformation the presence of two positive charges is unfavourable and one of the sodium cations is released (Scheme 2. 5 a, p. 35). Benzo-15-crown-5 (**11**, Figure 2. 2, p. 10) is normally not selective towards potassium cations, but as seen in Scheme 2. 5 b, p. 35, when two benzo-15-crown-5 moieties are nearby, they produce a cavity that is large enough to complex one K^+. The photo-isomerised *cis*-isomer (**163**) exhibits greater binding abilities for larger alkali metal cations than the *trans*-isomer (**162**). As seen in Scheme 2. 5 b, p. 35, the *cis*-isomer could be used to transport larger cations. The *cis*-isomer (**163**) can complex the larger K^+, and when this is removed from the light, it transformed to the *trans*-isomer (**162**), thus releasing the cation (Scheme 2. 5 b, p. 35).



Scheme 2. 5. The butterfly-like motion of an azobenzene derivative.

Shinkai *et al.*[43] also synthesised azocyclophane type macrocycles with 29- (**164**), 32- (**165**) and 35-membered (**166**) rings. In the *cis*-form, these types of macrocycles form crown-type loops, which can be use for the binding of alkali metal cations.[43] They[43] found that **167** were selective for Na^+, **168** were selective for K^+, while **169** were selective for Rb^+. The log *K* (*o*-$C_6H_4Cl_2$:*n*-BuOH (86.8:13.2)) value for the interactions of these compounds with the respective cations are 3.14, 3.20 and 3.06, respectively.[43] The *cis*-form showed spherical recognition patterns in the binding of alkali metal cations, typically of those found for crown ethers in solution. In the *trans*-form, however, these macrocycles show a lack of affinity for any of the metal cations.



164 n = 1
165 n = 2
166 n = 3

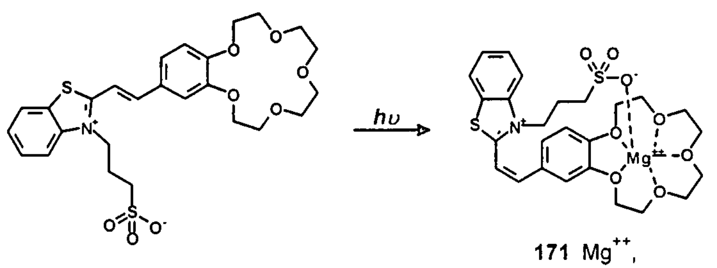
167 n = 1, Na$^+$, log *K* (*o*-$C_6H_4Cl_2$:*n*-BuOH (86.8:13.2)) = 3.14

168 n = 2, K$^+$, log *K* (*o*-$C_6H_4Cl_2$:*n*-BuOH (86.8:13.2)) = 3.2

169 n = 3, Rb$^+$, log *K* (*o*-$C_6H_4Cl_2$:*n*-BuOH (86.8:13.2)) = 3.0

Scheme 2. 6. The interconversion of an azocyclophane type of macrocycle with the use of UV-light and of temperature.

Azobenzene derivatives are not the only compounds that exhibit *cis*/*trans*-isomerism; alkenes also exhibit this isomerism. An example of this isomerism can be seen in Scheme 2. 7.



170 Mg^{++}, log *K* (MeCN) = 7.00

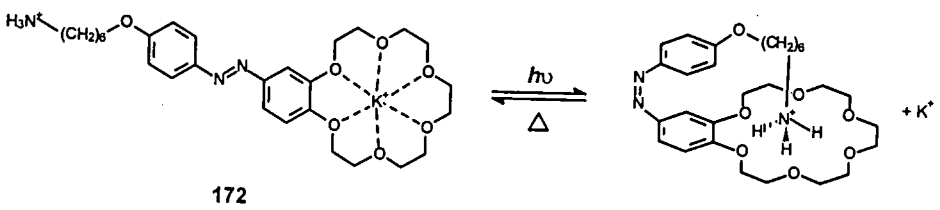
171 Mg^{++}, log *K* (MeCN) > 9.15

Scheme 2. 7. The interconversion between the *trans*- and *cis*-isomers of 170 to better complex cations, such as Mg^{2+}.

In the *cis*-form (**171**), the thethered sulphonate anion helps to stabilise the Mg^{2+}, but this stabilisation cannot occur in the *trans*-form (**170**). The log *K* (MeCN) value of > 9.15, for the reaction between Mg^{2+} and the *cis*-isomer (**171**), is much higher than the corresponding log *K* (MeCN) value of 7.00 for the *trans*-isomer (**170**, Scheme 2. 7).[44]

Another example of this interconversion between the *cis*- and *trans*-isomer of an azobenzene derivative (**172**) can be used to induce cation release as seen in

Scheme 2. 8. Shinkai *et al.*[45] synthesised a photoresponsive crown ether with a crown ether ring and an ammoniumalkyl group (**172**). This 'tail-biting' crown ether can only bind the intramolecular ammonium group in the *cis*-isomer (**173**). In the *trans*-isomer (**172**) the ammonium group cannot be complexed by the crown ether moiety (Scheme 2. 8) and a K^+ can thus be complexed. When this crown ether is photoisomerised to the *cis*-isomer (**173**), the ammonium tail can be complexed by the crown ether moiety, and thus the K^+ is subsequently released.



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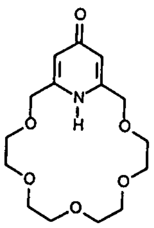
173

Scheme 2. 8. The 'tail-biting' ability of an azobenzene derivative.

2.5.3 pH switching

To accomplish pH switching, the macro ring must contain a proton ionisable group, such as 4-pyridone (**174**) or sulfonamido (**175**)[46] (Figure 2. 21). Izatt *et al.*[47] designed two proton-ionisable macrocycles, **176** and **177** 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 (Scheme 2. 9, p. 38). In these cases there is no co-anion present, due to the fact that the negative group is also associated with the complexed cation.[47]



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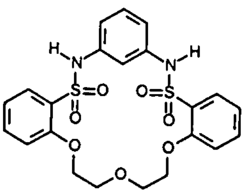
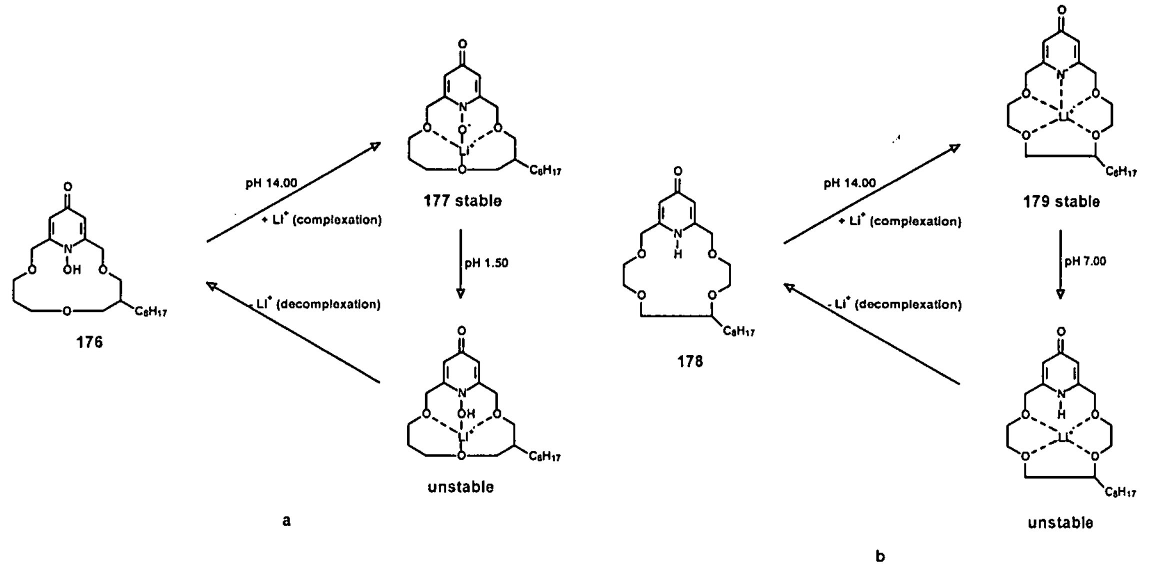


175

Figure 2. 21. Examples of proton ionisable groups for the use in pH switching.

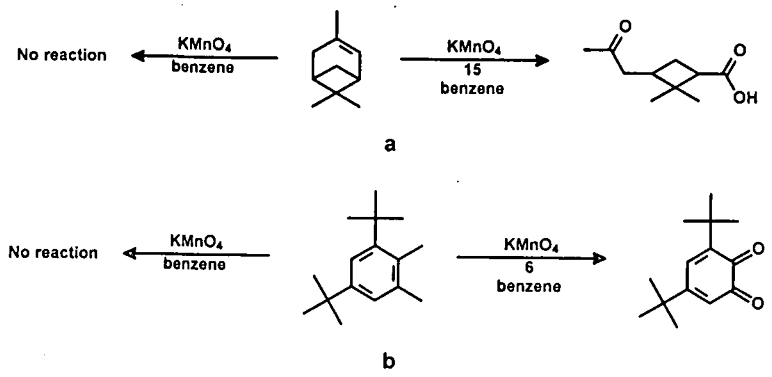
They[47] found that at pH levels ~14 the transport of metal ions, such as Li^+, was increased. The best cation transports occurred when the source phase pH was 14,[47] indicating that ionisation of the macrocycle was a necessary part of the transport process.



Scheme 2. 9. The cycle of Li^+ complexation and decomplexation by macrocycles exhibiting ionisable properties.

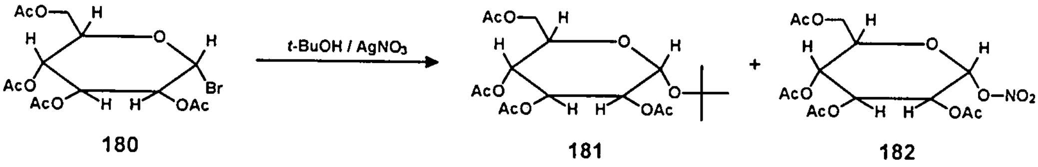
2.6 APPLICATIONS OF MACROCYCLES

Any chemical reaction where ions or ionic intermediates are involved, can be modified, or even improved, by the use of macrocycles. These reactions may include, among others:[8] nucleophilic substitutions, reactions with carbanions, C-C bond formation, additions, eliminations, oxidations, carbene generation, gas extrusions, reductions, rearrangements, isomerations, and polymerisations. In Scheme 2. 10, p. 39, benzene-solubilised permanganate is used as an oxidant, with the crown ether facilitating the solubility of the inorganic salt into the organic phase.[48]



Scheme 2. 10. The use of 'naked' permanganate oxidants in the presence of 15 and 6. By the addition of the macrocycle to the reaction mixture, complexation of the K^+ occurs, thus producing the 'naked' permanganate anion. The addition of the macrocycles also makes the $KMnO_4$ more soluble in lipophilic media, such as benzene.

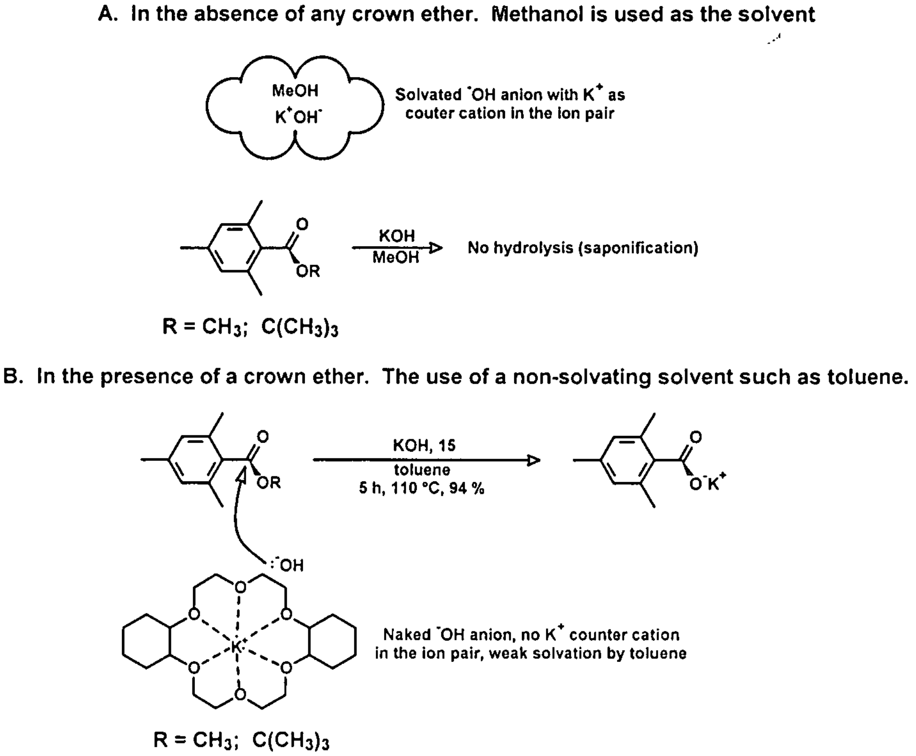
It can also be used to activate anions (Scheme 2. 11).[49] A good example of the activation of anions is the Koenings-Knorr reaction (Scheme 2. 11),[49] i.e. the conversion of acetobromo-glucose (**180**), with an alcohol in the presence of silver nitrate to the β-ester of nitric acid (**182**). In the absence of any macrocycles the only product formed is the β-glycoside (**181**), but upon the addition of a crown ether, e.g. **14**, the nitrate is activated, by the complexation of the silver by the crown ether, and the corresponding β-ester of nitric acid (**182**) is produced.



catalyst	Relative Yields (%)
14	181 : 0 ; 182 : 10
55	181 : 36 ; 182 : 64

Scheme 2. 11. Anion-activation – ligand controlled Koenings-Knorr reaction.

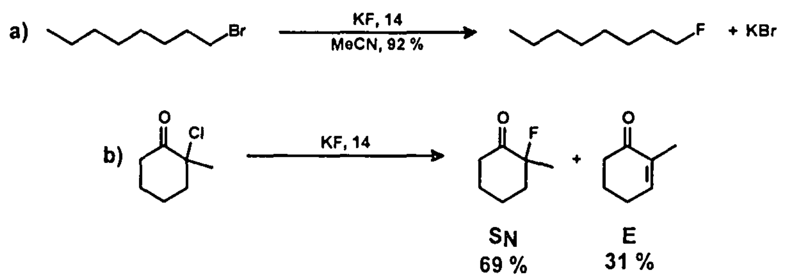
Another example of anion activation is the application of the so-called 'naked hydroxyl' anion in the hydrolysis of sterically hindered esters (Scheme 2. 12, p. 40).[8] The esters of the bulky mesitylenecarboxylic acid are easily saponified with KOH in the presence of **15**, while under normal conditions (i.e. in the absence of any crown ether), these esters are absolutely inert towards saponification with ethanolic KOH (Scheme 2. 12 A).[8] To explain this observation, one should recognise that in alcoholic media, the hydroxyl anion is highly solvated and therefore it is not able to gain access to the centre of the reaction. In the presence of **15**, the K^+ is complexed by the crown ether and this complex can then be transferred to a solvent that is less capable of solvating the hydroxide anion, e.g. toluene. Being 'naked', or less solvated, the hydroxide anion is able to reach the reaction site more easily (Scheme 2. 12 B), and is thus able to hydrolyse the sterically hindered ester.


A. In the absence of any crown ether. Methanol is used as the solvent

B. In the presence of a crown ether. The use of a non-solvating solvent such as toluene.

Scheme 2. 12. Hydrolysis of bulky esters with the 'naked hydroxyl' anion. The crown ether traps the K^+ so that no solvated K^+---^-OH ion pair can be formed. The ^-OH is highly reactive and can gain access to the reaction site more easily.

Fluoride anions are notoriously bad nucleophiles for nucleophilic substitutions, due to the fact that in solvents with good solubility for the fluoride anion, the fluoride anions are covered with a tight solvate wrapping.[50] In the presence of **15**, KF can be transferred to a solvent that is less able to solvate the fluoride anion, such as acetonitrile. 'Naked' or less solvated fluoride is not only a strong nucleophile, but also a strong base, so when proton elimination is favoured in a molecule, elimination products also arise in high yields (Scheme 2. 13, p. 41).[50]

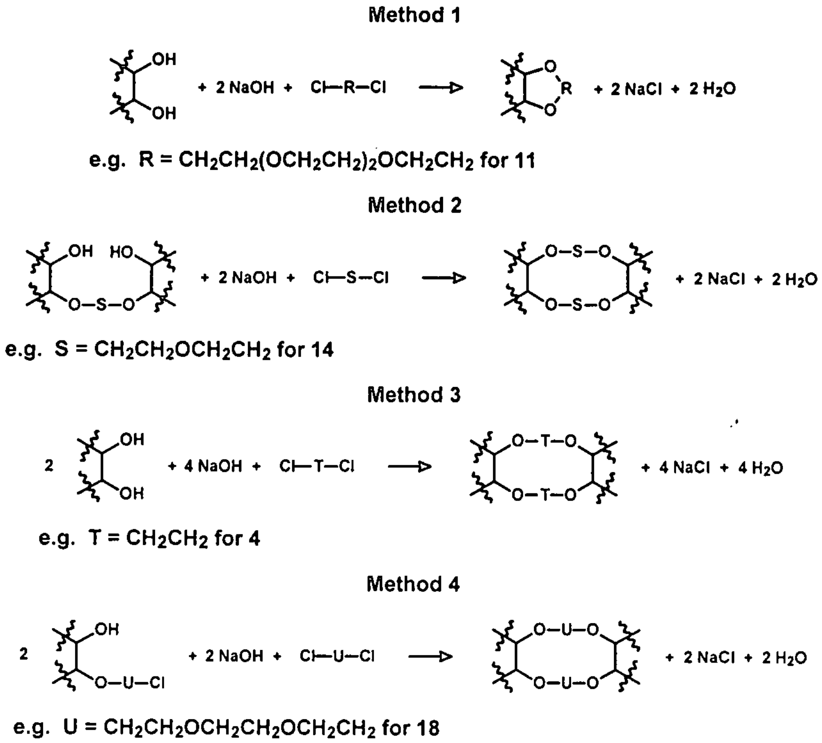


Scheme 2. 13. The use of the 'naked' fluoride anion as both nucleophile and base, in the presence of 14.

2.7 SYNTHESIS OF CROWN ETHERS

Many ways exists for the synthesis of crown ethers, but only four different methods are going to be discussed here. These four different synthetic pathways are shown in Scheme 2. 14, p. 42, where R, S, T and U represent divalent organic groups, which may or may not be identical.[2] Method 2 is the most versatile method for the synthesis of macrocycles containing two or more benzo groups, and it also gives the highest yields. It is evident that certain macrocyclic ether rings are preferentially formed; such as those containing five and/or six oxygen atoms in the ring, each separated from the next by two carbon atoms.[8]

One problem during the synthesis of crown ethers, are the formation of linear by-products, rather than the desired cyclic products. High dilution techniques were often used to enhance the cyclisation of these macrocycles over the oligomerisation.[51] Another way to overcome this problem is the use of the 'template effect'. The synthesis of crown ethers is usually done in the presence of a metal cation, which helps to stabilise the transition state leading to the formation of a cyclic macrocycle. This organisation effect is known as the 'template effect'.[51] The template effect helps to organise the nucleophilic- and the electrophilic-ends of the molecule, so that intramolecular products, or cyclic products (Scheme 2. 15, path a, p. 42), are formed rather than intermolecular products, or non-cyclic products (Scheme 2. 15, path b, p. 42).



Method 1

e.g. R = $CH_2CH_2(OCH_2CH_2)_2OCH_2CH_2$ for 11

Method 2

e.g. S = $CH_2CH_2OCH_2CH_2$ for 14

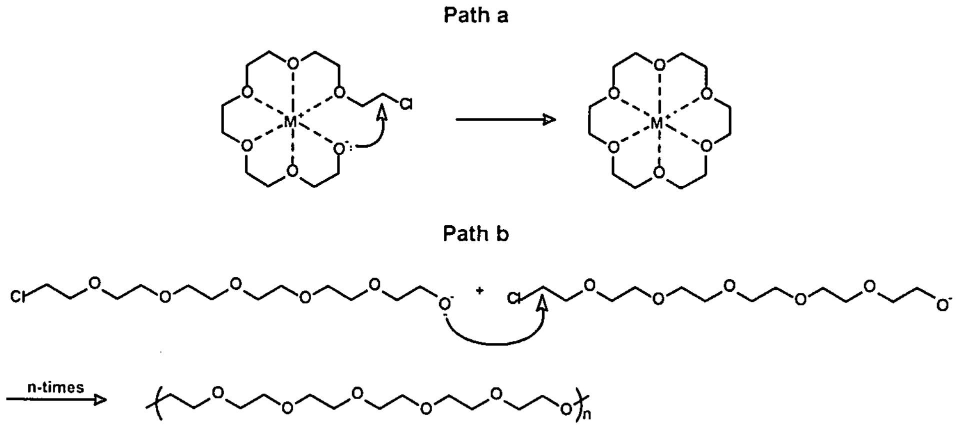
Method 3

e.g. T = CH_2CH_2 for 4

Method 4

e.g. U = $CH_2CH_2OCH_2CH_2OCH_2CH_2$ for 18

Scheme 2. 14. Four methods for the synthesis of crown ethers.

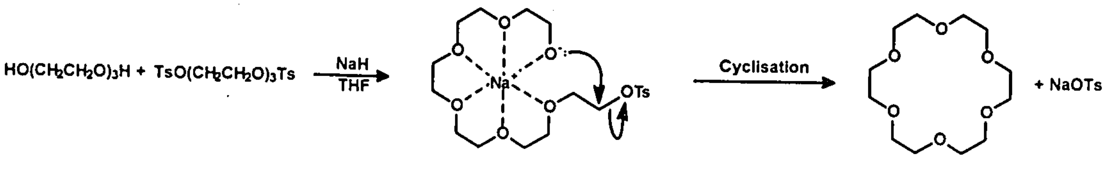


Path a

Path b

Scheme 2. 15. The principle of the template effect. The template effect leads to cyclic compounds, as seen in path a, while in the absence of M^+, no template is produced, and this results in the formation of linear compounds, as seen in path b.

In the case of poly(ethyleneoxy) reactants, the template process takes place through the action of the cation present in the reaction mixture. Due to the polar interactions between the electronegative oxygen atoms and the positive cation, the poly(ethyleneoxy) reactants tend to organise around the cation, as seen in Scheme 2. 16, p. 43.



6

Scheme 2. 16. An illustration to show how the template effect works in the synthesis of 6.

The formation of a circle, or semi-circle, around the cation enhances the likelihood of the two ends of the reacting molecule being close enough for the cyclisation reaction to take place. The initial reaction (in the absence of any template effect) leads to the formation of a hexa(ethyleneoxy) product, containing an alkoxide residue at one end and a tosylate leaving group at the other (Scheme 2. 16). Due to the affinity of the Na^+ for the oxygen atoms, the chain organises itself around the cation. This organisation effect allows the two reacting ends of the molecule to be in the vicinity of each other, and this allows ring closure. Therefore the template effect enhances cyclisation over oligomerisation.

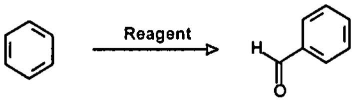
2.8 FUNCTIONALISATION OF MACROCYCLES

One of the goals of this study was to functionalise crown ethers for the ultimate anchoring of these functionalised crown ethers onto polymers or polymeric carriers. For this reason it was deemed necessary to discuss some functionalisation techniques. It is a well-known fact that it is easier to functionalise an aromatic ring than it is to functionalise an aliphatic chain. Therefore it is reasonable to utilise a crown ether that contains an aromatic ring, such as **11**, rather than **5** as the starting material to obtain functionalised molecules. These aromatic macrocycles react like anisole and/or veratrole, which can be halogenated, nitrated and condensed with formaldehyde,[8] and this substitution usually occurs at the 4'-position. A few examples of 4'-substituted-benzo-15-crown-5 compounds, or 4'-R-benzo-15-crown-5, are known and include R = H,[2] $C(CH_3)_3$,[52] CH_3,[53] CHO,[54] $CH(OH)CH_2NHCH_3$,[55] $CH_3C(O)$,[9] NO_2, NH_2,[56] Br, COOH and $COOCH_3$.[57]

According to Izatt *et al.*,[9] the functionalisation of the macrocycle has an effect on its ability to complex cations. For example, the presence of an electron-withdrawing group, such as the nitro group, in 4,4'-dinitrodibenzo-18-crown-6, causes an increase in the decomplexation rate and simultaneously a decrease in the complexation rate, compared to that of **14**. However, 4'-formylbenzo-15-crown-5 does not exhibit a different complexation rate as compared to benzo-15-crown-5 (**11**).[58] This might be due to the fact that a single formyl group is not as electron-withdrawing as two nitro groups.

As this study includes several synthetic procedures, it is deemed appropriate to discuss the more frequently used techniques to functionalise aromatic compounds.

2.8.1 Formylation‡



Scheme 2. 17. The formation of an aromatic aldehyde.

The *Vilsmeier*, or the *Vilsmeier-Haack*, reaction is the most versatile method for the formylation of aromatic rings.[59] This reaction occurs between an aromatic compound and disubstituted formamides in the presence of phosphorus oxychloride.[60] *N*-Phenyl-*N*-methylformamide[59] is the reagent of choice, but other arylalkyl amides and dialkyl amides can also be used.

The *Gatterman reaction*[61] utilises $Zn(CN)_2$ and HCl to carry out the formylation. This reaction can be applied to alkylbenzenes, phenols and their ethers, and also to many heterocyclic compounds.[59]

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‡ As paragraph 2.8 discuss general synthetic procedures, reaction schemes do not necessarily imply crown ether derivatives, but focuses on aromatic compounds like benzene, in general.

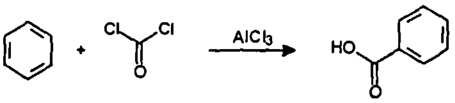
The *Reimer-Tiemann reaction*,[62] formylation with chloroform and hydroxide anions, is useful only for phenols and certain heterocyclic compounds such as pyroles and indoles.[59] A closely related reaction to the *Reimer-Tiemann reaction* is the *Duff reaction*.[63] In this reaction chloroform is replaced by hexamethylenetetramine, $C_6H_{12}N_4$, and this reaction can be applied to phenols and amines.[59] Table 2. 3 show other reagents that can be used in the formylation of aromatic compounds.

Table 2. 3. Miscellaneous reagents that can be used for formylation.

Reagent	Reference
Bisthionium ions	**64**
HF + SbF_5 and HF + BF_3 superacid systems as catalysts	**65**
Manganese(III) acetate, $[Mn_3O(OAc)_6(OAc)\text{-}(HOAc)]\cdot 5H_2O$	**66**
Dichloromethyl methyl ether formylates aromatic rings with Friedel-Crafts catalysts	**67**
Orthoformates	**68**
Formyl fluoride; HCOF; BF_3	**69**
CO + HCl + CuCl	**70**

The formylation of the *ortho* position of phenols can also be accomplished by using *para*-formaldehyde, $SnCl_4$ and a tertiary amine,[71] or 2-ethoxy-1,3-dithiolane.[72]

2.8.2 Carboxylation



Scheme 2. 18. The formation of an aromatic carboxylic acid.

Carboxylation can be accomplished by phosgene in the presence of a *Friedel-Crafts catalyst*,[73] but other reagents include: oxalyl chloride (**183**), urea hydrochloride (**184**), choral (**185**), carbamoyl chloride (**186**) and *N,N*-diethylcarbamoyl chloride[73] (Figure 2. 22, p. 46). Aromatic carboxylic acids can also be produced through the reaction between aromatic compounds with sodium palladium(II) malonate (**187**), in a mixture of acetic acid and acetic anhydride, or carbon tetrachloride.[74]

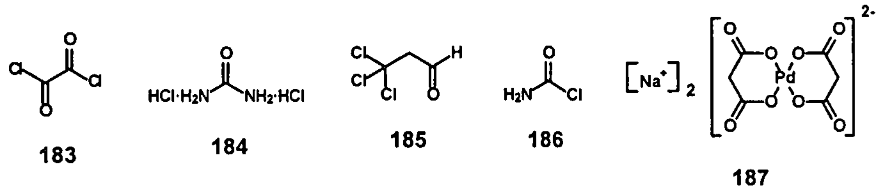
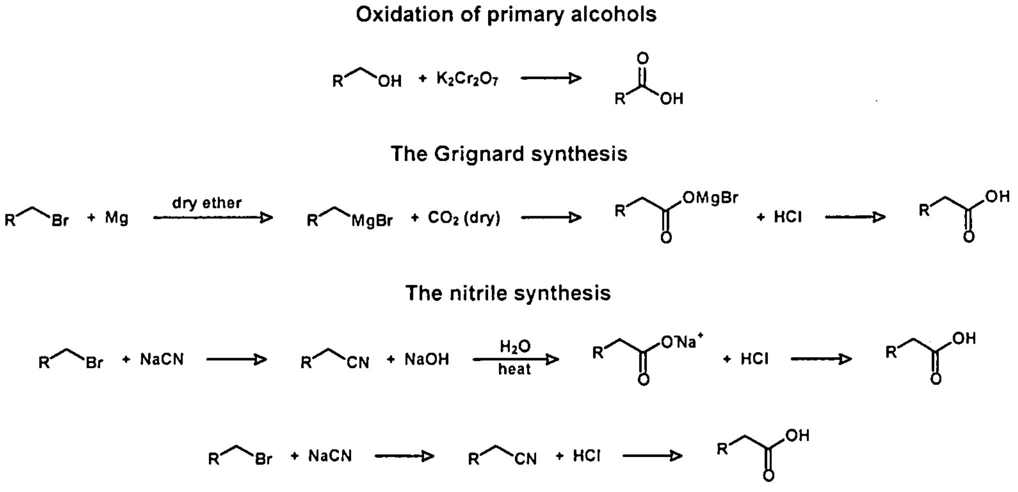


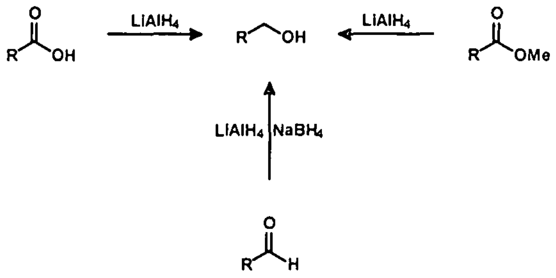
Figure 2. 22. The structures of some of the reagents used in the carboxylation of aromatic compounds.

Aromatic rings can also be carboxylated with carbon monoxide, under mild conditions, i.e. trifluoroacetic acid as solvent, palladium acetate as catalyst in the presence of a co-catalyst, such as sodium acetate.[75] The treatment of bromomagnesium, or aluminium phenoxide, with an excess of phosgene, produces the *ortho*-chloro carbonyl derivative of the phenol, which when treated with carbon disulphide, NH_4Cl and water, produces the corresponding carboxylic acid.[76] Alternative ways of producing carboxylic acids include the oxidation of primary alcohols, the Grignard synthesis, and the nitrile synthesis (Scheme 2. 19).[73]



Scheme 2. 19. Synthetic strategies towards carboxylic acids.

2.8.3 Formation of alcohols



Scheme 2. 20. The reduction of carbonyl containing compounds to alcohols by both $LiAlH_4$ and $NaBH_4$.

Aldehydes can be reduced to primary alcohols with $LiAlH_4$, with the advantage that it does not reduce carbon-carbon double, or triple bonds.[77] $LiAlH_4$ easily reduces aliphatic, aromatic, alicyclic and heterocyclic aldehydes, containing double or triple bonds and/or non-reducible groups such as NR_3, OH, OR and F.[77] $NaBH_4$ has a similar scope of reactions as $LiAlH_4$, but it is more selective and may be used with NO_2, Cl, COOR and CN-groups in the molecule.[77] In general $NaBH_4$ reduces carbonyl compounds in the order: (fastest) aldehydes > α,β-unsaturated aldehydes > ketones > α,β-unsaturated ketones (slowest).

The two oldest methods for the reduction of the carbonyl group of aldehydes and ketones are the *Clemmensen reduction* and the *Wolff-Kishner reduction*.[78] The *Clemmensen reduction* occurs when the aldehyde or ketone is treated with zinc amalgam and aqueous HCl.[79] The *Wolff-Kishner reduction* occurs when the aldehyde or ketone is heated with hydrazine hydrate and a base (usually NaOH or KOH).[80] The *Wolff-Kishner reduction* is now completely replaced by the *Huang-Minlon modification* and this reaction is carried out in diethylene glycol.[81] The *Clemmensen* and *Wolff-Kishner* reactions are complementary, since the first uses acidic conditions, while the latter uses basic conditions.

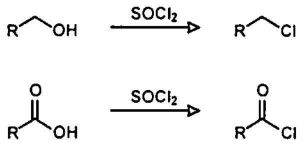
$LiAlH_4$ can easily reduce carboxylic acids to alcohols, under mild conditions, and even at room temperature.[82] Borane is particular effective for the reduction of the carboxyl group and can selectively reduce it in the presence of other functional groups, except double bonds. Double bonds are reduced to alkanes at the same rate as the carboxylic acid.[82] However, the reduction of carboxylic acids to produce alcohols is more sluggish to occur than the reduction of the corresponding ester to the same alcohol.

$LiAlH_4$ can also be used to reduce a wide variety of carboxylic esters.[83] $NaBH_4$ can reduce phenolic esters, especially those containing electron-withdrawing groups,[84] but the reaction with other esters is usually too slow, and it is therefore not feasible.[83] Table 2. 4 show other reagents that can be used to reduce the carbonyl group to produce an alcohol.

Table 2. 4. Miscellaneous reagents that can be used for the reduction of carbonyl compounds.

Reagent	Reference
Isopropyl alcohol and $Al(OCHMe_2)_3$ (*Meerwein-Ponndorf-Verley reduction)*	77
aqueous VCl_2	77
Sodium in EtOH (*Bouveault-Blanc procedure)*	85
9-Borabicyclo[3.3.1]nonane	86
BH_3-Me_2S	87
Zn + DMF	88
Zn-$ZnCl_2$-EtOH	89
H_2 + Ni/Al_2O_3	90
$LiAlH_4$-$AlCl_3$	91
Li-NH_3	92
$NaBH_4$-$AlCl_3$	93
Titanocene dichloride	94
H_2 + $CuCr_2O_7$	95
BF_3-OEt_2 + BH_3-SMe_2	96

2.8.4 Formation of aryl and acyl halides



Scheme 2. 21. The conversion of alcohols to alkyl halides and carboxylic acids to acyl chlorides.

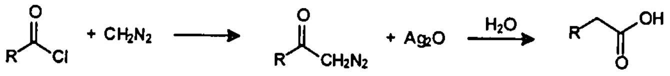
Alcohols can be converted into the corresponding alkyl halide[97] by the reaction of halogen acids, HX, and by inorganic acid halides, such as $SOCl_2$,[98] PCl_5,[99] PCl_3[100] and $POCl_3$.[97] Tertiary chlorides are easily made with concentrated HCl,[101] but primary and secondary alcohols react more slowly with HCl, and a catalyst, such as $ZnCl_2$, is usually required.[97] PBr_3[102] have also been used, although this is much more expensive than HBr or HI.[97]

The same inorganic acid halides that convert alcohols to alkyl halides can also be used to convert carboxylic acids to acyl halides.[103] This is the best method for the synthesis of acyl chlorides, although acyl bromides and iodides can also be synthesised in this manner.[103] Thionyl chloride is the reagent of choice, since the by-products are gasses and the acyl chloride can easily be isolated, but other reagents include oxalyl chloride, PX_3 and PX_5 (X = Cl and Br). Another mild reaction involves the reaction of the acid with Ph_3P in CCl_4, producing the acyl chloride without the formation of any acidic by-products.[104] Table 2. 5 show other reagents that can be used for the conversion of alcohols and carboxylic acids to their corresponding alkyl and acyl halides.

Table 2. 5. Miscellaneous reagents for the conversion of alcohols and carboxylic acids to their corresponding alkyl and acyl halides.

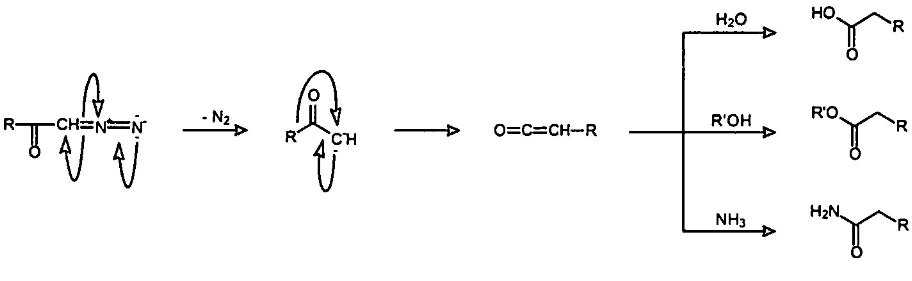
Reagent	Reference
R_3PX_2	**105**
Me_2SBr_2	**106**
Me_3SiCl-SeO_2	**107**
$PPh_3 + CCl_4$	**108**

2.8.5 The Arndt-Eistert synthesis



Scheme 2. 22. The Arndt-Eistert synthesis.

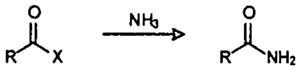
This method allows the synthesis of a carboxylic acid with an additional carbon atom compared to the parent carboxylic acid.[109] The first step in the reaction between an acid chloride and diazomethane is the formation of a diazoketone.[110] The rearrangement (known as the *Wolff rearrangement*) occurs in the second step upon treatment of the diazoketone with water and silver oxide or with silver benzoate and triethylamine.[110] This synthesis is a very convenient method for the increase of the carbon atoms in the side chain if the carboxylic acid is available. When an alcohol is used instead of water during the rearrangement step, an ester, RCH_2COOR', is produced, and when ammonia is used instead of water, the product is an amide, RCH_2CONH_2.[110] Other catalysts in place of silver oxide include colloidal platinum and copper, or the diazoketone can just be heated or photolysed in the presence of water, an alcohol, or ammonia, with no catalysts at all.[110] The photolysis method often gives better results than the silver catalysis. The mechanism (Scheme 2. 23) is generally regarded as involving the formation of a carbene.[110]



Scheme 2. 23. The mechanism involved in the *Arndt-Eistert synthesis*.

It can be seen from the mechanism in Scheme 2. 23, that a ketene is formed as an intermediate. The ketene then reacts with water, an alcohol, or ammonia to produce carboxylic acids, esters and amides, respectively.

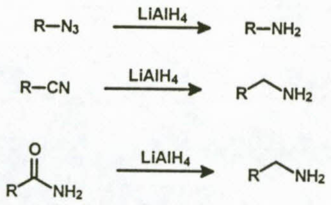
2.8.6 Formation of amides



Scheme 2. 24. The formation of amides by the reaction between acyl halides and ammonia.

The treatment of acyl halides with ammonia,[111] or substituted amines,[112] is a very general reaction to produce amides under mild conditions (room temperatures, short reaction times). The reaction is highly exothermic and must be carefully controlled, usually by cooling or dilution. Ammonia gives unsubstituted amides, primary amines gives *N*-substituted amides, and secondary amines gives *N,N*-disubstituted amides. When aqueous alkali is added to neutralise the liberated HCl, the reaction is known as the *Schotten-Baumann procedure.*[112] As seen in 2.8.5 amides can also be produced by the reaction of ketenes with NH_3, in a modified *Arndt-Eistert reaction.*

2.8.7 Formation of amines



Scheme 2. 25. The reduction of azides, nitriles and amides to produced amines.

Azides can easily be reduced to primary amines by the reaction with $LiAlH_4$.[113] Amides can also be reduced by $LiAlH_4$ and by catalytic hydrogenation, although, in the latter case, high temperatures and pressures are usually required.[82] The reduction of the amide to the amine with $LiAlH_4$ is more difficult than the reduction of other functional groups, such as the reduction of esters to alcohols, in the same molecule. These functional groups are often reduced without the reduction of the amide to the amine. Other reducing agents include $NaBH_4$, although not on its own, but in the presence of certain other reagents;[114] borane[115] and sodium in 1-propanol.[82]

2.8.8 Formation of nitriles

$R{-}X + CN^- \longrightarrow R{-}CN$

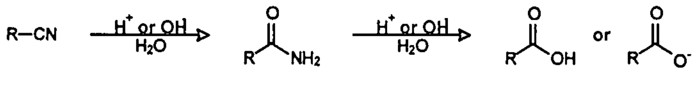
Scheme 2. 26. The formation of nitriles.

The reaction between alkyl halides and the cyanide anion is a convenient way to produce nitriles.[116] Primary, benzylic and allylic halides give the best yields and other groups in the molecules do not interfere with the synthesis of nitriles. This is also a convenient way to increase the carbon chain length by one carbon, and nitriles can be either hydrolysed to produce carboxylic acids or reduced to produced amines. Table 2. 6 show other reagents that can be used to produced nitriles.

Table 2. 6. Miscellaneous reagents for the formation of nitriles.

Reagent	Reference
CuCN	**117**
vinylic triflates, treated with LiCN, a crown ether and palladium catalyst	**118**
KCN, a crown ether, and a Pd(0) complex	**119**
primary, secondary and tertiary alcohols treated with NaCN, Me_3SiCl, and a catalytic amount of NaI in DMF-MeCN	**120**
$K_4Ni_2(CN)_6$	**121**

2.8.9 The hydrolysis of nitriles



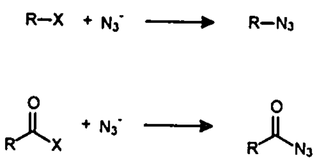
Scheme 2. 27. The hydrolysis of nitriles to produce amides and/or carboxylic acids.

Nitriles can be hydrolysed to carboxylic acids *via* the amide under basic[122] or acidic[123] conditions. When the amide is the desired compound there are a number of methods involving the correct selection of reagent to stop at the amide stage, see Table 2. 7. Nitriles can be hydrolysed without disturbing ester functions that may also be present in the same molecule, by the use of tetrachloro- or tetrafluorophthalic acid.[124]

Table 2. 7. Reagents that can be used to hydrolysed nitriles to amides.

Reagents	Reference
concentrated H_2SO_4	**124**
formic acid and HCl or HBr	**125**
30 % H_2O_2 in Me_2SO	**126**
MnO_2 on silica gel	**127**
sodium perborate in aqueous MeOH	**128**
$Hg(OAc)_2$ in HOAc	**129**
2-mercaptoethanol in a phosphate buffer	**130**
H_2O_2 + NaOH	**131**

2.8.10 Formation of azides



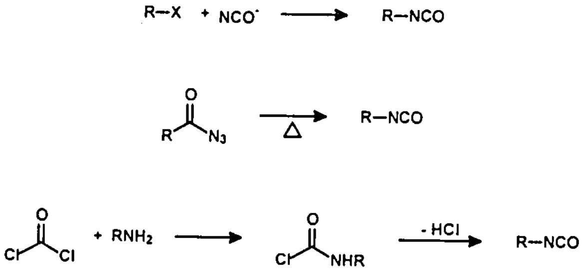
Scheme 2. 28. The formation of azides from alkyl and acyl halides.

Alkyl and acyl azides can be prepared by treating the corresponding alkyl and acyl halide with the azide anion,[132] or by using a phase transfer catalyst[133] or even ultrasound.[134] Other leaving groups rather than the halogens X = Cl, Br or I can be seen in Table 2. 8. NaN_3 and $ZnCl_2$ in CS_2[135] can be used to convert tertiary alkyl halides to tertiary alkyl azides. Tertiary alkyl azides can also be prepared from tertiary alcohols with NaN_3 and CF_3COOH[134] or with HN_3 and $TiCl_4$[136] or BF_3.[137]

Table 2. 8. Leaving groups other than the halides. Mesitylene (OMs), tosyl (OTs) and acetyl (OAc).

Leaving Groups	References
OH	138
OMs	134
OTs	132
OAc	139

2.8.11 Formation of isocyanates



Scheme 2. 29. The formation of isocyanates from alkyl halides, acyl azides and amides.

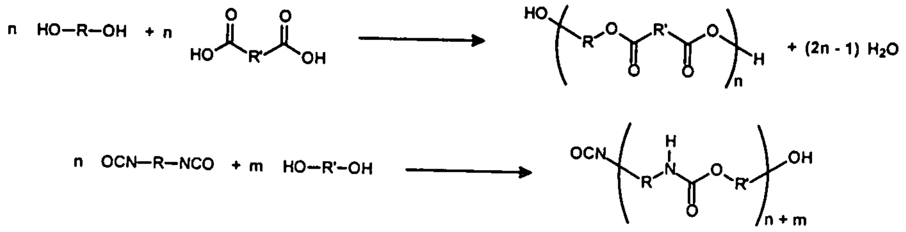
Isocyanates can be produced by either the reaction of an alkyl halide with the isocyanate anion,[140] or by the *Curtius rearrangement* from acyl azides,[141] or *via* the chloroformamides, ClCONHR, which is produced by the reaction between phosgene and primary aliphatic or aromatic amines.[142] The use of chloroformamides is one of the most common methods for the synthesis of isocyanates.[142] Primary alkyl halides have been converted to isocyanates by the use of sodium nitrocyanamide ($NaNCNNO_2$) and *m*-chloroperbenzoic acid.[141] The *Curtius rearrangement* involves the pyrolysis of acyl azides to produce isocyanates.[141] This reaction usually gives good yields of the isocyanate, if there is no water present in the system. The *Curtius rearrangement* is a very general reaction and can be applied to any azide: aliphatic, aromatic, alicyclic, heterocyclic and unsaturated.[143]

2.9 POLYMERS

Regarding this study program, the key to the use of macrocycles in water purification is a polymeric macrocycle carrier. The author deemed it appropriate to discuss some general polymer systems that are relevant to this study program. The desired polymeric macrocycle carrier should easily be functionalised and it should also be water-insoluble.

The term polymer was derived from the Greek words *poly* and *meros*, meaning many parts.[144] Staudinger[145] showed that one of the major routes in the synthesis of long chain molecules (i.e. polymers), is the successive addition of unsaturated molecules in a chain reaction to produce polymers (Scheme 2. 30). Carothers[145] identified condensation reactions (modern terminology is 'step reaction') as another major route in the production of polymeric materials, and for many years these remained the principal routes in the synthesis of organic polymers (Scheme 2. 31, p. 55).

Scheme 2. 30. An example of a chain polymerisation reaction.



Scheme 2. 31. Examples of step polymerisation reactions.

In this study both kinds of polymers were used, although both kinds of polymers were not synthesised. Scheme 2. 30, p. 54, shows an example of a chain reaction polymer as is the case in the synthesis of poly(vinyl chloride), while the formation of polyesters and polyurethanes (Scheme 2. 31) illustrate step reaction polymerisation, with or without the elimination of a small molecule.

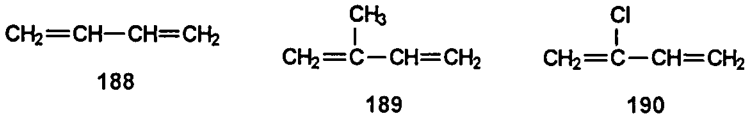
The polymerisation reactions that occur in the chain reaction mechanism, are typically those involving unsaturated monomers, and this polymerisation is usually initiated by the chemical generation of a reactive centre, which usually are free radicals, but anions or cations may also be used.[144] The polymerisation reaction proceeds readily without the destruction of the reactive centre. The chain polymerisation consists of three phases:

1. initiation;
2. propagation;
3. and termination.

2.9.1 Insoluble polymers

In this study no step reaction polymers were synthesised, but commercially available hydroxy terminated polybutadiene (HTPB, **199**) was used as an important pre-polymer. HTPB (**199**) is manufactured by the free radical polymerisation of 1,3-butadiene (**188**) and a number of geometric isomers are observed in this pre-polymer.

These geometric isomerisms involve the various possible structures that may result from the polymerisation of 1,3-dienes. Three of the more important examples of this type of 1,3-diene monomers can be seen in Figure 2. 23; 1,3-butadiene (**188**), 1,3-isoprene (**189**) and 1,3-chloroprene (**190**).



$CH_2{=}CH{-}CH{=}CH_2$ **188**

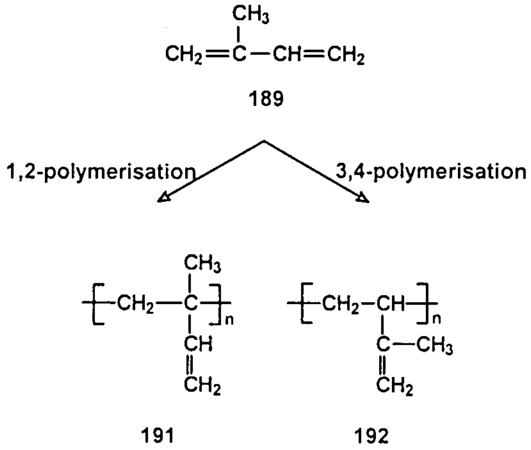
$CH_2{=}C(CH_3){-}CH{=}CH_2$ **189**

$CH_2{=}C(Cl){-}CH{=}CH_2$ **190**

Figure 2. 23. Three important 1,3-dienes monomers.

To illustrate the possible modes of polymerisation of these compounds, consider the following reactions that isoprene (**189**) can undergo:[146]

1. 1,2- and 3,4-polymerisation. For this type of polymerisation, **189** behaves as mono-olefins, since the second double bond is relegated to the status of a substituent group. Due to the reactivity of the latter, it can be involved in cross-linking reactions. For isoprene (**189**), 1,2-polymerisation (**191**) and 3,4-polymerisation (**192**) yield different products (Scheme 2. 32).

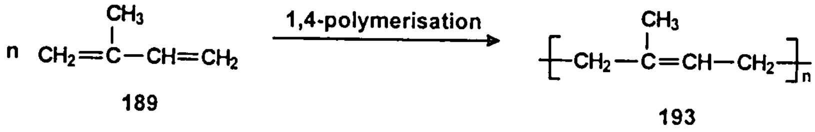


Scheme 2. 32. An example of 1,2- and 3,4-polymerisation reactions utilising isoprene (189).

Polymers **191** and **192** can exhibit three different taxicities, so a total of six structures can result from this monomer when only one of the olefin groups are involved in the backbone formation.

2. 1,4-polymerisation. This mode of polymerisation produces a polymer with an alternating double bond along the backbone of the chain. Again using

isoprene (**189**), the synthesis of polyisoprene (**193**, Scheme 2. 33) may serve as an example of this type of polymerisation.



Scheme 2. 33. An example of 1,4-polymerisation reactions of isoprene (189).

The adjacent chain sections can either be the *cis*-isomer (**194**) or the *trans*-isomer (**195**) with respect to the double bond, producing the following geometrical isomers (Figure 2. 24, p. 57).

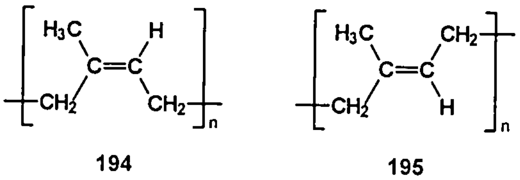
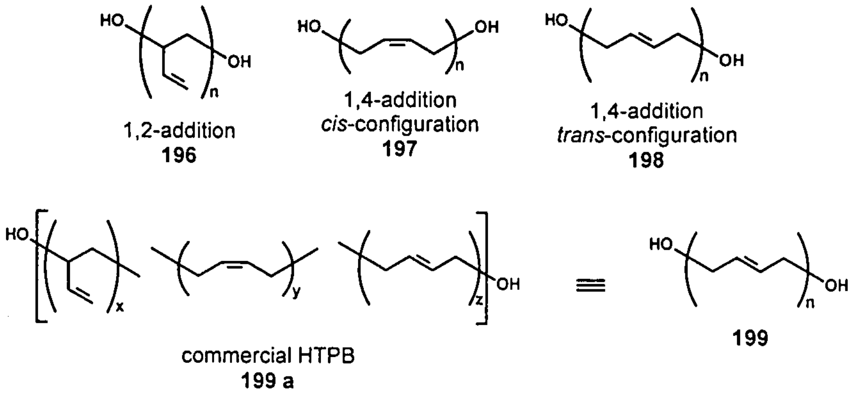


Figure 2. 24. The geometrical isomers of 1,4-polymerisation reactions of isoprene (189).

The HTPB (**199**) used in this study invariably consists of a mixture of 1,2- and 1,4-polymerisation fragments of 1,3-butadiene in the same molecule, and also of *cis*- and *trans*-configurations, as can be seen in Figure 2. 25, p. 58. The hydroxy functionality, i.e. the amount of hydroxy groups per molecule, of free radical induced commercial available HTPB, is between 2.2 and 2.6 and this is the cause for the limited cross-linking ability of this polymer during condensation reactions to form polyurethanes. HTPB (**199**) is *inter alia* used in the solid fuel industry as an elastomeric solid propellant matrix.[147] Curing of HTPB (**199**) with, for example, isophorone diisocyanate (**200**, Scheme 2. 34, p. 58) leads to the formation of an insoluble elastomer **201**, insoluble because of the limiting cross-linking capability of HTPB (**199**). Elastomer **201** is capable of carrying 9 times its own mass of solid particles (Al_2O_3, NH_4ClO_4, Al, etc.) in a solid propellant.[148] The 1,2-polymerisation fragments of HTPB (see structure **199 a**, Figure 2. 25, p. 58) were also utilised to immobilise the high burning rate catalyst, ferrocene, in a solid propellant matrix[148] (Figure 2. 26, p. 58) to produce butacene (**202**).



1,2-addition
196

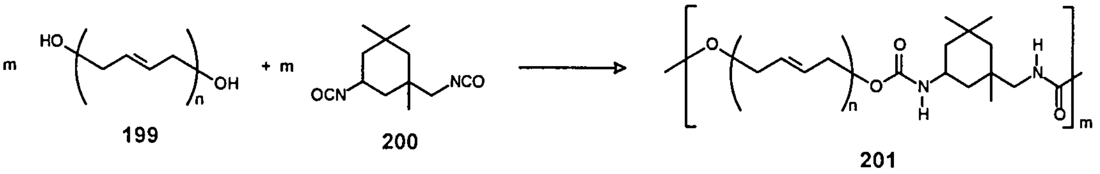
1,4-addition
cis-configuration
197

1,4-addition
trans-configuration
198

commercial HTPB
199 a

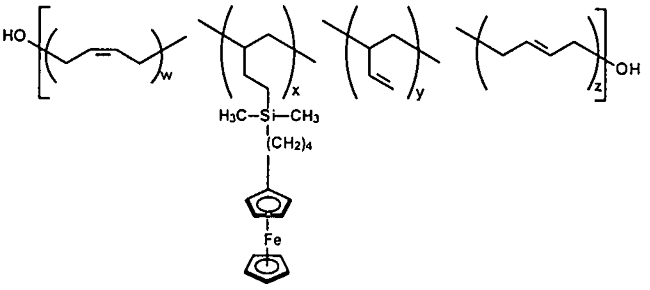
199

Figure 2. 25. Compounds 196, 197 and 198 illustrate the possible structures that can be obtained if 1,3-butadiene is polymerised, to give hydroxy terminated polybutadiene (HTPB). However, commercial HTPB (199a), invariably has all three structures, in a random distribution, in its backbone. Throughout this thesis, whenever reference to HTPB is made, it is understood to be compound 199a, but for simplicity the full structure of HTPB will hereafter be simplified by 199. It is explicitly understood, though, that when structure 199 is drawn, it is just an abbreviated way of indicating structure 199a.



199 **200** **201**

Scheme 2. 34. The formation of an elastomer from HTPB (199) and isophorone diisocyanate (200). Although structure 201 indicates a linear polymer, in actual fact it is slightly cross-linked due to the hydroxy content of HTPB (199) of 2.2 – 2.6 equivalents.



202

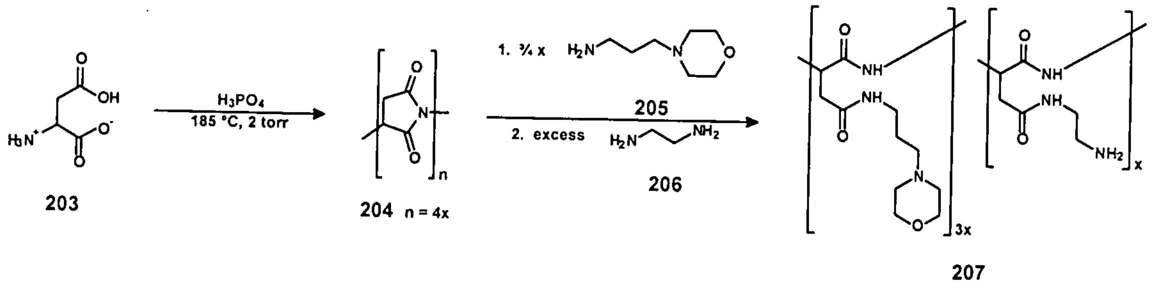
Figure 2. 26. An example of the use of the 1,2-polymerisation fragments that can be used in the immobilisation of ferrocene on HTPB.

Elastomer **201** is insoluble in most solvents due to the limiting cross-linking ability of HTPB (**199**). One of the goals set for this study was the grafting of water-soluble side chains onto a water-insoluble polymeric support, such as polymer **201**.

2.9.2 Soluble polymers

One of the approaches used in this study to anchor crown ether derivatives onto a polymer, were to first graft a water-soluble polymer onto the surface of elastomer **201** and then to anchor the crown ether derivatives onto the grafted side chains (see Chapter 3, paragraphs 3.5 and 3.6, p. 112 – 135). For this purpose we chose two types of water-soluble polymers to graph onto elastomer **201**. The first was previously developed as a water-soluble polymeric drug carrier, while the second one was developed to minimise the smoke trail of rockets and to provide more energy to a solid propellant.

The water-soluble polymeric drug carrier in question, polymer **207** (Scheme 2. 35) is derived from aspartic acid (**203**).[149]

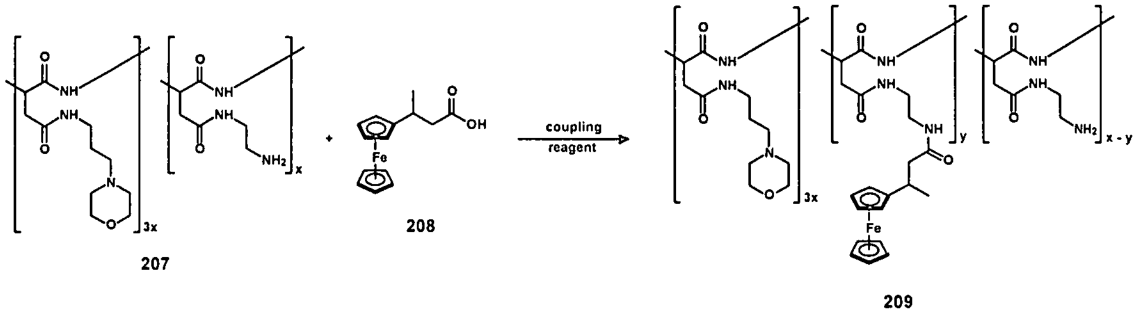


Scheme 2. 35. The synthesis of a water-soluble polymeric carrier derived from aspartic acid.

The introduction of morpholino groups as side chains onto the polymer main chain, made polymer **207** very water-soluble. The introduction of amine containing side chains in polymer **207** provided an active site to which a drug can be anchored.[149]

Polymer **207** was used to anchor a variety of antineoplastic material, including rhodium,[150] platinum[151] and titanium-based compounds.[152] However, the first series of drug polymer conjugates that were tested for biological activity, so far, made use of ferrocene as the active antineoplastic material.[153] One of the compounds tested for anticancer activity, polymer **209**, is shown in Scheme 2. 36, p. 60.[154] This polymer/ferrocene conjugate was found to be about

700 % (almost one order of magnitude) more effective than the free ferrocene drug **208**.[153]



Scheme 2. 36. The anchoring of a ferrocene derivative onto the water-soluble polymer 207.

In this study we used polymer **207** as a platform to anchor crown ethers onto this water-soluble polymer. The anchoring of the antineoplastic material was done in the presence of a suitable coupling reagent. According to a study on the effectiveness of different coupling reagents, in order to anchor carboxylic acids to the amine side chains, the most effective coupling reagent was *O*-benzotriazolyl-*N,N,N',N'*-tetramethyluronium hexafluorophosphate (**212**, Figure 2. 27), compared to *N*-hydroxybenzotriazole (**210**, Figure 2. 27) and *N*-hydroxysuccinimide (**211**, Figure 2. 27).[152] This prompted us to use *O*-benzotriazolyl-*N,N,N',N'*-tetramethyluronium hexafluorophosphate (**212**) as the coupling reagent for the anchoring of our carboxylic acid derivatised crown ethers onto the polymeric carrier **207**.

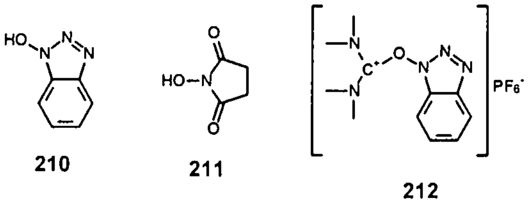
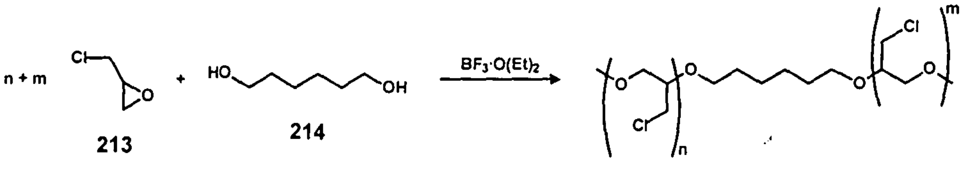


Figure 2. 27. Examples of different coupling reagents that can be used to obtain a suitable coupling between a carboxylic acid group and an amine group.

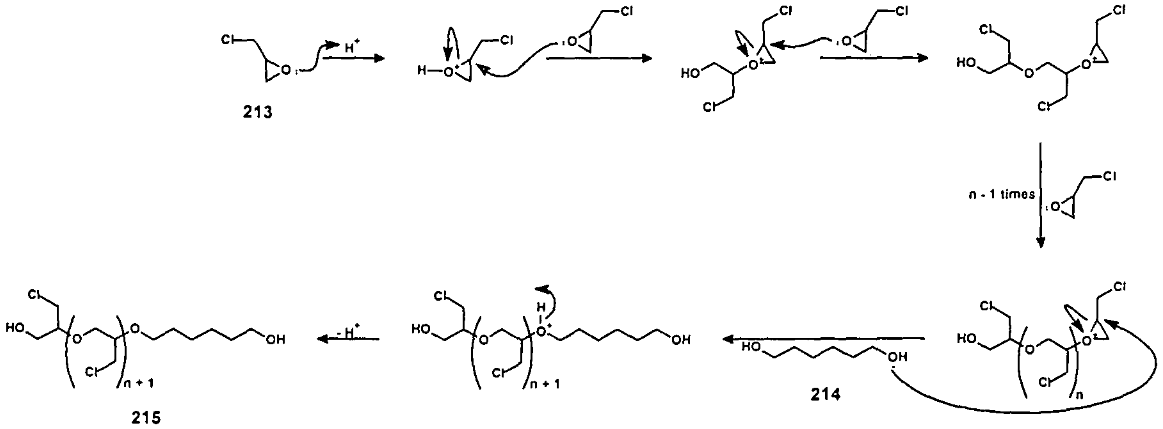
The second type of polymer that was considered important for this study was developed to decrease the amount of smoke emitted from rockets.[155] This polymer (a polyether derivative) is obtained by the cationic ring-opening polymerisation of epichlorohydrin (**213**) to produce hydroxy terminated polyepichlorohydrin (**215**) as seen in Scheme 2. 37. Polyethers, such as polyepichlorohydrin (**215**), exhibit a relative flexible polymeric backbone, due to the free rotation around the ether oxygen.[156]



213 214 215

Scheme 2. 37. The synthesis of polyepichlorohydrin (215) from epichlorohydrin (213).

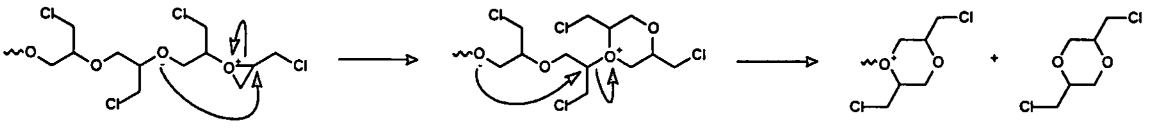
Polyepichlorohydrin (**215**) is usually synthesised by the cationic ring-opening polymerisation reaction of epichlorohydrin (**213**), in the presence of $BF_3{\cdot}O(C_2H_5)$, as the catalyst.[157] Two mechanistic pathways for the cationic ring-opening polymerisation reaction of epichlorohydrin (**213**) exist. The first is labelled the active chain end mechanism and is illustrated in Scheme 2. 38. In this mechanism there is always an excess of epichlorohydrin (**213**) present and the growing point of the polymer is not destroyed before all the starter-monomers are used up. The dialcohol (**214**) is finally added to create a polymer which is hydroxy terminated.



213 215

Scheme 2. 38. The cationic ring-opening polymerisation of epichlorohydrin (213) according to the active chain end mechanism.

This method of polymerisation does have the disadvantage of possible thermal runaway. When thermal runaway occurs, the chain length in the polymeric backbone is severely reduced by the elimination of substituted dioxanes from the polymeric backbone, as indicated in Scheme 2. 39.

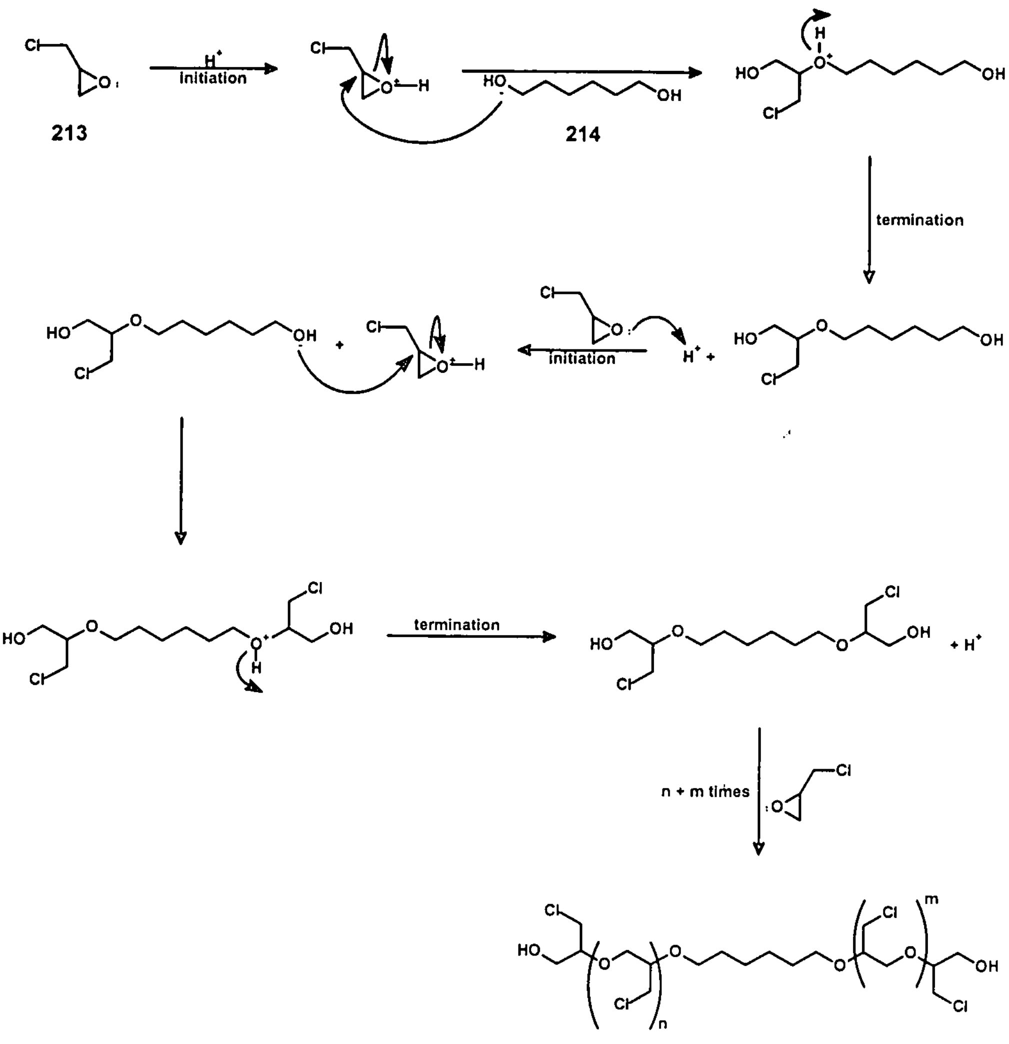


216

Scheme 2. 39. Mechanism of elimination of derivatives of dioxane (216) from the growing polyepichlorohydrin (215). Dioxane elimination is accelerated with increase in the temperature of the reaction.

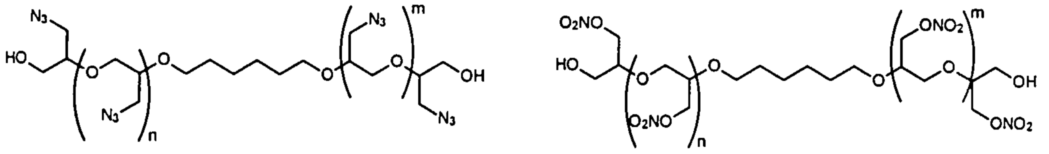
In order to reduce the risk of thermal runaway, the synthesis of polyepichlorohydrin (**215**) need to be performed in such a way as to never have an excess of the starting monomer, i.e. epichlorohydrin (**213**), in the mixture. Very slow addition of the monomer to the dialcohol **214** (the reactant order is also reversed compared to the active chain end mechanism, as illustrated in Scheme 2. 38, p. 61) satisfied this need, but this leads to a change in the mechanism. This mechanism is labelled the active monomer mechanism and is illustrated in Scheme 2. 40, p. 63. In this mechanism, the growing point of the polymer is terminated after each separate epichlorohydrin (**213**) attack on the dialcohol (**214**). Provided that the addition is slow enough, there is no excess of the starting monomer. This turns out to be quite favourable due to the fact that the side reactions are reduced and there is no threat of thermal runaway.

To obtain more energetic materials in the solid propellant industry, the use of functionalised polyepichlorohydrin derivatives have received much attention.[158] These include the synthesis of azide[159] (glycidyl azide polymer (**217**)) and nitrate[160] (poly(glycidyl nitrate) (**218**)) functionalised polyepichlorohydrin derivatives, as seen in Figure 2. 28, p. 63. Both of these functionalised polymers were more energetic than polyepichlorohydrin (**215**) itself.



215

Scheme 2. 40. Cationic ring-opening of epichlorohydrin (213) according to the active monomer mechanism. This mechanism limits the probability of elimination of substituted dioxanes as illustrated in Scheme 2. 39, p. 62.



217 218

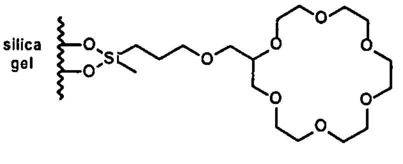
Figure 2. 28. Examples of more energetic derivatives of polyepichlorohydrin (215).

2.9.3 Polymers containing crown compounds

As one of the goals set for this study was to anchor crown ether derivatives onto polymeric carriers, the author deemed it appropriate to discuss existing polymeric crown ether derivatives.

Due to the selectiveness of crown ethers for specific metallic cations, polymeric crown derivatives will be useful in the recovery of metallic cations from a complex solution of cations. Examples of these polymeric crown ether derivatives, include crown ethers anchored to silica gel (**219**),[161] polystyrene based polymers (**220**),[162] poly(methacrylate) based polymers (**221** and **222**),[163] polyurethane based polymers (**223**, **224**, **225** and **226**)[164] and polythiophene based polymers (**227** and **228**)[165] as can be seen in Figure 2. 29, p. 65.

According to Izatt *et al.*[161], the silica gel bound crown ether, polymer **219**, produced a permanent bond, and this polymer could be used indefinitely to perform separations, recoveries and determinations without the loss of the crown ether moiety. They[161] also found that the polymer bound crown ether exhibited the same affinity for metallic cations as the unbound parent macrocycle. Blanton and Salley[162] used polymer **220**, in conjunction with a tin catalyst to reduce alkyl halides to the corresponding hydrocarbon. Tachon *et al.*[163] synthesised polymers **221** and **222** to determine their conductivity ability. They complexed Li^+, and tested these polymers for their conductivity ability. Lemaire *et al.*[164] synthesised a variety of polyurethane-based polymeric crown ether derivatives. These polymers were soluble in organic solvents and they found that it bound Li^+ and Na^+ more efficiently than commercially available chelating polymers.[164] Higgins[165] reported that the polythiophene based crown ether polymers **227** and **228**, exhibit a colour change when these polymers complex metallic cations. These could thus act as a visual reference for the presence of either Na^+ or K^+.



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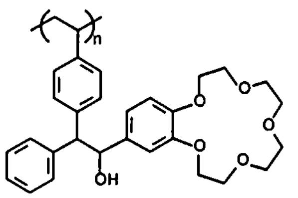
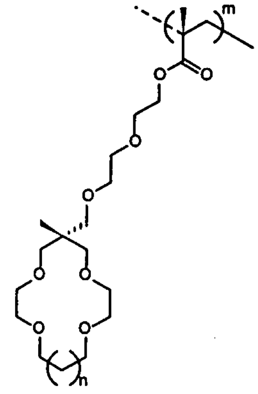
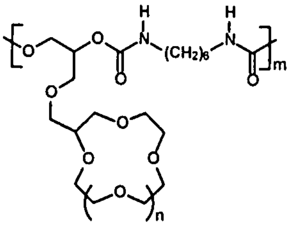


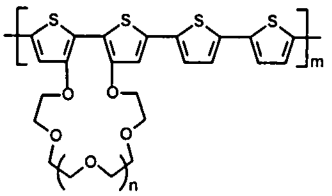
220



221 n = 0
222 n = 1



223 n = 1
224 n = 2
225 n = 3
226 n = 4



227 n = 1
228 n = 2

Figure 2. 29. Examples of polymeric crown ether compounds.

2.10 CONCLUDING REMARK

The more common uses of polymers are found in plastics, e.g. polyethylene bottles, polyesters in clothing, elastomers for tyres and elastic bands or polyurethane paints. More sophisticated uses of polymers are found in medicine, e.g. polymeric drug carriers,[149] supports in solid propellants,[148] the anchoring of catalysts on carrier polymers[154] and as marine paint additive that supports tin as a poison for molluscs.[166]

Although the complexation ability of crown ethers has been known for over three decades,[2] new applications of these special macrocycles are still being discovered. Applications of these macrocycles include the use in NMR as NMR discriminating agents,[167] in ion selective electrodes for mercury(II),[168] in enantiomeric separations in capillary-electrophoresis,[169] and in dyes for the identification of metal ions.[170]

This study attempts to lay foundations towards the use of polymer-bound crown ethers as complexation agents for the removal of group I and II cations from industrial wastewater.

CHAPTER 3

RESULTS AND DISCUSSION

3.1 INTRODUCTION

The synthetic goals of this study were to synthesise various monomeric and polymeric crown ether compounds that could be used to remove Na^+ from industrial wastewater, while supported on a solid support.

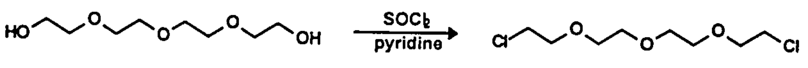
To describe how this was achieved, this chapter will be divided into the following parts:

1. The synthesis of various crown ethers.
2. The functionalisation of these crown ethers to allow anchoring onto a solid support.
3. The synthesis of various pre-polymer crown ether carriers.
4. The anchoring of crown ethers to the pre-polymeric carriers.
5. The anchoring of the pre-polymer crown ether derivatives onto a solid support.

3.2 SYNTHESIS OF CROWN ETHERS

This section will include the syntheses of benzo-15-crown-5 (**11**), benzoaza-15-crown-5 (**241**) and aza-15-crown-5 (**253**). The dialcohol precursors used in the synthesis of these crown ethers were all converted to the dichloride compounds by using the general procedure described by Pedersen.[2] The reaction involves the chlorination of a dialcohol, such as tetraethylene glycol (**229**), with thionyl chloride, to afford the alkyl dichloride derivative **230** (Scheme 3. 1, p. 69).

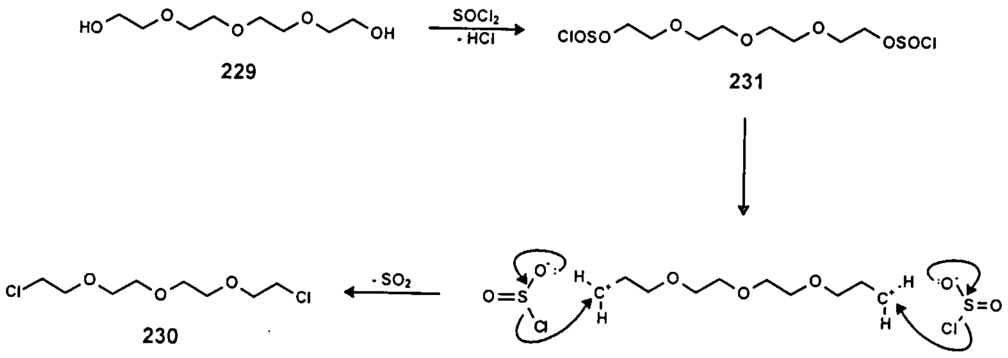
During this reaction the compound is changed from one containing a poor-leaving group, i.e. the alcohol group, to one containing a better leaving group, i.e. the chloride group. This change is accomplished by nucleophilic substitution of the hydroxyl group with a chloride group as shown in Scheme 3. 1, p. 69.



229 **230**

Scheme 3. 1. The chlorination of tetraethylene glycol (229) to produce 1,11-dichloro-3,6,9-trioxaundecane (230).

The first step in the reaction between alcohols and thionyl chloride is the formation of an alkyl chlorosulphite, such as **231**, as seen in Scheme 3. 2. Conversion of the alkyl chlorosulphite **231** to an alkyl chloride **230** involves a S_Ni mechanism (*substitution nucleophilic internal*),[171] and is probably the most important example of this mechanism to date. The first step in this mechanism is (the same as the very first step in a S_N1 mechanism) dissociation into an intimate ion pair[172] involving SO_2Cl^- and a carbocation as in **232**. Then, in the second step, the leaving group, SO_2Cl^-, in particular the Cl part, attacks the carbocation, whilst simultaneously detaching itself from the rest of the leaving group in the process. This leads to the formation of the alkyl dichloride **230** and concomitant SO_2 release.

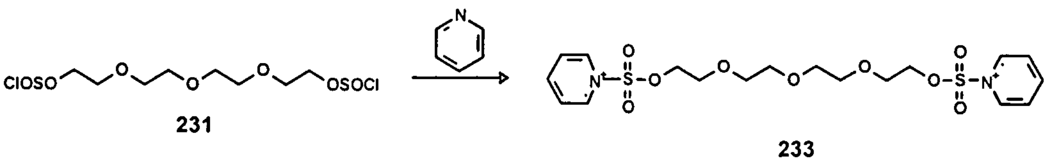


229 **231** **232** **230**

Scheme 3. 2. The S_Ni mechanism during the synthesis of alkyl dichlorides from dialcohols.

Thionyl chloride is the reagent of choice when converting alcohols to alkyl chlorides, due to the formation of the gaseous by-products HCl (g) and SO_2 (g). The yields of these chlorination reactions are usually high (> 90 %).

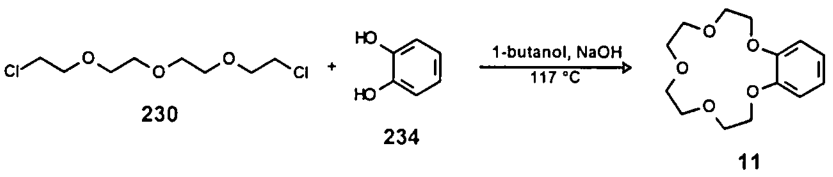
When pyridine is added, as a catalyst and HCl scavenger to the reaction, the intermediate alkyl chlorosulfite **231** reacts with the pyridine to produce **233**, as can be seen in Scheme 3. 3, p. 70.



Scheme 3. 3. The reaction between pyridine and the alkyl chlorosulphite 231.

1,11-Dichloro-3,6,9-trioxaundecane (**230**) is a liquid that was obtained in pure form after solvent removal, and washing of the benzene[‡] solution with water.

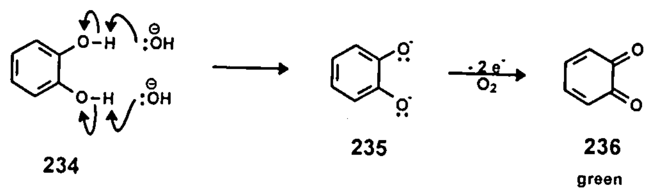
Although it is possible to condense dialcohols, such as tetraethylene glycol (**229**) with catechol (**234**), with a simultaneous release of water, the yields of such reactions are low. In contrast, the condensation of alkyl dichloride compounds, such as 1,11-dichloro-3,6,9-trioxaundecane (**230**) with catechol (**234**), to produce benzo-15-crown-5 (**11**), as the case in Scheme 3. 4, is much higher yielding reactions.



Scheme 3. 4. The synthesis of benzo-15-crown-5 (11) by the condensation reaction between 1,11-dichloro-3,6,9-trioxaundecane (230) and catechol (234).

Often when the synthesis of benzo-15-crown-5 (**11**) was performed in air, the colour of the reaction mixture changed from colourless to green. This green colour can be ascribed to the formation of *o*-quinone (**236**) in the reaction mixture, due to base catalysed oxidation of catechol by oxygen (Scheme 3. 5, p. 71).

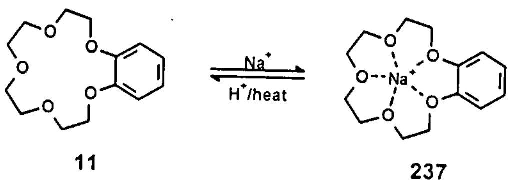
[‡] CAUTION: Benzene is a carcinogen and all reactions with it were conducted in an efficient fume hood, using gloves.



Scheme 3. 5. The formation of *o*-quinone (236) due to the oxidation of the dianion of catechol (234) by oxygen present in the reaction mixture.

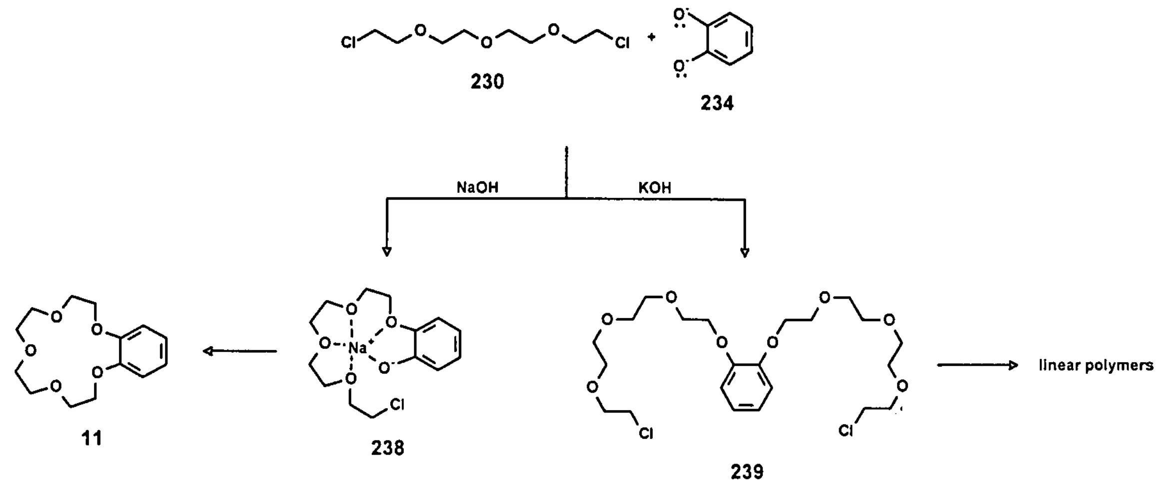
No formation of a green colour was observed when catechol (**234**) was mixed with NaOH in oxygen-free conditions, i.e. under a nitrogen atmosphere.

The synthesis of benzo-15-crown-5 (**11**) requires a base. Here the hydroxyl anion was used to deprotonate catechol (**234**) to produce a nucleophile (**235**) that is able to attack 1,11-dichloro-3,6,9-trioxaundecane (**230**). Two sources of hydroxyl anions were experimented with; NaOH and KOH. This was done because when NaOH is used as the base, condensation of catechol with 1,11-dichloro-3,6,9-trioxaundecane (**230**) would produce a benzo-15-crown-5 (**11**) with a Na^+ filled cavity as seen in Scheme 3. 6. Heating of **237** in an acid media had to be performed to remove Na^+ from the cavity of **237**.



Scheme 3. 6. Na^+ cations may be trapped in the cavity of benzo-15-crown-5 (11) during its synthesis.

It was expected that the use of KOH rather than NaOH as the base in the formation of benzo-15-crown-5 derivatives would result in a metal free crown ether, free of any complexed K^+, because benzo-15-crown-5 (**11**) is not a good co-ordinator of K^+. However, in converting from NaOH to KOH for this synthesis, the yields of benzo-15-crown-5 (**11**) decreased from about 60 % to less than 10 %. This decrease in the yield can be explained by the template effect (Chapter 2, p. 42 – 43), namely that the correct metal cation, in this case the Na^+, is required to direct the long alkyl ether chains towards cyclised product formation (i.e. crown ether formation), rather than linear polymeric ether products (Scheme 3. 7, p. 72).



Scheme 3. 7. The template effect during the synthesis of benzo-15-crown-5 (11).

The synthetic procedure for benzo-15-crown-5 (**11**) produced a dark black, highly viscose liquid. Purification of benzo-15-crown-5 (**11**) from this dark black liquid was achieved by column chromatography for small-scale reactions (< 10 g) or by soxhlet extractor utilising hexane for larger (> 10 g) scale reactions. Benzo-15-crown-5 (**11**) is commercially available at a price of R 308 / g, but during this study, benzo-15-crown-5 (**11**) was synthesised in 30 g batches for a total price of R 10 / g. Benzo-15-crown-5 (**11**) is only moderately soluble in warm hexane, and when cooled it crystallises as white needles, melting point (m.p.) 77 – 79 °C. The yields of benzo-15-crown-5 (**11**) were usually relatively high (50 – 60 %) when the soxhlet extraction method of purification was followed.

As one of the goals of this study, see Chapter 1, is the removal of Na^+ from industrial wastewater, it would be of no use if the ligand, here benzo-15-crown-5 (**11**), was not able to complex the desired cation, here Na^+. A previous study, done by the author,[58] was concerned with this aspect of complexation of Na^+ by benzo-15-crown-5 (**11**) and its derivatives. It was showed that benzo-15-crown-5 (**11**)[58] could complex Na^+ from a sodium source phase into an organic phase. It must be stressed that for the present study this complexation was not done, but for the benefit of the reader, it was deemed essential to discuss some of the results from that study. It was showed that benzo-15-crown-5 (**11**) could complex Na^+ and that this complexation was pH dependent,[58] see Figure 3. 1, p. 73. As seen in Figure 3. 1, p. 73, the most (± 30.61 %) Na^+ is complexed when the pH of the solution is 9.99, and the least (± 15.16 %) Na^+ is complexed when the pH of the solution is 3.02.

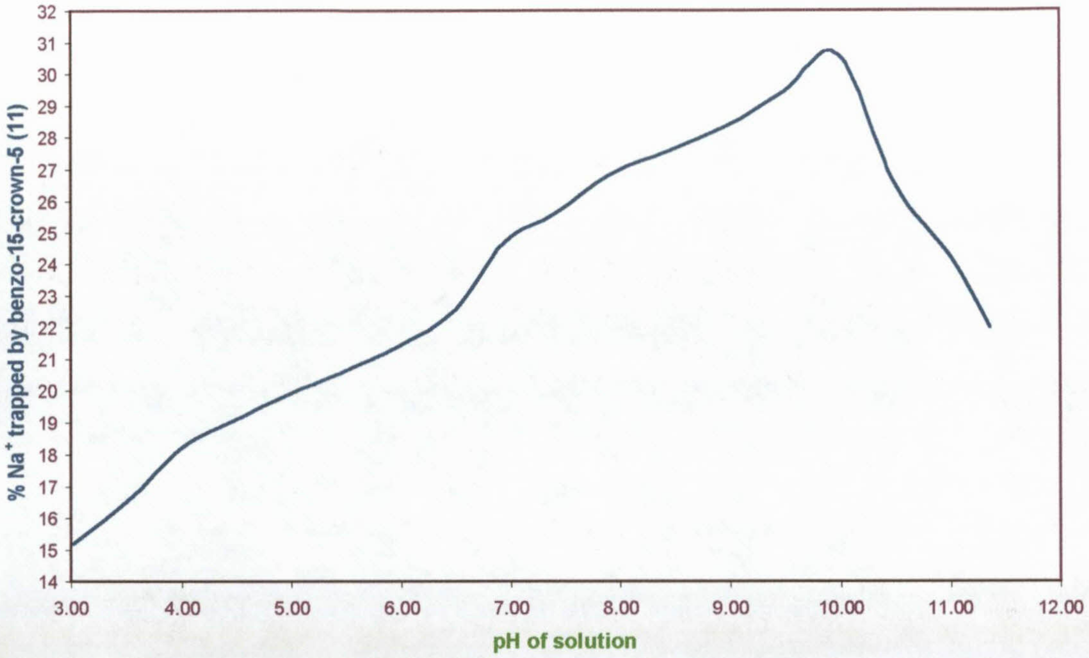
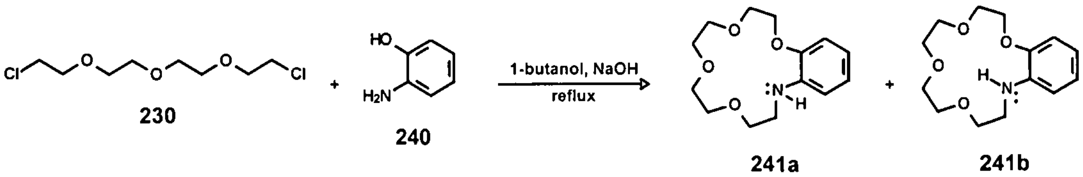


Figure 3. 1. The effect of pH on Na^+ complexation by benzo-15-crown-5 (11).

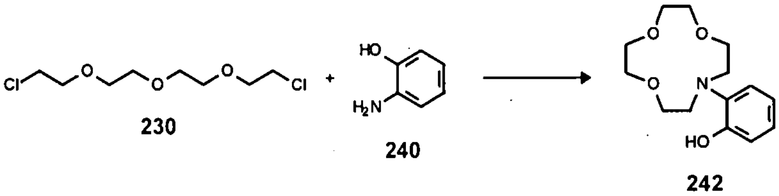
The next type of Na^+ scavenger synthesised was a nitrogen containing crown ether. This choice was made because the aza group can more easily be protonated than the oxygen atoms of benzo-15-crown-5 (**11**). This protonation, to give a positively charge cationic crown ether, would allow easier release of the complexed Na^+ from the nitrogen containing crown ether than from benzo-15-crown-5 (**11**) (see Chapter 2, paragraph 2.5.3, p. 37). For this reason benzoaza-15-crown-5 (**241**) was synthesised. The synthesis of azacoronands, such as benzoaza-15-crown-5 (**241**), is similar to that of the classic crown ethers, except that catechol (**234**) is replaced by 1,2-aminophenol (**240**) as precursor. Although a nitrogen atom replaced one of the oxygen atoms in catechol, the cyclisation mechanism stays the same. To obtain a nitrogen containing sodium cation scavenger, 1,11-dichloro-3,6,9-trioxaundecane (**230**) was treated with the dianion of 1,2-aminophenol, under the influence of NaOH, to produce benzoaza-15-crown-5 (**241**) in low yields (< 20 %), as shown in Scheme 3. 8, p. 74.



Scheme 3. 8. The synthesis of benzoaza-15-crown-5 (241).

Due to the free rotation of the hydrogen atom and the lone electron pair around the nitrogen atom, **241a** and **241b** only differ in the location of the hydrogen. In **241a**, the hydrogen atom is located outside the macroring, while in **241b** the hydrogen atom is located inside the macroring. For a stable crown ether-cation complex, it is wise for the directed lone pair to be located inside the macroring.

The low yields of benzoaza-15-crown-5 (**241**) can be ascribed to the formation of other smaller *N,N*-dialkyl macrocycles, such as **242**, as shown in Scheme 3. 9.



Scheme 3. 9. The formation of smaller macrocycles during the synthesis of benzoaza-15-crown-5 (241).

The synthesis of benzoaza-15-crown-5 (**241**) also produces a dark black, highly viscose liquid. Hydrochloric acid is used to neutralise the excess NaOH, and this can also protonate benzoaza-15-crown-5 (**241**) to produce the hydrochloride salt, which render it insoluble in lipophilic solvents, such as chloroform and hexane. Therefore the purification of benzoaza-15-crown-5 (**241**) needs to be modified to accommodate this new protonated species, in order to increase the yields significantly. One method that was employed to purify benzoaza-15-crown-5 (**241**) was to dissolve this dark black liquid into an aqueous solution with a pH of about 8, and then to extract the product into chloroform. After the organic layer was separated, the purification of benzoaza-15-crown-5 (**241**) was again done by chromatography or soxhlet extraction, to produce the yellowish-white crystalline aza product. Chloroform extraction of the product from the basic aqueous solution increased yields from about 15 % to between 35 – 45 %.

Benzoaza-15-crown-5 (**241**) was tested for its Na$^+$ complexation ability. It was assumed that by containing an aza group, this macrocycle would exhibit a better pH dependence during the complexation of cations than would benzo-15-crown-5 (**11**). The results of this pH dependence during the complexation by Na$^+$ by benzoaza-15-crown-5 (**241**) can be seen in Figure 3. 2. If one look at the blue (—) line (showing the pH dependence of benzoaza-15-crown-5 (**241**) in complexing Na$^+$) it is clear that a downward trend is can be observed.

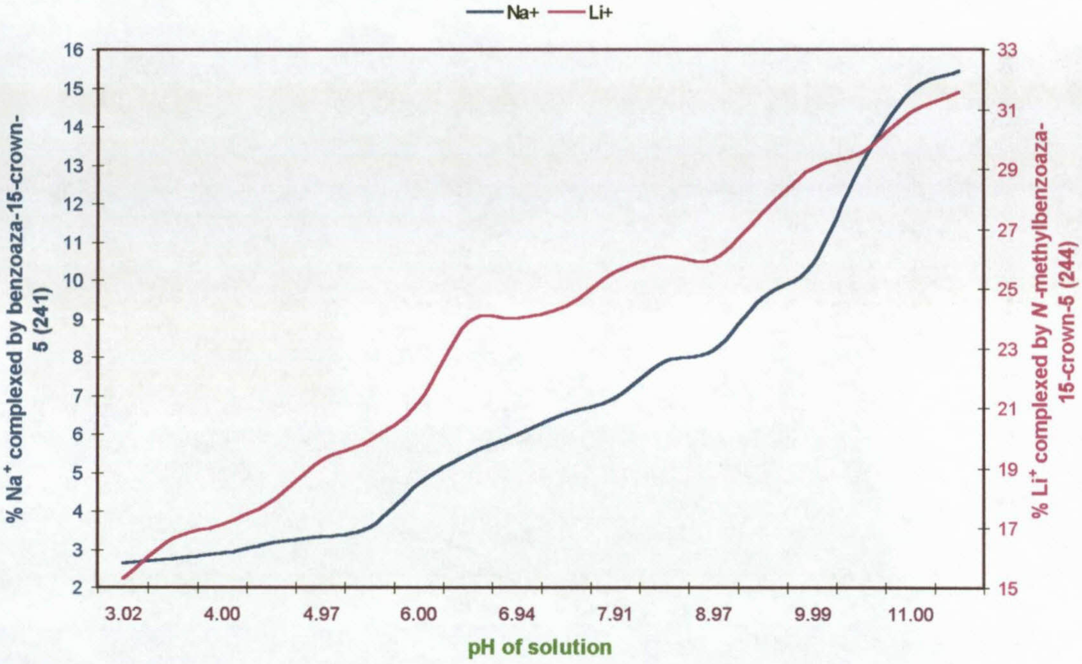
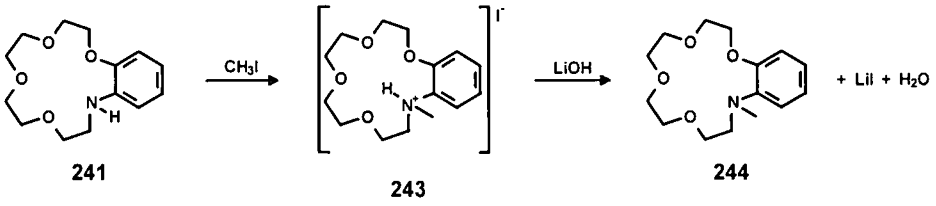


Figure 3. 2. The effect of pH on Na$^+$ (blue (—) line) and Li$^+$ (pink (—) line) complexation by benzo-15-crown-5 (241) and *N*-methylbenzoaza-15-crown-5 (244).

Although there is a pH dependence of benzoaza-15-crown-5 (**241**) for the complexation of Na$^+$, it is clear that the amount of Na$^+$ complexed by the two ligands is not the same. In the complexation of Na$^+$ by benzo-15-crown-5 (**11**), 30.61 % equivalents Na$^+$ was complexed by this crown ether, while benzoaza-15-crown-5 (**241**) only managed 15.45 % Na$^+$. This low complexation can be ascribe to the direction of the lone pair of the nitrogen atom of benzoaza-15-crown-5 (**241**). The presence, or absence, of the hydrogen atom does not direct the lone electron pair[11] of the nitrogen atom to the inside of the aza-crown ether macrocyclic ring (Scheme 3. 8, p. 74). This situation does not preclude the complexation of cations, but it only make the final crown ether-cation complex less stable, due to the fact that not all the donor atoms are involve in the complexation of Na^+.

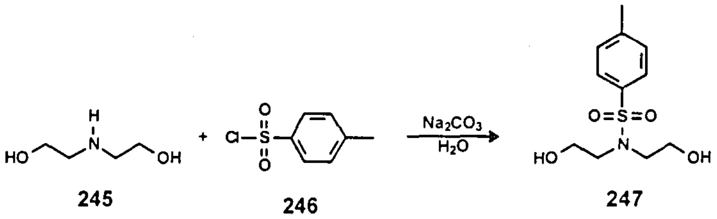
If one can, however, force the lone electron pair of the nitrogen atom to the inside of the macrocyclic ring, one would create a suitable environment for complexation, and thus produce a more stable crown ether-cation interaction, coupled with the same pH dependence of complexation. For this reason it was decided to methylate benzoaza-15-crown-5 (**241**) with methyl iodide to produce *N*-methylbenzoaza-15-crown-5 (**244**) as shown in Scheme 3. 10.



Scheme 3. 10. The synthesis of *N*-methylbenzoaza-15-crown-5 (244).

By the addition of a methyl group to benzoaza-15-crown-5 (**241**), it was hoped that this would force the lone electron pair of the nitrogen atom of benzoaza-15-crown-5 (**241**) in a more suitable position for the complexation of cations, i.e. inside the ring, but outside, because the CH_3-group cannot fit inside the macrocyclic ring of **244**. When the lone electron pair of the nitrogen atom is involved in the complexation of a cation, the total stability of the crown ether-cation complex is increased, but the pH dependence of complexation of cations would still remain. If one look at the pink (—) line in Figure 3. 2, p. 75 (showing the pH dependence of *N*-methylbenzoaza-15-crown-5 (**244**) in its complexation of Li^+), one can clearly see that there is still a pH dependence of cation complexation of *N*-methylbenzoaza-15-crown-5 (**244**). It is also clear that the amount of Li^+ complexed by *N*-methylbenzoaza-15-crown-5 (**244**), 31.56 %, is comparable with the amount of Na^+ complexed by benzo-15-crown-5 (**11**), 30.61 %. This result shows that by the slight modification of a ligand, one can change the preference of the ligand towards a certain cation. In this example, the preference of a ligand was changed from Na^+ to Li^+ by the addition of a methyl group.

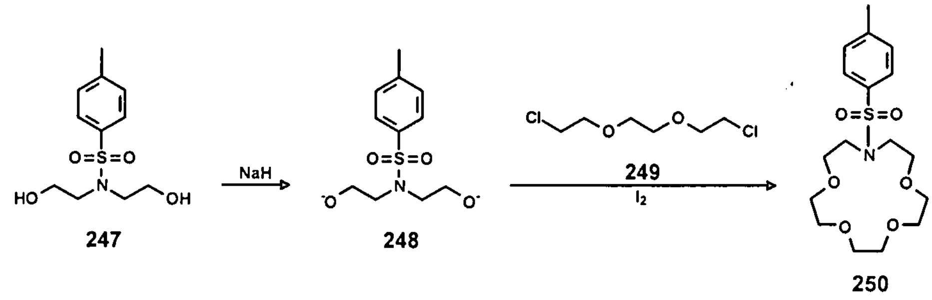
Conformational rigidity or flexibility of macrocycles has a significant influence on their selective behaviour.[4] By incorporating the benzo group as a substituent of aza-15-crown-5 macrorings (i.e. compound **241** for example) the conformational stability of the crown ether-cation complex is enhanced and the flexibility and/or rigidity of the macrocycle is increased.[4] In order to overcome this lower stability and higher rigidity of macrocycle **241**, aza-15-crown-5 (**252**) was synthesised. The first step in the synthesis of aza-15-crown-5 (**252**, Scheme 3. 15, p. 80) is the protection of the nitrogen atom of diethanolamine (**245**), as shown in Scheme 3. 11. This was done to ensure the formation of a cyclic macrocycle and not a bicyclic macrocycle.



Scheme 3. 11. The protection of the nitrogen atom in diethanolamine (245) with toluene-*p*-sulphonyl chloride (246).

In this protection reaction the nitrogen atom of diethanolamine (**245**) serves as a nucleophile, displacing the chloride atom of toluene-*p*-sulphonyl chloride (**246**) to produce *N*-*p*-tolylsulphonyl diethanolamine (**247**). This reaction needs to be performed in the presence of a weak base, such as Na_2CO_3, and at relative high (95 °C) temperatures to ensure that only the *N*-tosylated product is produced. *N*-*p*-Tolylsulphonyl diethanolamine (**247**) was isolated as a white solid, m.p. 129 – 131 °C, after it crystallised from the reaction mixture.

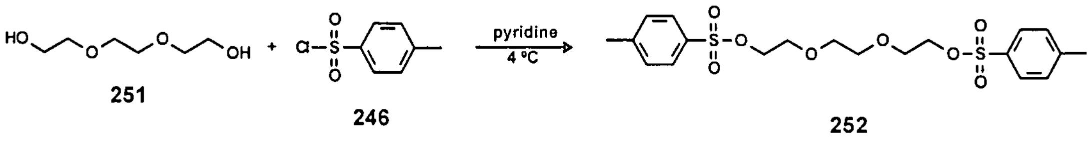
After the nitrogen atom of diethanolamine was protected by toluene-*p*-sulphonyl chloride, the cyclisation of *N*-*p*-tolylsulphonyl diethanolamine (**247**) to produce *N*-tolylsulphonyl aza-15-crown-5 (**249**) was attempted. This cyclisation was at first attempted with 1,8-dichloro-3,6-dioxaoctane (**248**), in the presence of iodine, according to Scheme 3. 12, p. 78. This reaction involves the deprotonation of *N*-*p*-tolylsulphonyl diethanolamine (**247**) by NaH and the subsequent cyclisation of the dianion **248** with 1,8-dichloro-3,6-dioxaoctane (**249**) to produce *N*-tolylsulphonyl aza-15-crown-5 (**250**), as shown in Scheme 3. 12, p. 78.



Scheme 3. 12. The attempted synthesis of *N*-tolylsulphonyl aza-15-crown-5 (249) from the reaction between *N*-*p*-tolylsulphonyl diethanolamine (247) and 1,8-dichloro-3,6-dioxaoctane (248).

This reaction, however, was unsuccessful and is probably due to the relatively poor leaving ability of the chloride groups. Iodine is often used in organic synthesis to enhance the leaving ability of chloride derivatives. The addition of iodine to the reaction depicted in Scheme 3. 12, however, also did not produce the desired product.

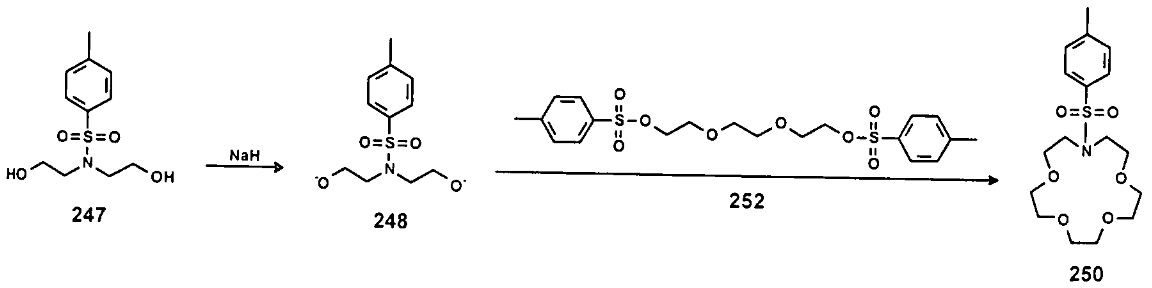
After this failure, it was decided to synthesise a compound that contains a better leaving group than chloride and/or iodide. The tosyl group is a much better leaving group than the chloride group and is often used in organic synthesis as a means of protection and as a leaving group. For this reason triethylene glycol bis-toluene-*p*-sulphonate (**252**) was synthesised by the reaction between triethylene glycol (**251**) and toluene-*p*-sulphonyl chloride (**246**), as shown in Scheme 3. 13.



Scheme 3. 13. The synthesis of triethylene glycol bis-toluene-*p*-sulphonate (252) from the reaction between triethylene glycol (251) and toluene-*p*-sulphonyl chloride (246).

The tosyl group is such a good leaving group that the synthesis of triethylene glycol bis-toluene-*p*-sulphonate (**252**) must be done at low temperatures, i.e. 4 °C. This reaction gave the product **252** as a white crystalline solid, m.p. 78 – 81 °C that must be stored at a temperature of about 4 °C to ensure that decomposition does not occur.

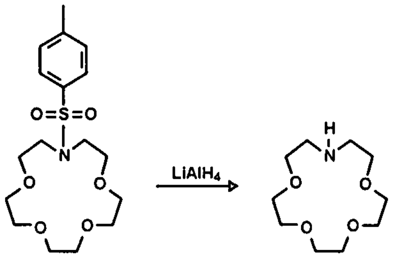
The cyclisation of *N*-*p*-tolylsulphonyldiethanolamine (**247**) and triethylene glycol bis-toluene-*p*-sulphonate (**252**) could then be accomplish. *N*-*p*-Tolylsulphonyldiethanolamine (**247**) was first converted to the corresponding dianion **248**, by treating it with the strong base NaH. During this synthesis a brownish solid was observed after about 1 – 1.5 h. This solid can be ascribed to the formation of the hydrophilic disodium salt of *N*-*p*-tolylsulphonyldiethanolamine. After the addition of triethylene glycol bis-toluene-*p*-sulphonate (**252**) this solid was dissolved to ultimately produce the protected crown ether *N*-tolylsulphonyl aza-15-crown-5 (**250**), according to Scheme 3. 14.



Scheme 3. 14. The synthesis of *N*-tolylsulphonyl aza-15-crown-5 (250) from the reaction between *N*-*p*-tolylsulphonyl diethanolamine (247) and triethylene glycol bis-toluene-*p*-sulphonate (252).

The author found that *N*-tolylsulphonyl aza-15-crown-5 (**250**) could be purified by column chromatography, using hexane:acetone 8:2 as the eluting liquid and by recrystallisation from hexane to liberate the macrocycle as a white crystalline product, m.p. 78 – 81 °C.

The final step in the synthesis of aza-15-crown-5 (**253**) is the deprotection of the nitrogen atom of *N*-tolylsulphonyl aza-15-crown-5 (**250**), by treating *N*-tolylsulphonyl aza-15-crown-5 (**250**) with $LiAlH_4$, as seen in Scheme 3. 15, p. 80. This gave aza-15-crown-5 (**253**) as a white solid, m.p. 36 – 39 °C.



250 253

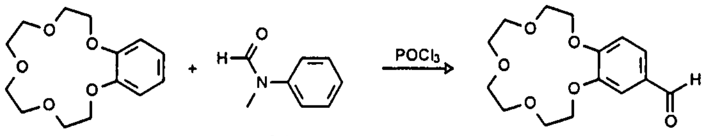
Scheme 3. 15. Deprotection of *N*-tolylsulphonyl aza-15-crown-5 (247) with LiAlH$_4$ liberates aza-15-crown-5 (252).

The overall yield of aza-15-crown-5 (**253**) was low (< 20 %), although the yields of the various reaction steps was high (> 80 %).

3.3 FUNCTIONALISATION OF CROWN ETHERS

In order to obtain a series of benzo-15-crown-5 derivatives that could ultimately be anchored onto a polymeric carrier, it was necessary to functionalise benzo-15-crown-5 (**11**), benzoaza-15-crown-5 (**241**), aza-15-crown-5 (**253**) in such a way that it could be anchored onto a suitable functionalised polymer *via* a covalent bond. For the purpose of this study, alcohol-, carboxylic acid- and amine-functionalised crown ethers were chosen as target compounds.

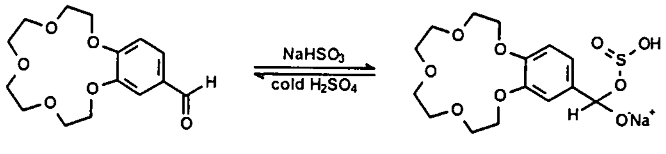
En route to the first alcohol, 4'-formylbenzo-15-crown-5 (**255**) was synthesised under *Vilsmeier* or *Vilsmeier-Haack* conditions[54] according to Scheme 3. 16.



11 254 255

Scheme 3. 16. The synthesis of 4'-formylbenzo-15-crown-5 (255).

The *Vilsmeier* reaction,[54] is the most common method for the formylation of aromatic rings, and involves the reaction of an aromatic group with *N*-methylformanilide (**254**) in the presence of phosphoryl chloride. During the purification of 4'-formylbenzo-15-crown-5 (**255**), one can treat it with sodium hydrogensulphite, which precipitate the aldehyde, as seen in Scheme 3. 17.



255 **256**

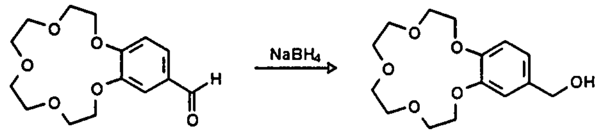
Scheme 3. 17. The purification of 4'-formylbenzo-15-crown-5 (255) with sodium hydrogensulphite.

Compound **256** is a salt that could easily be removed from the reaction mixture and it gave 4'-formylbenzo-15-crown-5 (**255**) upon treatment with sulphuric acid. This procedure produced 4'-formylbenzo-15-crown-5 (**255**) as a clean product. However, it was found that sulphuric acid-induced decomposition of **256** in liberating clean 4'-formylbenzo-15-crown-5 (**255**) was very much temperature dependent. Yields were often low (20 – 30 %) and on a warm day yields would fall to below 5 %. Although column chromatography is a viable alternative purification method, this is not the purification method of choice for large-scale reactions. It was found that, as in the case of benzo-15-crown-5 (**11**), 4'-formylbenzo-15-crown-5 (**255**) are sparingly soluble in warm hexane and could thus be crystallised from it after a soxhlet extraction. This purification method drastically increased the yields of the overall reaction to between 50 – 60 % and gave 4'-formylbenzo-15- crown-5 (**255**) as a white crystalline solid, with m.p. 77 – 81 °C.

The goals of this study, see Chapter 1, was to anchor functionalised crown ether derivatives onto a solid support for the purpose of removing Na$^+$ from a sodium contaminated source phase. Being the first functionalised crown ether that was synthesised, it was decided to see if this functionalisation would influence the Na$^+$ complexation of the crown ether moiety in any way. It was found that the aldehyde functionalisation did not alter the Na$^+$ complexation ability of 4'-formylbenzo-15-crown-5 (**255**), compared to benzo-15-crown-5 (**11**).

To obtain the first alcohol functionalised derivative of benzo-15-crown-5, 4'-formylbenzo-15-crown-5 (**255**) was reduced with NaBH$_4$, to produce

4'-(hydroxymethyl)benzo-15-crown-5 (**257**), as a white solid, m.p. 45 – 47 °C (Scheme 3. 18).



255 **257**

Scheme 3. 18. The synthesis of 4'-(hydroxymethyl)benzo-15-crown-5 (257) by the treatment of 4'-formylbenzo-15-crown-5 (255) with $NaBH_4$.

4'-(Hydroxymethyl)benzo-15-crown-5 (**257**) may be anchored, for example, onto a polymeric carrier that has isocyanate functional groups on it *via* a urethane bond, or to an acid functionalised polymer *via* an ester functional group. 4'-(Hydroxymethyl)benzo-15-crown-5 (**257**) has one methylene (i.e. CH_2) spacer separating the benzo-15-crown-5 moiety from the alcohol functional group. However, it was envisaged that the sodium cation scavenging properties of a crown ether that is immobilised on a polymer support, may be influence by the distance between the polymeric support and the crown ether moiety. It was thus decided to systematically lengthen the side chain length between the alcohol functional group and the benzo-crown ether moiety from one methylene spacer (as in 4'-(hydroxymethyl)benzo-15-crown-5 (**257**)) all the way up to four methylene spacers. For this purpose, the series of carboxylic acid derivatives **258** – **261** showed in Figure 3. 3, p. 83, were deemed the most appropriate precursors, not only for alcohol synthesis, but also for the synthesis of amine functionalised crown ethers.

4'-Carboxybenzo-15-crown-5 (**258**) was synthesised, by the multistep synthetic route depicted in Scheme 3. 19, p. 83, from 4'-formylbenzo-15-crown-5 (**255**).

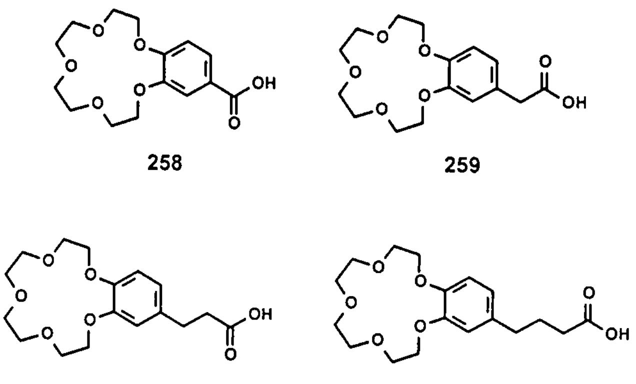
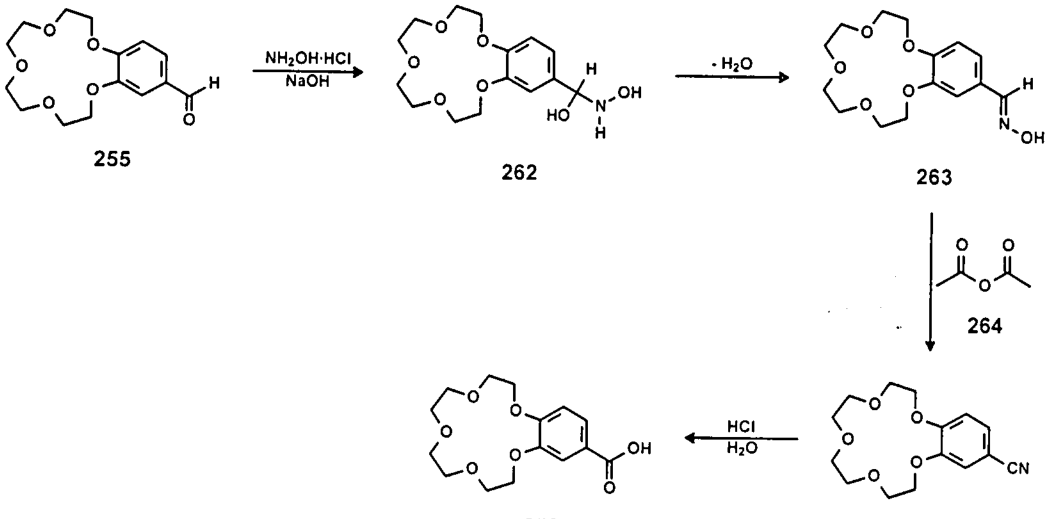


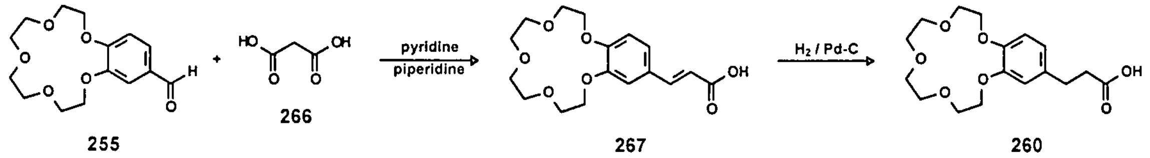
Figure 3. 3. A series of carboxylic acid functionalised benzo-15-crown-5 derivatives for the ultimate anchoring of these onto the polymeric carriers.



Scheme 3. 19. The multistep synthesis of 4'-carboxybenzo-15-crown-5 (258) from 4'-formylbenzo-15-crown-5 (255).

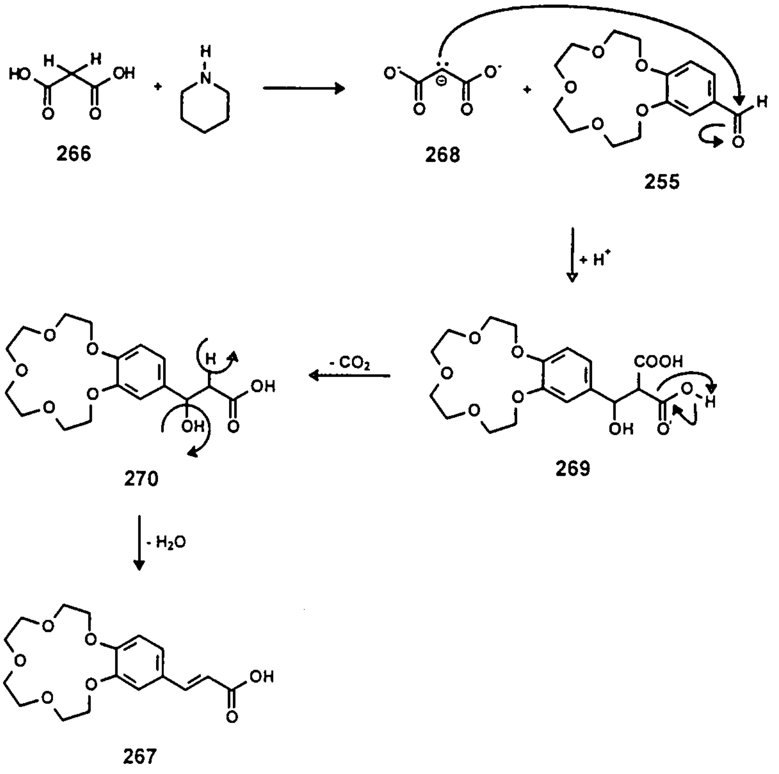
The first part of the reaction involves the addition of hydroxylamine (by nucleophilic attack of the nitrogen atom of hydroxylamine on the carbonyl carbon of 4'-formylbenzo-15-crown-5 (**255**)) to produce the oxime functionalised compound, 4'-(oximinomethyl)benzo-15-crown-5 (**263**) after the dehydration of the intermediate **262** in high yields (> 95 %)[173]. The product, 4'-(oximinomethyl)-benzo-15-crown-5 (**263**) can be purified by crystallisation from 50 % aqueous ethanol (v/v), to obtain 4'-(oximinomethyl)benzo-15-crown-5 (**262**) as a white solid, m.p. 61 – 64 °C. Dehydration of **263** by acetic anhydride (**264**), liberates the nitrile functionalised compound 4'-cyanobenzo-15-crown-5 (**265**), also in high yield (> 95 %). This product needs to be washed thoroughly with water to remove the acetic acid formed. After the organic layer is removed the product can be obtained as a white solid, m.p. 81 – 84 °C. Finally, hydrolysis of 4'-cyanobenzo-15-crown-5 (**265**) in the presence of HCl produces 4'-carboxybenzo-15-crown-5 (**258**) in high yield (> 80 %). Although basic hydrolysis of 4'-cyanobenzo-15-crown-5 (**265**) is also possible, the acid hydrolysis was preferred, due to the fact that the crown ether moiety is a selective sodium cation scavenger. NaOH catalysed hydrolysis of 4'-cyanobenzo-15- crown-5 (**265**) would produce a crown ether with a Na^+ filled cavity, rather than one with an empty cavity. The purification of 4'-carboxybenzo-15-crown-5 (**258**) could be accomplished by recrystallisation from 20 % aqueous ethanol solution (v/v), to produce a white solid, m.p. 188 – 191 °C.

The synthesis of 4'-(propanoic acid)benzo-15-crown-5 (**260**), was easily accomplished from 4'-formylbenzo-15-crown-5 (**255**) *via* the intermediate 4'-(acrylic acid)benzo-15-crown-5 (**267**, Scheme 3. 20). To obtain 4'-(acrylic acid)benzo-15-crown-5 (**267**) a *Knoevenagel condensation reaction*[174] between 4'-formylbenzo-15-crown-5 (**255**) and malonic acid (**266**) in the presence of piperidine and pyridine was performed.



Scheme 3. 20. The synthesis of 4'-(propanoic acid)benzo-15-crown-5 (260), according to a *Knoevenagel type reaction*, followed by the hydrogenation of 4'-(acrylic acid)benzo-15-crown-5 (267).

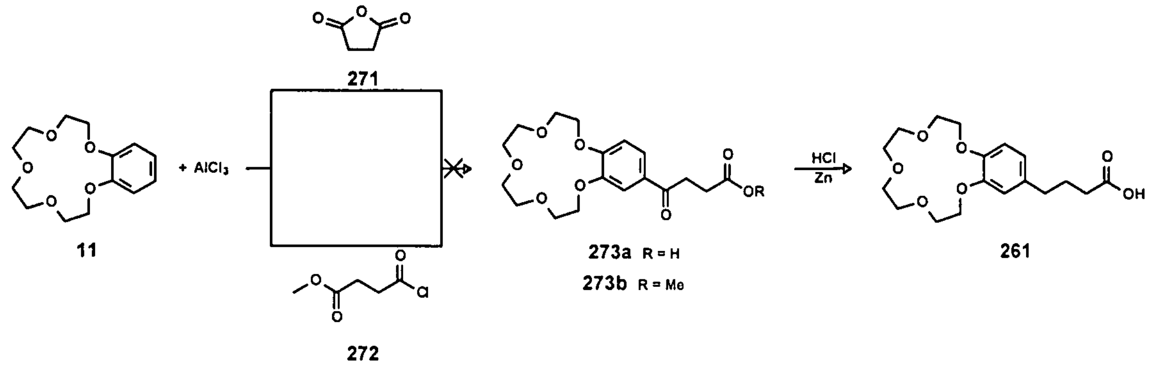
This reaction involves the deprotonation of the very acidic α-hydrogen of malonic acid (**266**) by piperidine to produce the carbanion **268**. The carbanion **268** then attacks the carbonyl carbon of 4'-formylbenzo-15-crown-5 (**255**) to produce **269**. Compound **269** then undergoes a series of rearrangements followed by decarboxylation and finally dehydration to produce the α,β-unsaturated acid 4'-(acrylic acid)benzo-15-crown-5 (**267**) in high yields (> 80 %).



Scheme 3. 21. The mechanism for the formation of the α,β-unsaturated acid derivative 4'-(acrylic acid)benzo-15-crown-5 (267).

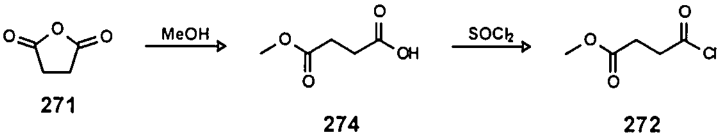
Although the *cis*-isomer of this α,β-unsaturated acid, 4'-(acrylic acid)benzo-15-crown-5 (**267**), is also possible, only the *trans*-isomer was isolated due to the high temperatures used during the synthesis of 4'-(acrylic acid)benzo-15-crown-5 (**267**). The α,β-unsaturated acid 4'-(acrylic acid)benzo-15-crown-5 (**267**) was subsequently transformed into the saturated acid compound, 4'-(propanoic acid)benzo-15-crown-5 (**260**), in high yields (> 90 %) by heterogeneous hydrogenation over 10 % palladium-on-carbon as the catalyst (Scheme 3. 20, p. 84).

The synthesis of 4'-(butanoic acid)benzo-15-crown-5 (**261**) proved to be very troublesome. The first synthetic strategy pursued during the course of this study was *Friedel-Crafts acylation* of benzo-15-crown-5 (**11**) with succinic anhydride (**271**) and/or methyl succinyl chloride (**272**) and the subsequent *Clemmensen reduction* of **273** to produce 4'-(butanoic acid)benzo-15-crown-5 (**261**), as depicted in Scheme 3. 22, p. 86.



Scheme 3. 22. The attempted synthesis of 273 from the reaction between succinic anhydride (271) and methyl succinyl chloride (272), with benzo-15-crown-5 (11), respectively. In practice it was found that *Friedel-Crafts acylation* experimental conditions destroyed the macrocyclic ring.

Methyl succinyl chloride (**272**) was obtained from the reaction between succinic anhydride (**271**) and methanol to yield the mixed acid ester **274** followed by chlorination with thionyl chloride, as seen in Scheme 3. 23. During the synthesis of methyl succinate (**274**) the methanol acted both as solvent and nucleophile. Methyl succinate (**274**) is a white solid with m.p. 54 – 57 °C, while methyl succinyl chloride (**272**) is a yellowish liquid.

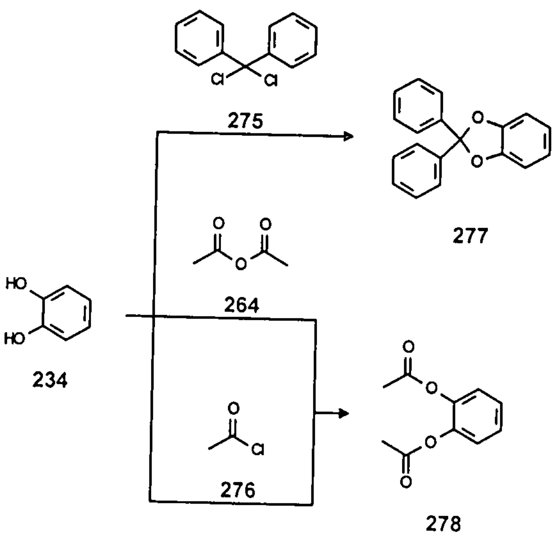


Scheme 3. 23. The synthesis of methyl succinyl chloride (272) from succinic anhydride (271).

The reaction depicted in Scheme 3. 22, however, did not give the desired product **273**, and ^{1}H NMR suggested that the macrocyclic ring of **273** was destroyed during its synthesis. This destruction of the macrocyclic ring can be ascribed to the use of the *Friedel-Crafts catalyst* aluminium chloride, $AlCl_3$, and liberated HCl, both of which catalyses ether bond cleavage.

It was therefore decided to first protect catechol (**234**), then to convert this protected compound to a carboxylic acid derivative with succinic anhydride (**271**) or methyl succinyl chloride (**272**), and finally to obtain the carboxylic acid functionalised 4'-(butanoic acid)benzo-15-crown-5 (**261**) by the deprotection of the catechol (**234**) and the subsequent cyclisation with 1,11-dichloro-3,6,9-trioxaundecane (**230**).

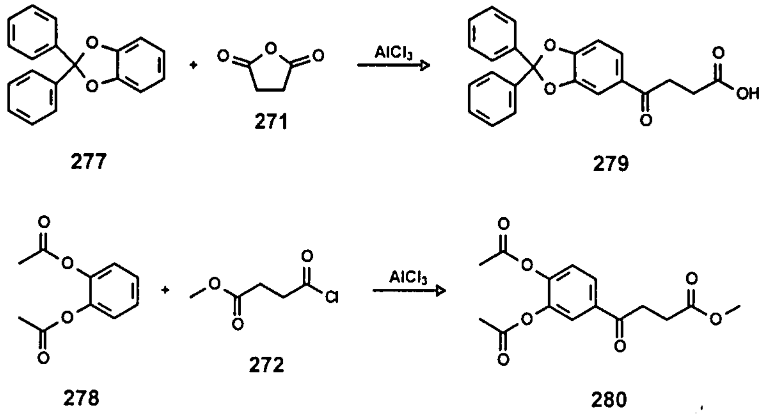
The protection of the alcohol groups of catechol (**234**) was achieved by using two different methods of protection. The first method involved oxetane formation with the diphenylmethane group as shown in compound **277**, while the second method involved acetylation of the alcohol groups with both acetic anhydride (**264**) and acetyl chloride (**276**) *via* ester groups as shown in compound **278**. The protection of catechol (**234**), with both these groups can be seen in Scheme 3. 24.



Scheme 3. 24. The protection of catechol (234) by diphenyldichloromethane (275) and acetic anhydride (264) or acetyl chloride (276) to produce an oxetane (277) or a diester (278), respectively.

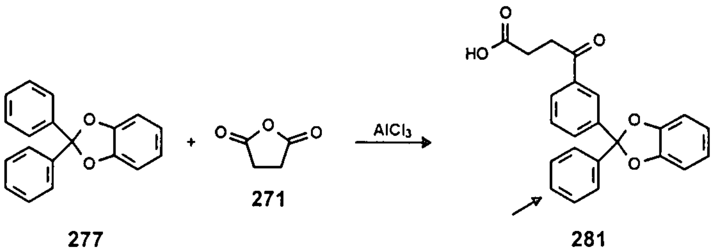
The reaction between catechol (**234**) and diphenyldichloromethane (**275**) gave the oxetane **277** as a black viscose liquid, while the reaction between catechol (**234**) and acetic anhydride (**264**) or acetyl chloride (**276**) gave the diester **278** as a white solid, m.p. 62 – 63 °C.

After this protection step, oxetane **277** and the diester **278** was treated with succinic anhydride (**271**) and methyl succinyl chloride (**272**) respectively, as shown in Scheme 3. 25, p. 88.



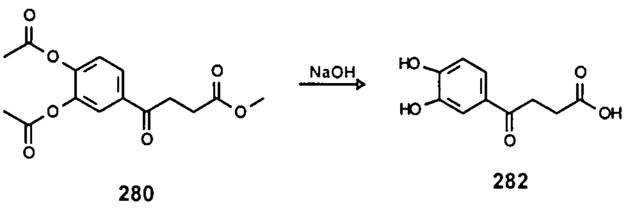
Scheme 3. 25. The *Friedel-Crafts acylation* of the oxetane 277 and the diester 278 with succinic anhydride (271) and methyl succinyl chloride (272), respectively.

The reaction between the oxetane **277** and succinic anhydride (**271**) did not give **279** as acylation was found to occur on the wrong benzene ring(s) as shown in Scheme 3. 26. However, acylation of **278** with the mixed ester/acid chloride **272** to give **280** was successful.



Scheme 3. 26. One of the possible side reactions during the *Friedel-Crafts acylation* of the oxetane 277 and succinic anhydride (271). Acylation could also occur on the second non-catechol phenyl ring (indicated by the arrow).

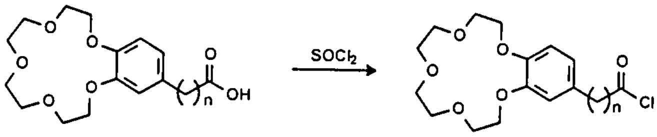
In order to obtain a crown ether derivative from the protected catechol **280**, hydrolyses of the ester groups, as shown in Scheme 3. 27, were first performed.



Scheme 3. 27. The deprotection of the triester 280 to produce the derivatised catechol 282.

Although the triester **280** were successfully converted to **282**, this route was also abandoned to obtain 4'-(butanoic acid)benzo-15-crown-5 (**261**) due the rigorous multistep synthesis and low yields of the intermediates.

The *Arndt-Eistert* synthesis[175] (elongation of the chain length of a carboxylic acid derivative with one methylene group by diazomethane) on the other hand was expected to be less rigorous and it is not expected to destroy the macrocyclic crown ether ring, as was the case with *Friedel-Craft acylation* (Scheme 3. 22, p. 86). In order for the *Arndt-Eistert* synthesis to be successful, a carboxylic acid functionalised derivative must first be converted to the corresponding acyl chloride, as depicted in Scheme 3. 28. For the purpose of this study, to obtain the acids 4'-(ethanoic acid)benzo-15-crown-5 (**259**) and 4'-(butanoic acid)benzo-15-crown-5 (**261**) (Figure 3. 3, p. 83), the acids 4'-carboxybenzo-15-crown-5 (**258**) and 4'-(propanoic acid)benzo-15-crown-5 (**259**) was converted to acid chlorides 4'-(carbonyl chloride)benzo-15-crown-5 (**283**) and 4'-(propanoyl chloride)benzo-15-crown-5 (**284**), respectively. This reaction is very similar to that of the chlorinations of the dialcohols (Scheme 3. 1, p. 69). Thionyl chloride was the chlorination reagent of choice, because the by-products are all gases and the acyl chloride can easily be isolated in very high yields (> 95 %).

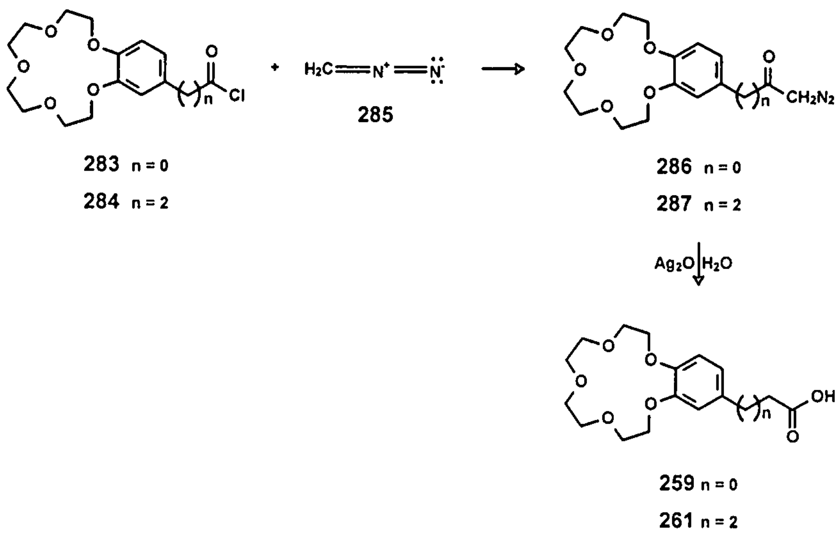


258 n = 0
260 n = 2

283 n = 0
284 n = 2

Scheme 3. 28. The conversion of the carboxylic acid derivatives 4'-carboxybenzo-15-crown-5 (258) and 4'-(propanoic acid)benzo-15-crown-5 (260) to the corresponding acid chlorides 4'-(carbonyl chloride)benzo-15-crown-5 (283) and 4'-(propanoyl chloride)benzo-15-crown-5 (284), respectively.

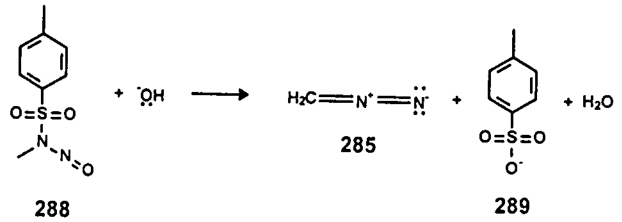
Carboxylic acids 4'-(ethanoic acid)benzo-15-crown-5 (**259**) and 4'-(butanoic acid)benzo-15-crown-5 (**261**) were subsequently synthesised from these two acids according to the *Arndt-Eistert reaction*, as seen in Scheme 3. 29, p. 90.



Scheme 3. 29. The synthesis of carboxylic acids 4'-(ethanoic acid)benzo-15-crown-5 (259) and 4'-(butanoic acid)benzo-15-crown-5 (261) from the acyl chlorides 4'-(carbonyl chloride)benzo-15-crown-5 (283) and 4'-(propanoyl chloride)benzo-15-crown-5 (284), respectively.

First, the acid chlorides 4'-(carbonyl chloride)benzo-15-crown-5 (**283**) and 4'-(propanoyl chloride)benzo-15-crown-5 (**284**) were reacted with diazomethane[$] (**285**) to produce the diazo ketone compounds **286** and **287**. When these diazo ketones compounds **286** and **287** were reacted with water in the presence of silver oxide, the carboxylic acids 4'-(ethanoic acid)benzo-15-crown-5 (**259**, m.p. 95 – 98 °C) and 4'-(butanoic acid)benzo-15-crown-5 (**261**, m.p. 78 – 81 °C), with one more carbon atom than the parent compound, were obtained. During this reaction the methylene group is not inserted into the side chain, but migration of the side chain (the so-called *Wolf rearrangement*)[175] took place to produce the carboxylic acids 4'-(ethanoic acid)benzo-15-crown-5 (**259**) and 4'-(butanoic acid)benzo-15-crown-5 (**261**). Diazomethane (**285**) is obtained by the reaction between diazald (**288**) and ethanolic potassium hydroxide in the presence of diethyl ether, as depicted in Scheme 3. 30, p. 91.

[$] CAUTION: Diazomethane is extremely explosive and poisonous. Appropriate safety precautions must be taken during its synthesis. Fume-hood, gloves, etc.



Scheme 3. 30. The synthesis of diazomethane (285) from diazald (288).

The series of carboxylic acids-functionalised benzo-15-crown-5 derivatives in Figure 3. 3, p. 83, were thus successfully synthesised, although not all of them directly from the parent compound benzo-15-crown-5 (**11**).

Due to the ease of synthesis of the carboxylic acid functionalised derivatives of benzo-15-crown-5 as seen in Figure 3. 3, p. 83, it was decided that amide functionalised derivatives of benzo-15-crown-5 would also be synthesised, and that these would then subsequently be reduced to the corresponding amine functionalised derivatives of benzo-15-crown-5. The series of amide functionalised derivatives of benzo-15-crown-5 can be seen in Figure 3. 4.

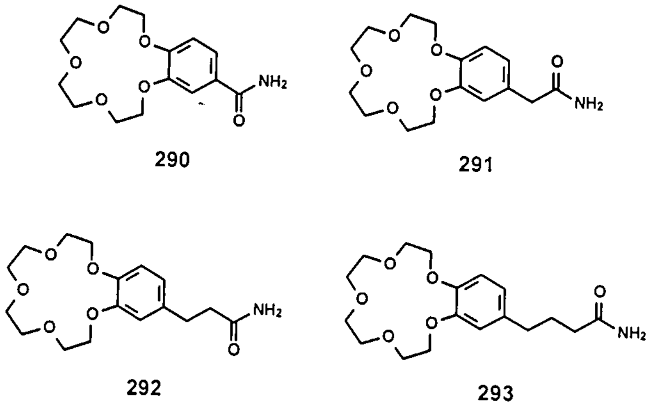
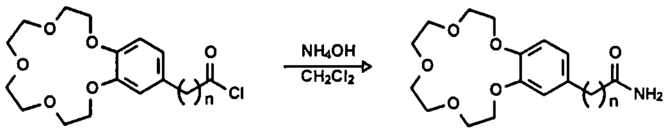


Figure 3. 4. A series of amide functionalised derivatives of benzo-15-crown-5.

4'-Amidobenzo-15-crown-5 (**290**) and 4'-(propylamide)benzo-15-crown-5 (**292**) was synthesised from the reaction between the acid chlorides 4'-(carbonyl chloride)benzo-15-crown-5 (**283**) and 4'-(propanoyl chloride)benzo-15-crown-5 (**284**) and aqueous ammonium hydroxide in a biphasic reaction system, as seen in Scheme 3. 31, p. 92.

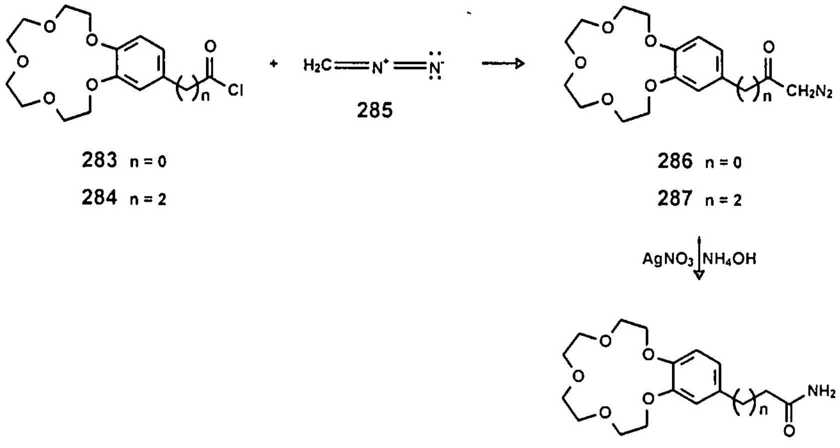


283 n = 0
284 n = 2

290 n = 0
292 n = 2

Scheme 3. 31. The synthesis of 4'-amidobenzo-15-crown-5 (290) and 4'-(propylamide)benzo-15-crown-5 (292) from 4'-(carbonyl chloride)benzo-15-crown-5 (283) and 4'-(propanoyl chloride)benzo-15-crown-5 (284), respectively.

Yields exceeded > 80 % at room temperature, to give the products as yellow solids, m.p. 188 – 189 °C (4'-amidobenzo-15-crown-5 (**290**)) and 119 – 120 °C (4'-(propylamide)benzo-15-crown-5 (**292**)). The other two amides, 4'-(ethylamide)benzo-15-crown-5 (**291**) and 4'-(butylamide)benzo-15-crown-5 (**293**) were synthesised according to a modified *Arndt-Eistert reaction*, as depicted in Scheme 3. 32.



283 n = 0
284 n = 2

286 n = 0
287 n = 2

291 n = 0
293 n = 2

Scheme 3. 32. The synthesis of 4'-(ethylamide)benzo-15-crown-5 (291) and 4'-(butylamide)benzo-15-crown-5 (293) from 4'-(carbonyl chloride)benzo-15-crown-5 (283) and 4'-(propanoyl chloride)benzo-15-crown-5 (284), respectively.

Instead of using water and silver oxide, as in Scheme 3. 29, p. 90, ammonium hydroxide and silver nitrate, Scheme 3. 32, were used to produce the amides 4'-(ethylamide)benzo-15-crown-5 (**291**) and 4'-(butylamide)benzo-15-crown-5 (**293**) with one more methylene group in the side chain than the parent acid chloride. 4'-(Butylamide)benzo-15-crown-5 (**293**) was obtained as a yellow solid, m.p. 113 – 115 °C. 4'-(Ethylamide)benzo-15-crown-5 (**291**) could, however, not successfully be synthesised according to Scheme 3. 32, p. 92. Several attempts failed. Alternative synthetic methods may involve *inter alia* the photolysis of the diazo ketone **286** to produce 4'-(ethylamide)benzo-15-crown-5 (**291**), but this reaction was not investigated, due to the fact that 4'-(ethylamide)benzo-15-crown-5 (**291**) was not regarded as an essential component of this study.

The reduction of the amide functionalised derivatives 4'-amidobenzo-15-crown-5 (**290**), 4'-(propylamide)benzo-15-crown-5 (**292**) and 4'-(butylamide)benzo-15-crown-5 (**293**) to the amine functionalised derivatives, 4'-(aminomethyl)benzo-15-crown-5 (**294**), 4'-(aminopropyl)benzo-15-crown-5 (**296**) and 4'-(aminobutyl)benzo-15-crown-5 (**297**), to obtain a series of amino functionalised derivatives of benzo-15-crown-5, as seen in Scheme 3. 33, were performed. This reduction is very similar to the reduction of carboxylic acids to alcohols. $LiAlH_4$ was used as the reducing agent and the reaction produces the amines in good yields (± 80 %). 4'-(Aminomethyl)benzo-15-crown-5 (**294**) was isolated as a yellow solid, m.p. 85 – 88 °C, while 4'-(aminopropyl)benzo-15-crown-5 (**296**) and 4'-(aminobutyl)benzo-15-crown-5 (**297**) were light yellow liquids.

290 n = 0
291 n = 1
292 n = 2
293 n = 3

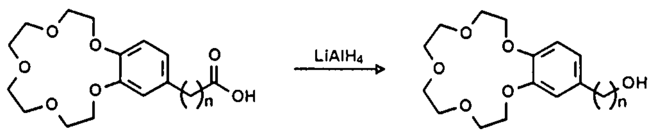
294 n = 1
295 n = 2
296 n = 3
297 n = 4

Scheme 3. 33. $LiAlH_4$ reduction of the amide derivatives 290, 292 and 293 to the corresponding amine derivatives 4'-(aminomethyl)benzo-15-crown-5 (294), 4'-(aminopropyl)benzo-15-crown-5 (296) and 4'-(aminobutyl)benzo-15-crown-5 (297). The unavailability of 4'-(ethylamide)benzo-15-crown-5 (291) implied that 4'-(aminoethyl)benzo-15-crown-5 (295) could not be synthesised.

The unavailability of 4'-(ethylamide)benzo-15-crown-5 (**291**) implied that 4'-(aminoethyl)benzo-15-crown-5 (**295**) could not be obtained following the path shown in Scheme 3. 33. Although several alternative methods for the synthesis of 4'-(aminoethyl)benzo-15-crown-5 (**295**) were experimented with, including a

Hofmann rearrangement reaction on 4'-(propylamide)benzo-15-crown-5 (**292**) under the influence of Br_2 and NaOH, and the chlorination of 4'-(hydroxymethyl)benzo-15-crown-5 (**257**) with $SOCl_2$, followed by cyanation and the subsequent $LiAlH_4$ reduction, all of these methods failed. Although it would have been good to have 4'-(aminoethyl)benzo-15-crown-5 (**295**) as part of the amine series of this study, the available time for this study eventually caused the author to stop pursuing the synthesis of 4'-(aminoethyl)benzo-15-crown-5 (**295**). This decision was made after due consideration was given to the fact that the available amines **294**, **296** and **297** would sufficiently demonstrate whether amine functionalised crown ethers can be anchored onto a solid support and whether these polymeric devices can be used to remove Na^+ from factory wastewater.

The $LiAlH_4$ reduction of the carboxylic acid functionalised derivatives 4'-carboxybenzo-15-crown-5 (**258**), 4'-(ethanoic acid)benzo-15-crown-5 (**259**), 4'-(propanoic acid)benzo-15-crown-5 (**260**) and 4'-(butanoic acid)benzo-15-crown-5 (**261**) to the alcohol functionalised derivatives 4'-(hydroxymethyl)benzo-15-crown-5 (**257**), 4'-(hydroxyethyl)benzo-15-crown-5 (**298**), 4'-(hydroxypropyl)-benzo-15-crown-5 (**299**) and 4'-(hydroxybutyl)benzo-15-crown-5 (**300**), to obtain a series of alcohol functionalised derivatives of benzo-15-crown-5, as seen in Scheme 3. 34 were performed. 4'-(Hydroxymethyl)benzo-15-crown-5 (**257**) was also synthesised by $NaBH_4$ reduction of 4'-formylbenzo-15-crown-5 (**255**, Scheme 3. 18, p. 82), and the author found the latter synthesis gave higher yields than the $LiAlH_4$ reduction of 4'-carboxybenzo-15-crown-5 (**258**, Scheme 3. 34).



258 n = 0
259 n = 1
260 n = 2
261 n = 3

257 n = 1
298 n = 2
299 n = 3
300 n = 4

Scheme 3. 34. $LiAlH_4$ reduction of the carboxylic acid derivatives 258, 259, 260 and 261 to the corresponding alcohol functionalised derivatives 4'-(hydroxymethyl)benzo-15-crown-5 (257), 4'-(hydroxyethyl)benzo-15-crown-5 (298), 4'-(hydroxypropyl)benzo-15-crown-5 (299) and 4'-(hydroxybutyl)benzo-15-crown-5 (300).

In conclusion to this part of this study then, four different series of benzo-15-crown-5 derivatives has been synthesised. These include 17 new benzo-15-crown-5 derivatives containing the carboxylic acids- (Figure 3. 3, p. 83), the amides- (Figure 3. 4, p. 91), the amines- (Scheme 3. 33, p. 93) and alcohol-functionalities (Scheme 3. 18, p. 82, and Scheme 3. 34, p. 94). Most of these compounds were anchored onto the polymeric carriers for the ultimate use as sodium cation scavenging devices, but this will be discussed in paragraph 3.5.

3.3.1 Infrared spectroscopy comparison between selected benzo-15-crown-5 functionalised derivatives

The 17 newly synthesised benzo-15-crown-5 derivatives, as well as their precursors, display a variety of functional groups. The IR spectra of selected benzo-15- crown-5 derivatives can be seen in Figure 3. 5, p. 96. Although a whole series of side chain lengths were synthesised, for the conservation of space, it was decided to compare only selected IR spectra of benzo-15-crown-5 functionalised derivatives, i.e. benzo-15-crown-5 (**11**), 4'-formylbenzo-15-crown-5 (**255**), 4'-carboxybenzo-15-crown-5 (**258**), 4'-amidobenzo-15-crown-5 (**290**) and 4'-(aminomethyl)benzo-15-crown-5 (**294**). If one examine Figure 3. 5, p. 96, and one look at the IR spectrum of benzo-15-crown-5 (**11**, dark red (—) line), the most characteristic signals are the ones originating from the aromatic ring (2872 – 2914 and 1458 – 1593 cm^{-1}) and from the ether bonds (1077 – 1239 cm^{-1}). These two sets of signals occur in all of the other spectra, and therefore they will not be discussed for the other compounds in the series, but only the characteristic signals of the other functional signals present in these compounds. If one examine the IR spectrum of 4'-formylbenzo-15-crown-5 (**255**, green (—) line) the carbonyl signal at 1686 cm^{-1}, is clearly observed. The carbonyl signal at 1686 cm^{-1} is also visible in the IR spectrum of 4'-carboxybenzo-15-crown-5 (**258**, blue (—) line), and the hydroxy group can also be seen at 2593 – 2664 and 3210 – 3450 cm^{-1}. In the examination of the IR spectrum of 4'-amindobenzo-15-crown-5 (**290**, red (—) line) the presence of the amino group (3160 – 3364 cm^{-1}), the amide 1 (1644 cm^{-1}) and the amide 2 (1581 cm^{-1}) signals is evident. The amide 1 and amide 2 signals disappear when 4'-amidobenzo-15-crown-5 (**290**, red (—) line) is converted to

4'-(aminomethyl)benzo-15-crown-5 (**294**, pink (—) line), and the amino signals at 1590 cm^{-1} and 3315 – 3550 cm^{-1} can be seen.

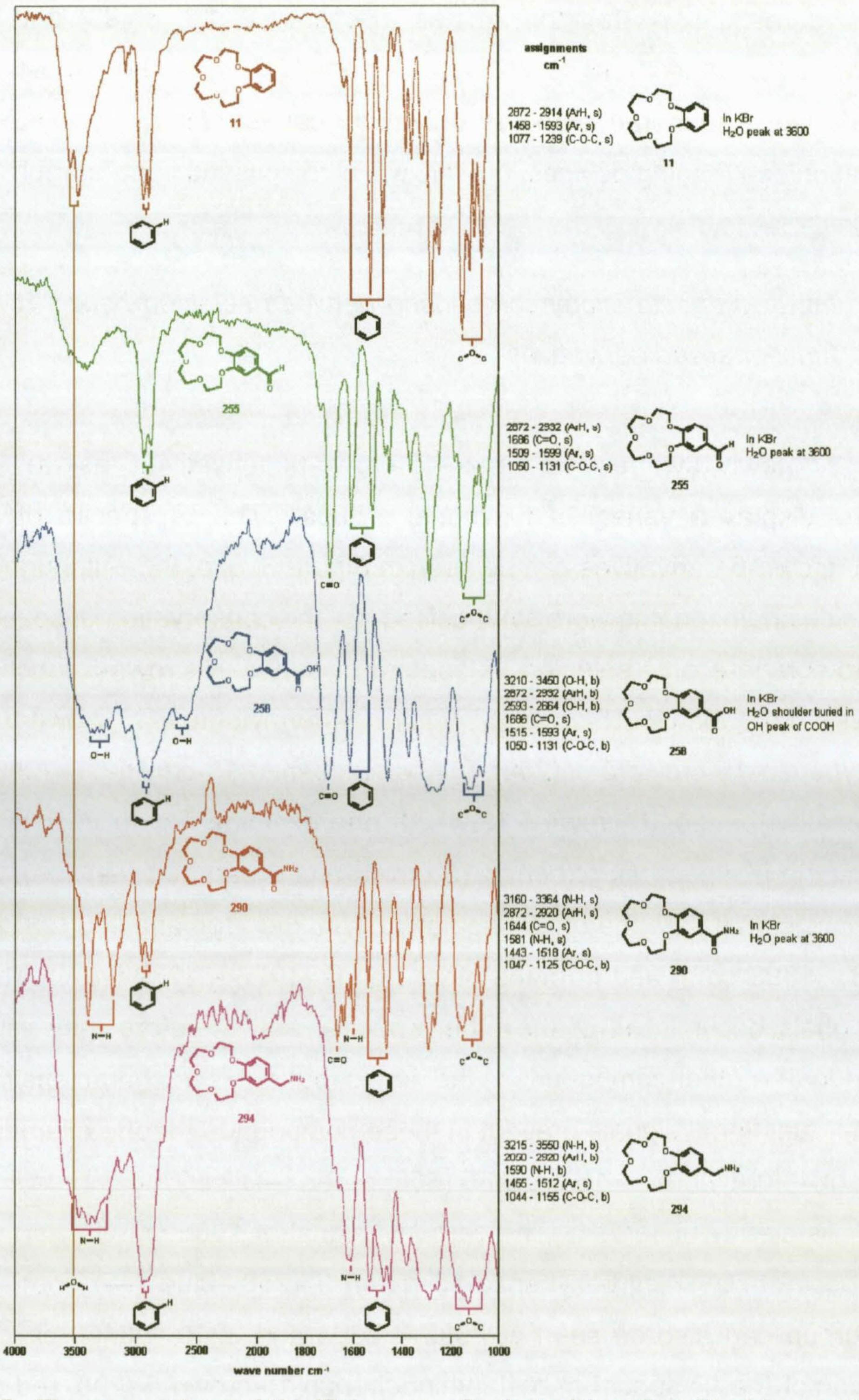


Figure 3. 5. The comparison of the IR spectra of selected functionalised benzo-15-crown-5 derivatives. The dark red (—) line indicates the IR spectrum of benzo-15-crown-5 (11); the green (—) line indicates the IR spectrum of 4'-formylbenzo-15-crown-5 (255); the blue (—) line indicates the IR spectrum of 4'-carboxybenzo-15-crown-5 (258); the red (—) line indicates the IR spectrum of 4'-amidobenzo-15-crown-5 (290); and the pink (—) line indicates the IR spectrum of 4'-(aminomethyl)benzo-15-crown-5 (294).

3.4 SYNTHESIS AND FUNCTIONALISATION OF THE POLYMERIC CARRIERS

3.4.1 *Introduction*

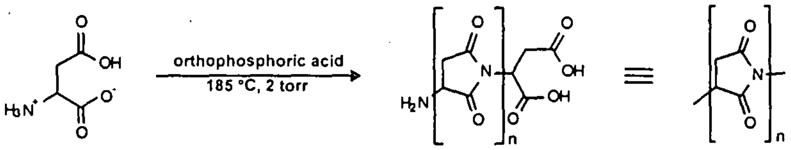
Three classes of polymeric carriers intended to anchor crown ether derivatives on were prepared in this study. These included:

1. Water-soluble polymers.
2. Polymers that are soluble in organic media.
3. Cross-linked elastomers that are insoluble in both water and in organic media.

3.4.2 *Water-soluble polymers*

The first water-soluble polymer was synthesised to have amine functionalised side chains that could react with carboxylic acid functionalised crown ethers, to produce a water-soluble crown ether polymeric conjugate.

As a precursor to such a polymer, polysuccinimide (**204**) was first obtained by the thermal polymerisation of DL-aspartic acid (**203**) in the presence of orthophosphoric acid at low pressure (*ca.* 2 torr), as depicted in Scheme 3. 35, as a white solid and molecular mass of *ca.* 70 000 g/mol.[176]



203 204a 204

Scheme 3. 35. The thermal polymerisation of DL-aspartic acid (203) to produce polysuccinimide (204). Throughout this thesis, whenever reference to polysuccinimide is made, it is understood to be compound 204a, but for simplicity the full structure of polysuccinimide will henceforth be simplified by 204. It is explicitly understood, though, that when structure 204 is drawn, it is just an abbreviated way of indicating structure 204a.

Polysuccinimide (**204**) is not water-soluble but due to its reactiveness could be converted into various polyaspartamide derivatives that are water-soluble. First the imide rings of polysuccinimide (**204**) was opened by nucleophilic attack utilising two different amines in two consecutive reactions, to obtain the water-soluble polymer **207** according to Scheme 3. 36, p. 99. The amine nucleophiles were chosen in such a way that certain properties could be build into the polymer. The first amine nucleophile, *N*-(3-aminopropyl)morpholine (**205**), was chosen to enhance the water-solubility and to separate the eventual active amine sites in the final polymer **207**. In doing this, any side reactions (such as cross-linking reactions) during the anchoring of a crown ether onto this polymer would be minimised. The second amine nucleophile, ethylenediamine (**206**), was used to provide the all-important active site for the anchoring of a crown ether onto the polymer. Ethylenediamine (**206**) is difunctional: one of the amine groups attacks the polymer opening the imide rings of polysuccinimide (**204**), while the second amine group serves as the all-imported active site. Utilising the correct experimental conditions, i.e. low temperatures and the correct sequence of nucleophile addition, ensured that no noticeable cross-linking took place, and gave a final water-soluble polymer, polymer **207**, with a theoretical envisaged ratio of 3:1 *N*-(3-aminopropyl)morpholine:ethylenediamine.

The final, experimental monomer ratio[*], [#] of the water-soluble polymer **207** was determined with the use of ^{1}H NMR spectroscopy.[149] The ^{1}H NMR spectra of this polymer can be seen in Figure 3. 6.

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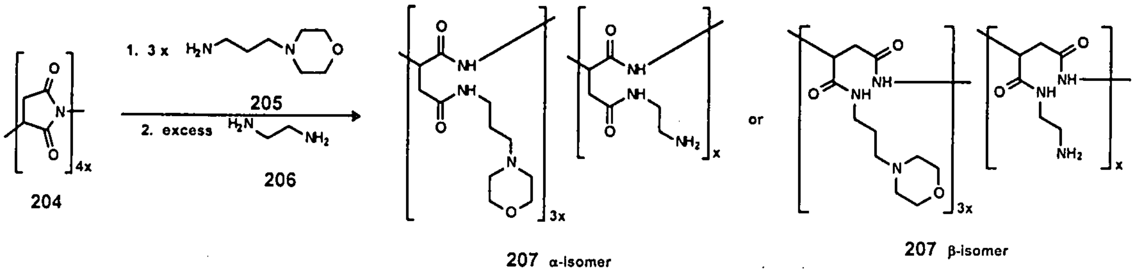
[*] The side chain fragments of the water-soluble polymers **207** and **302**, p. 102, and their derivatives, follows a random distribution. The structures shown only denote the stoichiometric ratio between the side chains, but does not imply a regular or ordered pattern of monomer distribution.

[#] Nucleophilic attack by the amines on polysuccinimide (**204**) can lead to α- and β-isomers. The structure for polymer **207** is that of both α- and β-isomers, but in future diagrams, only the α-isomer will be shown. It should be understood that there is always a mixture of the α- and β-isomers in the final product.



Scheme 3. 36. The synthesis of the water-soluble polymeric carrier 207 by the nucleophilic ring opening of polysuccinimide (204). Shown are exclusively the α-isomer of polymer 207 and the β-isomer of polymer 207. In practice, various combinations and mixtures of the α- and β-isomers are found.*, #

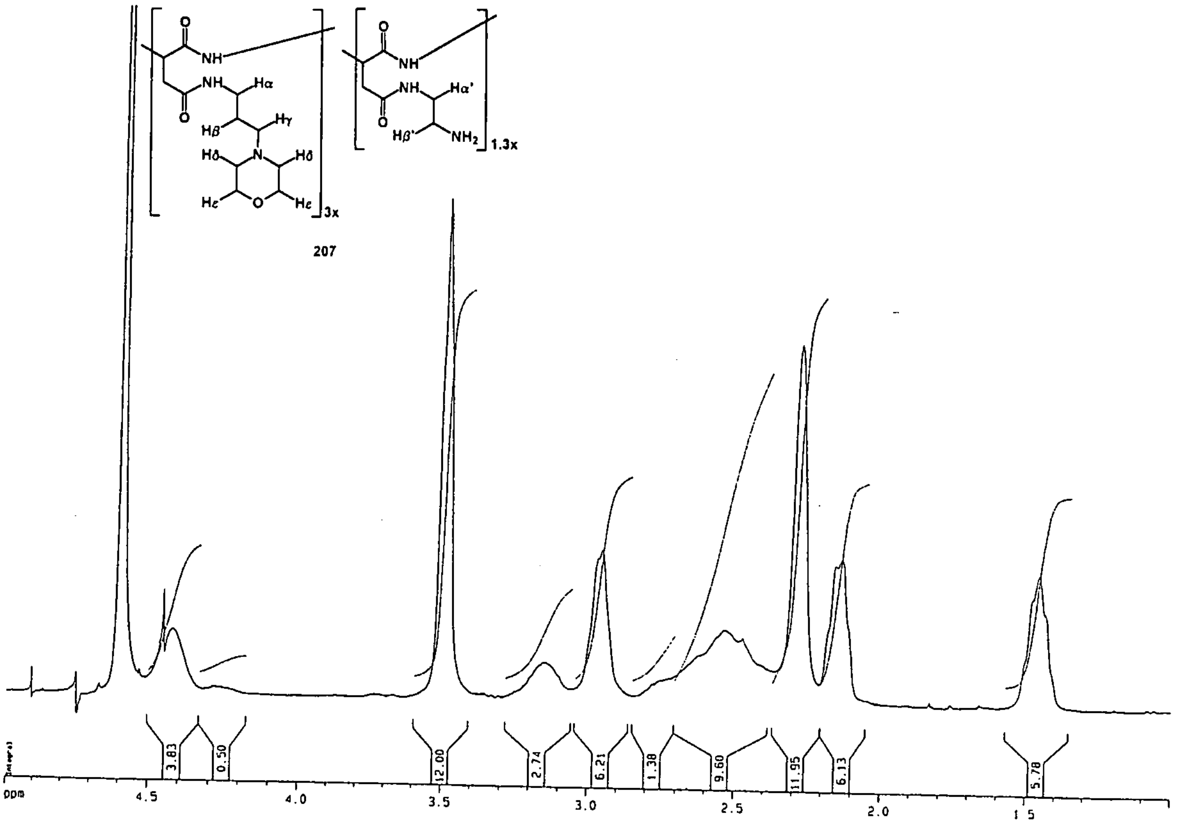


Figure 3. 6. The ^{1}H NMR spectra of the water-soluble polymer 207.

When the ^{1}H NMR spectrum of the water-soluble polymer **207** is studied, Figure 3. 6, the signal of the twelve (4 x 3 = 12) ε-protons of the morpholine side group is found at 3.40 – 3.51 ppm and have an integral value of 12.00. This corresponds to $\frac{12}{12} = 1$ integral unit per proton. The combined spectral region of 2.05 – 3.29 ppm have an integral value of 6.13 + 11.95 + 9.60 + 1.38 + 6.21 + 2.74 = 38.01. The known protons that is found in this region is {[(6 α-protons) + (6 γ-protons) + (12 δ-protons)] from the morpholine side chain} + {(6 asp-CH_2 protons) from the main chain linked to the morpholine groups} = 30 protons. The integral value associated with these 30 protons is therefore 30 x 1 = 30 protons. The unaccounted integral value is thus 38.01 – 30 = 8.01. The only unaccounted protons is the α'-, β'- and asp-CH_2 protons originating from the ethylenediamine moiety of the water-soluble polymer **207**. These six (6) protons implies that the water-soluble polymer **207** contains $\frac{8.01}{6} = 1.34$ ethylenediamine moieties. A ratio of 3:1 *N*-(3-aminopropyl)-morpholine:ethylenediamine was aimed for during the synthesis of the water-soluble polymer **207**. This ratio was remarkably well achieved, as can be seen from the previous discussion. The final monomer ratio of the water-soluble polymer **207** was determined as 3:1.34 *N*-(3-aminopropyl)-morpholine:ethylenediamine.

As shown in Scheme 3. 36, p. 99, the β-isomer of the water-soluble polymer **207** also exist in the final polymer. This β-isomer can also be seen on the ^1H NMR spectrum of the water-soluble polymer **207**. The aspartate CH_2 signal that corresponds to the β-isomer is found at 4.18 – 4.33 ppm. The experimental conditions employed (such as cooling to 0 °C) during the synthesis of the water-soluble polymer **207** is designed to minimise and/or totally eliminate the formation of this β-isomer. As seen in Figure 3. 6, p. 99, this β-isomer represent a small amount of the total repeating units in the final polymer (3.83 integral units for the α-isomer, compared to 0.50 integral units for the β-isomer).

Several different batches of this water-soluble polymer **207** were synthesised and the ratios between the *N*-(3-aminopropyl)morpholine:ethylenediamine was determined to be between 2.5:1 – 3.2:1. This difference in the desired ratio can be attributed to the difficulties associated with the weighing of liquid reagents, e.g. *N*-(3-aminopropyl)morpholine (**205**) and ethylenediamine (**206**). The addition of even one small extra drop of these reagents can cause the target ratio of 3:1 to be overshot.

The effect of pH on the ^{1}H NMR signals of the water-soluble polymer **207** was determined with a water-soluble polymer **207** batch containing a ratio of *N*-(3-aminopropyl)morpholine:ethylenediamine of 3:1.69, Figure 3. 7, p. 101. The top spectrum, in Figure 3. 7, p. 101, represents the ^{1}H NMR of the water-soluble polymer **207** at a pH ≅ 7, while the bottom spectrum represents the ^{1}H NMR spectrum of the water-soluble polymer **207** at a pH ≅ 14. If one closely examine these two ^{1}H NMR spectra, it is evident that several of the ^{1}H NMR signals have changed position. The signal at 3.20 – 3.40 ppm (in the top spectrum) has completely disappeared. On close examination of the bottom spectrum, it is evident that the integral value of the signal at 2.93 – 3.21 ppm has changed from 7.34 integral units (in the top spectrum) to 9.80 integral units (in the bottom spectrum).

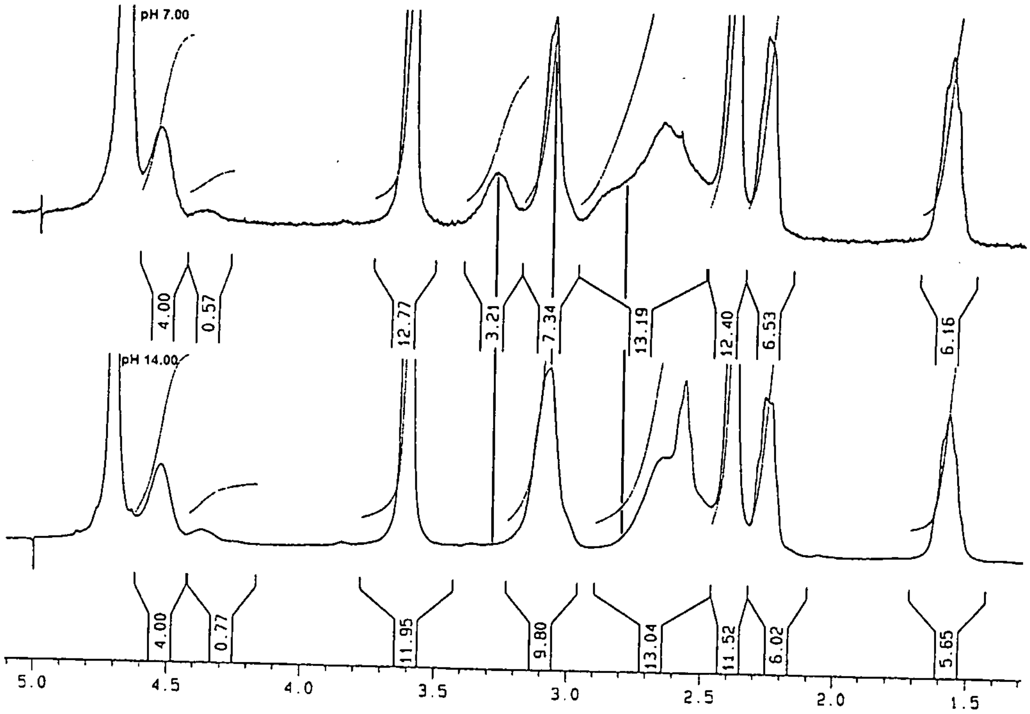
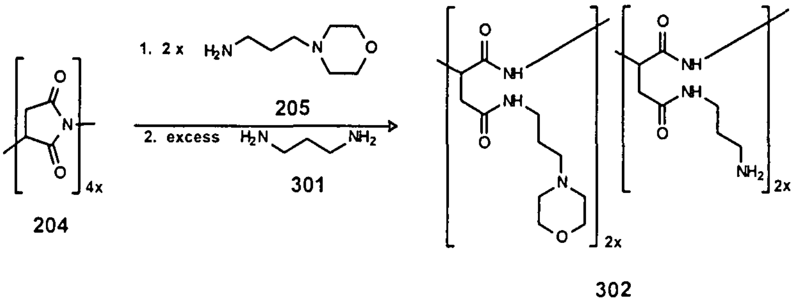


Figure 3. 7. The effect of pH on the ^{1}H NMR signals of the water-soluble polymer 207 having a ratio of *N*-(3-aminopropyl)morpholine:ethylenediamine of 3:1.69.

The ratios between the *N*-(3-aminopropyl)-morpholine:ethylenediamine is still in good agreement with each other, 3:1.69 for the water-soluble polymer **207** at pH ≅7 (top spectrum) and 3:1.75 for the water-soluble polymer **207** at pH ≅ 14 (bottom spectrum). This implies that the disappearance of the signal at 3.20 – 3.40 ppm can be attributed to a change in the environment of these protons, rather than the removal of protons from the water-soluble polymer **207**. The exact reason of this observation needs further research for clarification, but it was considered outside the boundaries of this study. One possibility is the fact that the intra- and intermolecular hydrogen bonding is broken at a high pH level, resulting in a change in the environment around the protons that resonate at 2.93 – 3.40 ppm.

A third amine nucleophile, propylenediamine (**301**), was also used to produce the water-soluble polymer **302** with the pendent amine group one methylene group further away from the polymeric backbone, than the amine group in the water-soluble polymer **207**. This reaction is the same as the one in Scheme 3. 36, p. 99, but rather than ethylenediamine (**206**), propylenediamine (**301**) was used to produce the water-soluble polymer **302**, as seen in Scheme 3. 37. The ratio between *N*-(3-aminopropyl)morpholine (**205**) and propylenediamine (**301**) was also changed from 3:1 to 2:2.

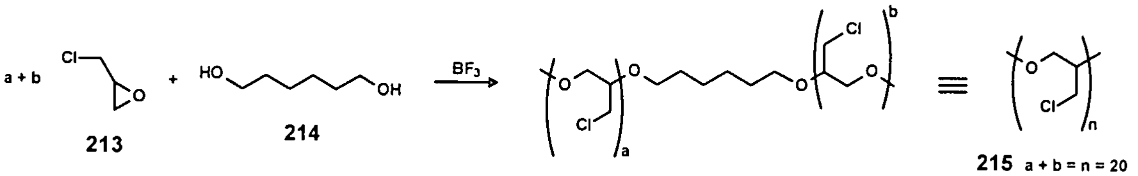


Scheme 3. 37. The synthesis of the water-soluble polymer 302 with the amine functionalities one methylene group further away from the polymeric backbone than in the water-soluble polymer 207. Also see footnote on page 99.

The final monomer ratio of the water-soluble polymer **302** was confirmed with the use of ^{1}H NMR spectroscopy following the guidelines described for the water-soluble polymer **207**, and by allowing for the additional methylene group in the propylenediamine side chain in polymer **302**, when compared with the ethylenediamine side chain in polymer **207**. Although a final monomer ratio of 2:2 was aimed for, ^{1}H NMR spectroscopy concluded that a final monomer ratio of 2:2.6 was obtained.

3.4.3 Organic soluble polymers

Next, the hydroxy terminated pre-polymer, polyepichlorohydrin (**215**), was synthesised utilising cationic ring-opening polymerisation techniques according to Scheme 3. 38, p. 103, to obtain a polymeric carrier that was soluble in organic media and that had pendant side groups to which a crown ether could be anchored.



213

214

215a

303a

215 a + b = n = 20

303 a + b = n = 205

Scheme 3. 38. The synthesis of polyepichlorohydrin (215). Throughout this thesis, whenever reference to polyepichlorohydrin is made, it is understood to be compound 215a or 303a, but for simplicity the full structure of polyepichlorohydrin will hereafter be simplified by 215 and 303. It is explicitly understood, though, that when structure 215 or 303 is drawn, it is just an abbreviated way of indicating structure 215a or 303a. Rounded to whole numbers, on average, n = 20 for 215 and n = 205 for 303.

The target molecular mass of polyepichlorohydrin of 2 000 g/mol was remarkable well achieved as indicated by the ^{1}H NMR spectrum of polyepichlorohydrin (**215**) and the molecular mass analysis of polyepichlorohydrin by gel permeate chromatography (Figure 3. 8 and Figure 3. 9, p. 105, respectively). This conclusion was reached as described below.

Utilising ^{1}H NMR spectroscopy to obtain the molecular mass, the following method was used: in the region 1.30 – 1.65 ppm, the signals of the hydrogen atoms on the four α-carbon middle section of the hexane linking unit is found (Figure 3. 8, p. 104). The integral value of 8.00 must therefore correspond to 8 protons, giving an integral value of 1.00 per proton. The rest of the NMR signals observe at 3.35 – 4.05 ppm must correspond to the signals of the remaining unassigned protons in the hexane unit (4 β-protons), all of the other protons adjacent to an ether linkage, and all the protons adjacent to the chloride atom. Four of the integral values in this region belong to the ß-protons of the hexane moiety. The remainder, $103.4 \approx 100$, belong to the epichlorohydrin repeating units in the polymeric backbone of **215**. Keeping in mind that each of the epichlorohydrin repeating units have 5 protons, there are therefore $\frac{100}{5} = 20$ epichlorohydrin repeating units in polyepichlorohydrin **215**, i.e. a + b = 20. The total molecular mass of polymer **215**, containing 20 epichlorohydrin units and 1 hexane unit, in the backbone, correspond to (20 x 92.5245 g/mol) + 116.1588 g/mol = 1 967 g/mol, which compares well with the target molecular mass of 2 000 g/mol.

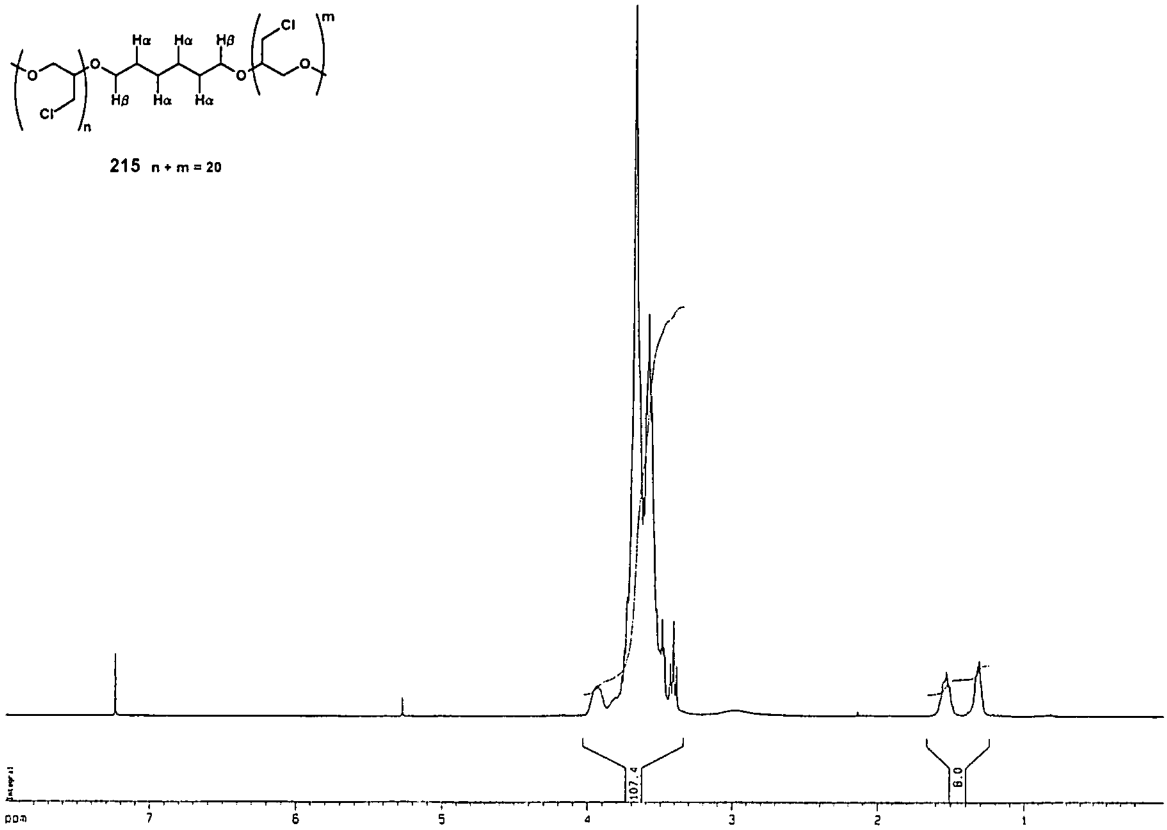
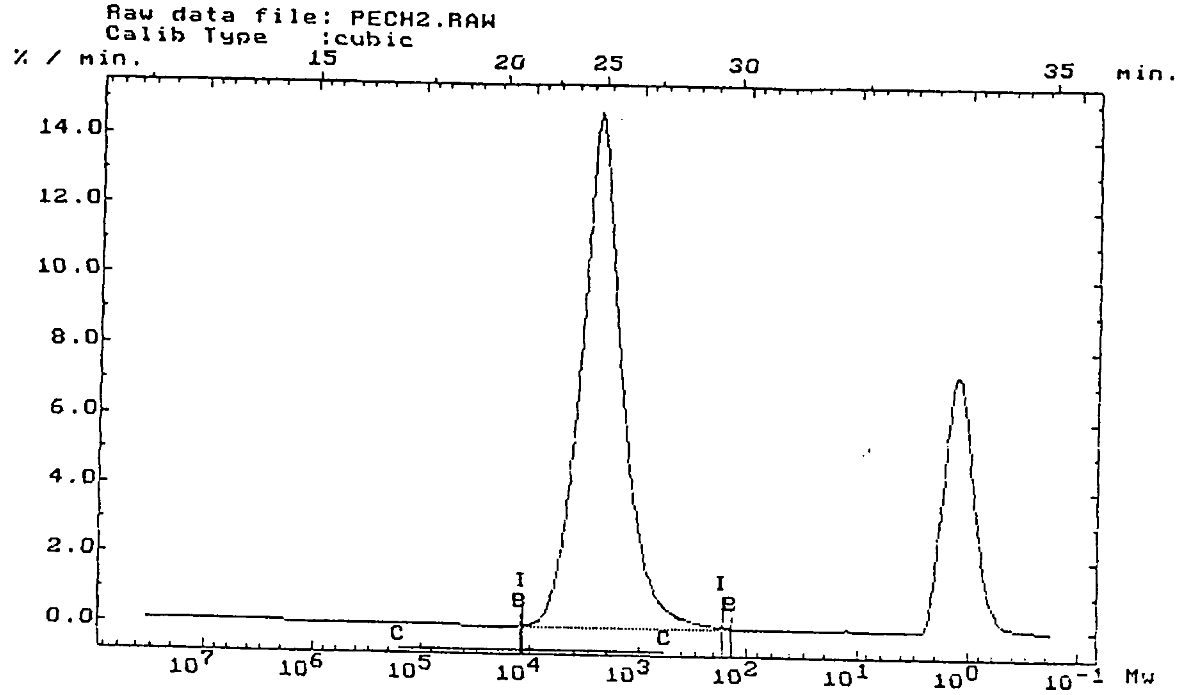


Figure 3. 8. The ^{1}H NMR spectrum of polyepichlorohydrin (215).

Gel permeation chromatography (courtesy of SOMCHEM) on polymer **215** resulted in the number average molecular mass to be 2 083 g/mol, and the polydispersity index, $\frac{M_w}{M_n}$, was found to be $\frac{2637}{2083} = 1.266$ (Figure 3. 9, p. 105).



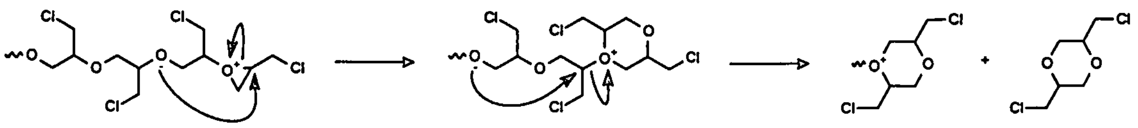
Reference Peak : 33.860, found at : 33.860
Calib Type : cubic
K[1] = 6.48416E+01 K[2] = -6.47253E+00
K[3] = 2.59984E-01 K[4] = -3.69805E-03

Baseline from 20.82 to 29.90
Integration range from 20.90 to 29.66

Mw = 2637
Mn = 2083
Mz = 3177
Polydisp. Index = 1.2662
Mz + 1 = 3769
10% at MW = 4196
90% at MW = 1329

Figure 3. 9. The molecular distribution of polyepichlorohydrin (**215**).

To achieve this remarkable result, the reader is referred to Chapter 2, p. 61 – 63, where two different mechanisms for cationic ring opening polymerisations were discussed. In order to eliminate undesired side reactions, such as dioxane derivatives elimination (Scheme 3. 39, p. 106), conditions had to be found in which there never was any build-up of unreacted epichlorohydrin (**213**) in the reaction mixture. This would force the reaction to proceed *via* the active monomer mechanism, and this resulted in an accurate target average molecular mass.[177] To comply with this requirement, epichlorohydrin (**213**) was added dropwise to hexane-1,6-diol (**214**) containing $BF_3{\cdot}O(C_2H_6)_2$, over a 24 hr period at a temperature of between 24 – 27 °C.



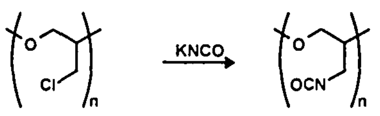
216

Scheme 3. 39. The mechanism of elimination of dioxane derivatives from the growing polyepichlorohydrin.

The reaction is very exothermic and care had to be taken to prevent thermal runaway. The slow addition required for obtaining the desired molecular mass also helped to prevent thermal runaway. Thermal runaway would invariably favour dioxane elimination from the growing chain (Scheme 3. 39) to liberate a polymer with molecular mass much less than desired.

From the amount of epichlorohydrin repeating units in polymer **215**, i.e. 20, it follows that polymer **215** has 20 side chains with the chloride group as potential active site for anchoring reactions. To increase the amount of these active sites, it was decided to synthesis a polyepichlorohydrin derivative with as many as possible epichlorohydrin repeating units in the polymeric chain. Utilising the same reaction conditions as that for the synthesis of polymer **215**, the polyepichlorohydrin derivative **303** was obtained, according to Scheme 3. 38, p. 103, with molecular mass of about 20 000 g/mol. The target molecular mass was 100 000 g/mol. To achieve higher molecular masses, further investigation is required for the development of suitable reaction conditions. However, in this study, this goal was not pursued as the derivative **303** was regarded as having a sufficiently large molecular mass for the water purification investigation at hand.

To obtain a polymer that could be anchored onto an elastomer, or one that could easily react with amine and hydroxy functionalised crown ethers, a polyepichlorohydrin derivative containing isocyanate groups rather than chloride groups was synthesised. This polyisocyanate compound, polymer **304**, was synthesised according to Scheme 3. 40, p. 107.



215 n = 20 **304** n = 20

303 n = 205 **305** n = 205

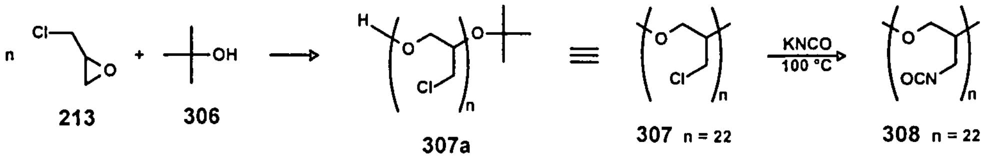
Scheme 3. 40. The synthesis of a polyisocyanate polymer 304 and 305 from the reaction between polyepichlorohydrin 215 and polyepichlorohydrin 303 and potassium isocyanate, respectively.

In order to obtain the polyisocyanate polymer **304**, several methods was studied to obtain the correct reaction conditions. These conditions are summarised in Table 3. 1. Reaction **number 6**, which made use of the phase transfer catalyst tetrabutylammonium bromide and a base, K_2CO_3, was found to be the best to convert polyepichlorohydrin **215** to the polyisocyanate polymer **304**.

Table 3. 1. The conditions employed to obtain the polyisocyanate polymer 304.

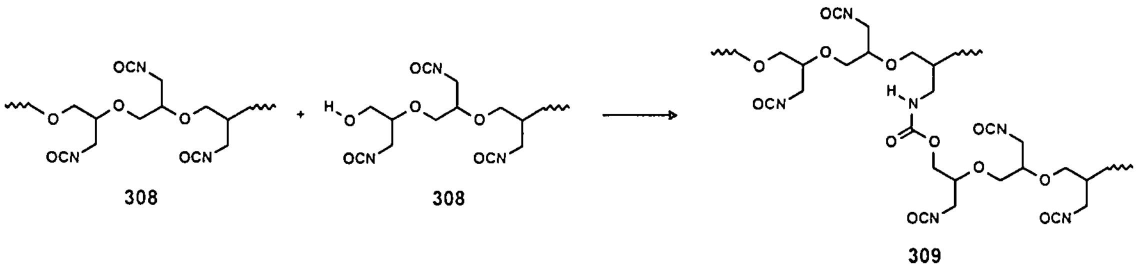
Reaction Number	Reaction Condition	% NCO Groups
1	KNCO / benzene / 16 h / 80 °C	< 2 %
2	KNCO / $N^+(CH_2CH_2CH_3)_4Br^-$ / K_2CO_3 / DMSO / 16 h / 150 °C	Insoluble cross-linked product
3	KNCO / DMF / 16 h / 120 °C	< 2 %
4	KNCO / $N^+(CH_2CH_2CH_3)_4Br^-$ / K_2CO_3 / DMF / 16 h / 100 °C / DMF evaporated	5 %
5	KNCO / $N^+(CH_2CH_2CH_3)_4Br^-$ / K_2CO_3 / DMF / 2 h / 100 °C / DMF evaporated	10 %
6	KNCO / $N^+(CH_2CH_2CH_3)_4Br^-$ / K_2CO_3 / DMF / 16 h / 100 °C / DMF extracted with hexane	15 %

One of the problems encountered during the synthesis of the polyisocyanate polymer **304** was that when the isocyanate groups was attached to the polymer, it then reacted with the alcohol groups of the hydroxy terminated polyepichlorohydrin **215**. When the concentration of the isocyanate group in polymer **304** becomes too high, it produced an insoluble cross-linked polymeric product. In order to prevent this side reaction, it was deemed necessary to synthesise a polyepichlorohydrin derivative containing at most one hydroxy group. For this reason the polyepichlorohydrin derivative **307** was synthesised using a mono-alcohol initiator, here *tert*-butanol (**306**), as seen in Scheme 3. 41, p. 108.



Scheme 3. 41. The synthesis of polyepichlorohydrin 307 and the isocyanate polymer 308. Throughout this thesis, whenever reference to polyepichlorohydrin 307 is made, it is understood to be compound 307a, but for simplicity the full structure of polyepichlorohydrin 307a will hereafter be simplified by 307. Rounded to whole numbers, on average, n = 22.

The molecular mass of polymer **307** was determined with the use of ^{1}H NMR spectroscopy as 1 840 g/mol, utilising the same techniques as discussed for polyepichlorohydrin (**215**), and keeping in mind that the alcohol used was *tert*-butanol (**306**). Polymer **307** was also converted to the isocyanate containing polymer **308**, using the same procedure as the synthesis of the polyisocyanate polymer **304**, as depicted in Scheme 3. 41. The fact that polymer **308** is not a dihydroxy terminated polymer meant that no cross-linking occurred. Polymer **308** can react with itself to form compounds of the type shown in Scheme 3. 42, but this reaction was actually regarded as an advantage, as it generated a polymer, polymer **309**, with more isocyanate groups. The greater abundance of isocyanate groups would allow immobilisation on an insoluble solid support with greater ease. To prevent the reactions shown in Scheme 3. 42, the hydroxy end-groups need, first, to be protected. This can be accomplished by the reaction of polymer **307** with methyl iodide to produce methoxy end-groups.



Scheme 3. 42. The linking of polymer 308 to itself, to produce a polymer 309.

The isocyanate peak in the IR spectrum of polymer **308** was clearly detected as shown in Figure 3. 10, at 2104 – 2140 cm^{-1}. The $\underline{CH_2}$-NCO was also detected on ^{1}H NMR spectroscopy (see the insert in Figure 3. 10, p. 109, the dashed spectrum), and from this it was concluded that nearly 50 % of the chloride groups were converted to isocyanate groups, i.e. n = 10.

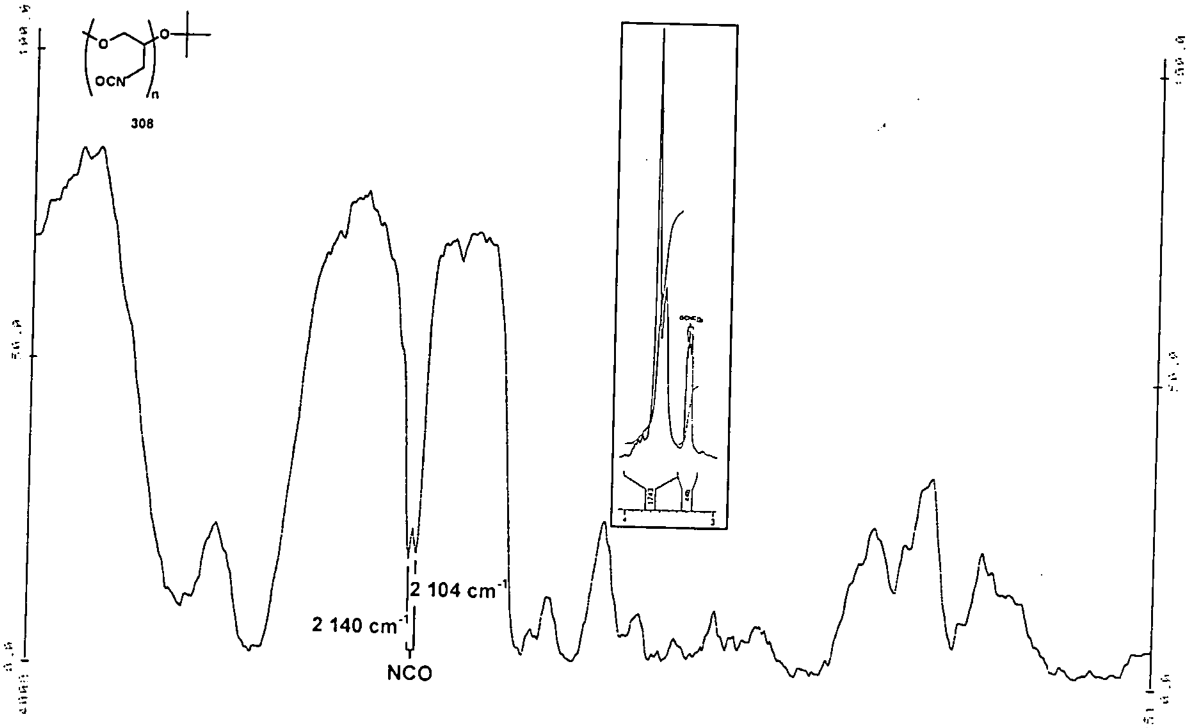
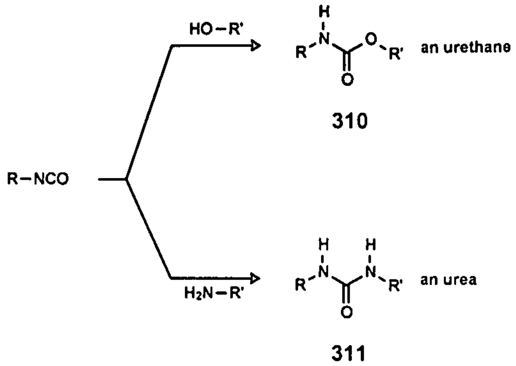


Figure 3. 10. The IR spectrum of the isocyanate polymer 308. The insert is a region of the ^{1}H NMR spectrum of the isocyanate polymer 308, showing the difference in the chloride functionalised side groups (3.40 – 4.00 ppm) *vs.* the isocyanate functionalised side groups (3.15 – 3.40 ppm).

These polyisocyanate polymers, polymer **304**, polymer **305** and polymer **308**, can react with alcohol or amine functionalised compounds, crown ethers for the purpose of this study, to either produces an urethane or an urea bond, as shown in Scheme 3. 43, p. 110.



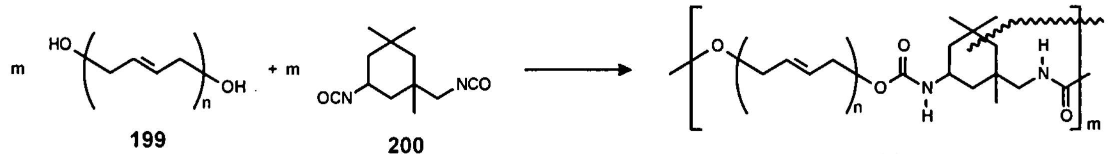
310

311

Scheme 3. 43. The reaction between an isocyanate derivative and either an alcohol or an amine functionalised compound to produce an urethane (310) and an urea (311), respectively.

3.4.4 Elastomeric solid supports

In order to obtain an insoluble elastomeric support that could be utilised to anchor crown ethers, hydroxy terminated polybutadiene (HTPB (**199**)) of approximate molecular mass 2 950 g/mol, was cured with isophorone diisocyanate (**200**) to produce an elastomeric insoluble cross-linked elastomer **201**, as shown in Scheme 3. 44.[147] Due to the fact that HTPB has a hydroxy content of between 2.2 – 2.6, the curing of HTPB was investigated with different ratios of isophorone diisocyanate (**200**), in order to obtain the correct curing conditions. It was found that a ratio of 1:1.25 (by moles) HTPB:isophorone diisocyanate was necessary to obtain the best elastomer. To obtain elastomer **201**, a mixture of HTPB (**199**) and isophorone diisocyanate (**200**) was thoroughly mixed, poured into a mould and placed in an oven for 24 h. After 24 h, the cured elastomer was taken out of the mould. A photo of this cured elastomer can be seen in Figure 3. 11, p. 112. **Photo 1** is schematically represented with the bottom structure in Figure 3. 11, p. 112, on the right. The structure that makes up the casted elastomer is shown inside this schematic representation. Special attention must be given to the imino groups that are shown in the rectangle and circle, respectively. The imino group that is circled is taken to be imbedded in the casted structure and is therefore totally inaccessible to any reactive molecule that cannot penetrate into the interior of the casted form. It therefore represents a "dead" moiety that cannot take part in any further reactions. However, the imino group that is highlighted with the rectangle is one that is on the surface of the casted form, in such an orientation, that it is accessible to any molecule that may come into contact with the casted elastomer **201**. If this molecule is a reactive species, it may react with this imino group. It is the aim of this study to try and attach a crown ether to the elastomeric support **201** *via* this imino group either directly or *via* intermediate spacers, such as polymer **308**. If this goal can be achieved, the elastomeric solid support **201** can be coated with sodium cation scavengers, here crown ethers, and it may open the route to a completely new technology in water purification.



199 200 201

Scheme 3. 44. The formation of a cured elastomer 201 from the reaction between HTPB (199) and isophorone diisocyanate (200). Although HTPB are shown to be difunctional, the hydroxy content of this polymer is actually 2.2 – 2.6. This implies that the product 201 is not a linear molecule as shown, but is actually slightly cross-linked. This cross-linking introduces the insolubility and elastomeric properties into 201. Whenever 201 or any of its derivatives are shown or used in this study, the reader should realise that it is really a cross-linked insoluble compound and not a linear compound as shown. The symbol 〰 represents this cross-linking bond. No significance must be read into the position of 〰 . The choice of where 〰 appears in the structures was driven by practical convenience and not chemical correctness. Chemically 〰 should originate from the HTPB moieties.

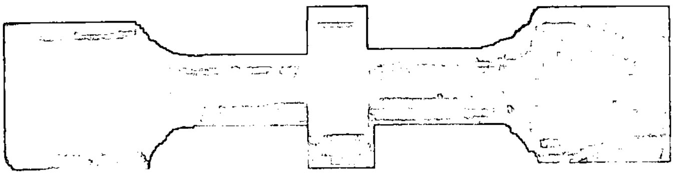
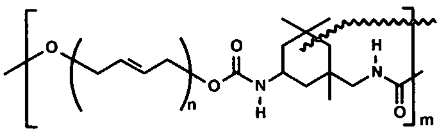
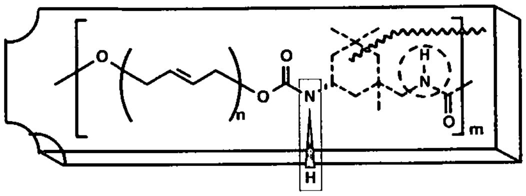


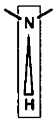
Photo 1



201



201



Indicates that this group stick out of the surface or is accessible on the surface of the casted elastomer. It can therefore take part in subsequent reactions, because it will be accessible to reactive groups (e.g. isocyanates).

Indicates that this group cannot take part in subsequent reactions, due to the fact that it is burried inside the matrix of the elsatomer and is therefore inaccessible for any reactive molecule.

Figure 3. 11. Bottom Right: A schematic representation of the final cured, cross-linked elastomer 201. The symbol 〰 is representative of the cured, cross-linking bonds, but no meaning should be attached to its indicated position. The photograph, photo 1, top, shows the form into which 201 were casted.

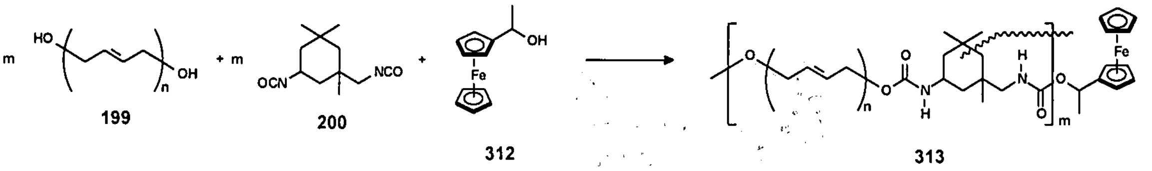
3.5 ANCHORING OF BENZO-15-CROWN-5 DERIVATIVES ONTO THE ELASTOMERIC CARRIER 201

In order to obtain a working model of a conveyer belt coated with crown ether sodium cation scavengers, it was necessary to anchor derivatives of benzo-15-crown-5 onto the insoluble elastomeric solid support **201**. For the first approach, the goal of anchoring an alcohol functionalised crown ether onto elastomer **201** was pursued.

The anchoring procedure was first experimented on with a cheaper and easier to synthesised alternative compound, 1-hydroxyethylferrocene (**312**), rather than an actual crown ether, due to the fact that the ferrocene dye **312** is a highly coloured compound and the effectiveness of the anchoring step could thus be visually evaluated.

Several different methods were used in order to obtain correct experimental conditions to allow surface anchoring of the ferrocene dye **312** onto elastomer **201**. Surface anchoring of any sodium cation scavenging ligand onto elastomer **201** is important because any ligand that is buried in the interior of the solid support would be inaccessible for any dissolved Na^+. These imbedded sodium cation scavenging ligands would therefore be wasted, as they cannot bind any Na^+. They would only serve to raise the cost of the ultimate device.

The first method employed was to add the ferrocene dye **312** to the liquid mixture of HTPB (**199**) and isophorone diisocyanate (**200**) before any curing had taken place. The reaction that took place is shown in Scheme 3. 45, p. 113.



Scheme 3. 45. The addition of the ferrocene dye 312, to a mixture of HTPB (199) and isophorone diisocyanate (200) to produce the slightly cross-linked elastomer 313. The cross-linking bond may be visualised with the symbol ~~~ , but no meaning must be given to the indicated binding position. The choice of the binding position showing the cross-linking bond was made merely because for practical limitations in demonstrating this bond schematically. See also Figure 3. 11, p. 112.

This method, however, led to the formation of an elastomer with the ferrocene dye **312** distributed throughout the polymeric matrix, i.e. on the surface and in the interior. This reaction was repeated but it was decided not to add the ferrocene dye **312** to the liquid mixture of HTPB (**199**) and isophorone diisocyanate (**200**), but to allow the latter mixture to cure for about 2 h, before the ferrocene dye **312** was added. The reaction in question is the same as that given in Scheme 3. 45. The material that was obtained from this reaction can be seen in Figure 3. 12, p. 114, (**photo 3**) and in Figure 3. 13, p. 115 (**photo 8**). **Photo 8** is a cross-section cut of polymer **313**. **Photo 8** clearly showed, from the yellow colour, that a great deal of the ferrocene dye **312** penetrated the interior of the polymer, thus rendering it useless for any participation in reactions.

After this initial failure, it was decided to first partially cure elastomer **201**, for 16 h, and then to add the ferrocene dye **312**. The reaction involved is the same as that depicted in Scheme 3. 45. As can be seen in Figure 3. 12, p. 114, (**photo 3**) and in Figure 3. 13, p. 115, (**photo 8**) migration of the ferrocene dye **312** still occurred to the solid support's interior, an undesirable result.

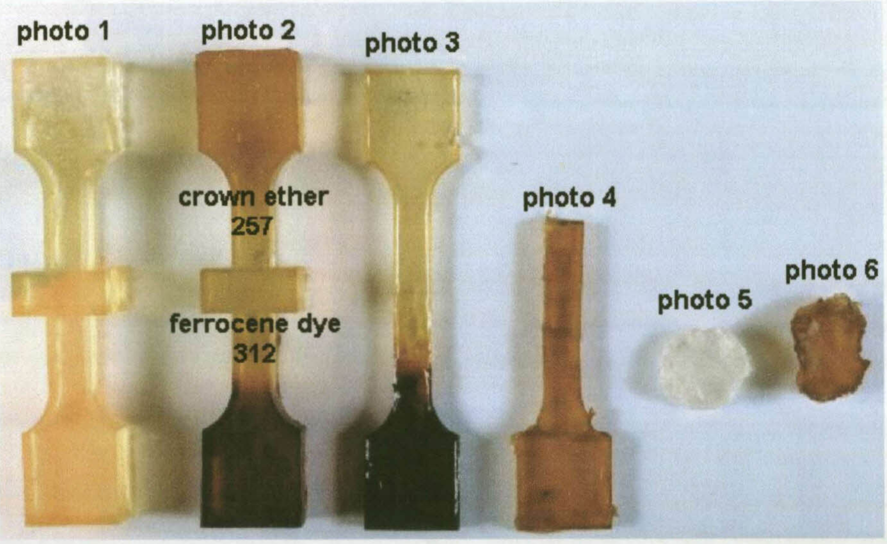


Figure 3. 12. The results of different methods of anchoring of 312 onto elastomer 201 to eventually obtain an elastomer containing 312 on the surface of the elastomer. Photo 1 represents the cured, cross-linked elastomer 201 (see Scheme 3. 44, p. 111 and Figure 3. 11, p. 112) after casting in the absence of any ferrocene dye and/or crown ether derivatives. Photo 2 is that of the alcohol derivative 4'-(hydroxymethyl)benzo-15-crown-5 (257, see Scheme 3. 49, p. 120) and the ferrocene dye 312 (see Scheme 3. 46, p. 116) bound mostly to the surface of elastomer 201. Photo 3 represents the reaction of the ferrocene dye 312 with the partially cured (2 h reaction) elastomer 201 (see Scheme 3. 45, p. 113). The dark area at the bottom of photo 3 is the ferrocene dye 312 imbedded in the matrix of the elastomer and on the surface of the elastomer. Photo 4 represents the elastomer produced by the reaction between the ferrocene dye 312, HTPB (199) and isophorone diisocyanate (200) to produce elastomer 313 (see Scheme 3. 45, p. 113), after 16 h of cured time. It can clearly be seen that the yellow ferrocene dye 312 is distributed throughout the entire matrix of the elastomer, not only on the surface. Photo 5 represents the cured, cross-linked elastomer 201, only casted into another form. Photo 6 represents the reaction of elastomer 201 and the ferrocene dye 312 in a solvent such as dichloromethane. Solvents such as dichloromethane produce a gel-like polymer. The yellow ferrocene dye 312 can be seen inside the matrix of the elastomer, as well as on the surface of the elastomer.

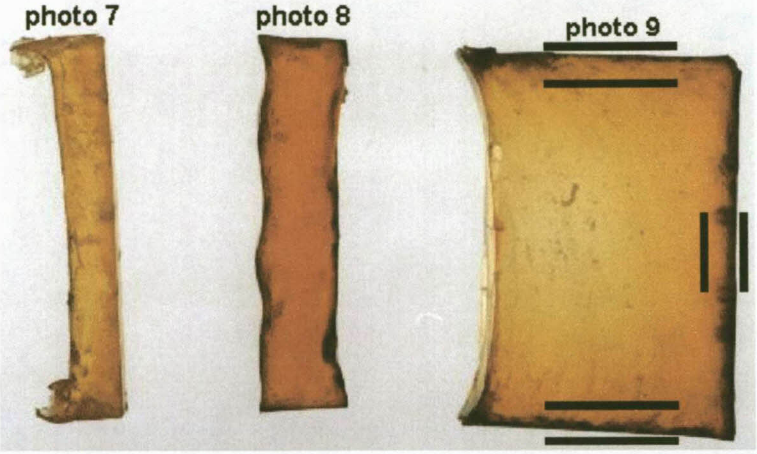
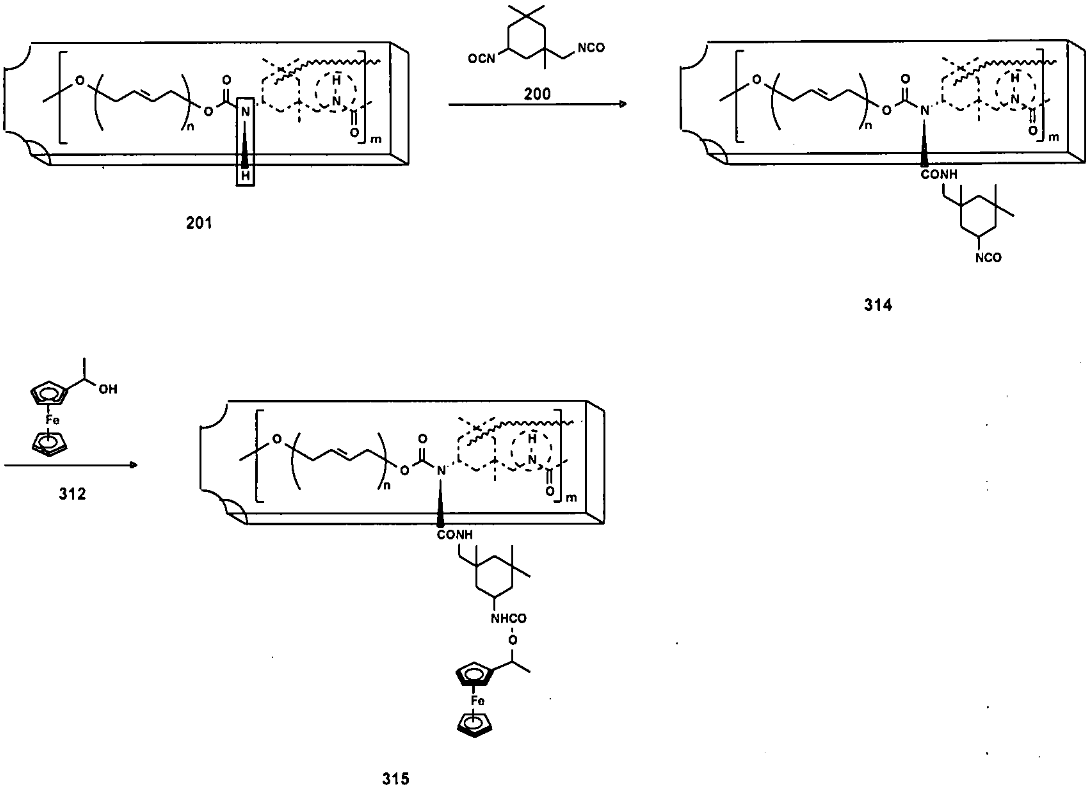


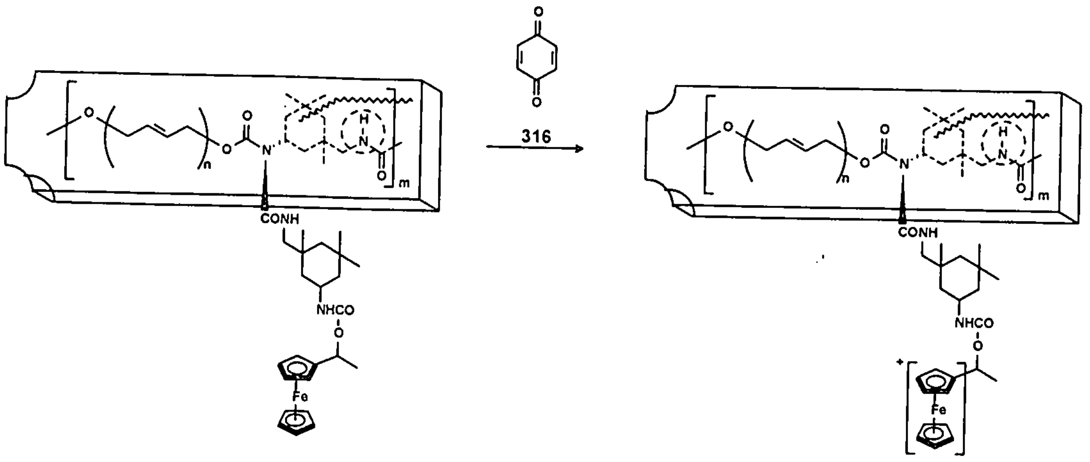
Figure 3. 13. A cross-section of the elastomers obtained from the reaction of the ferrocene dye 312 and elastomer 201. Photo 7 represents the cross-section of the elastomer produced by the reaction between the ferrocene dye 312, HTPB (199) and isophorone diisocyanate (200), see Scheme 3. 45, p. 113. The yellow colour of the ferrocene dye 312 can be seen inside the matrix of the elastomer, as well as on the surface. Photo 8 represents the elastomer produced by the reaction between the ferrocene dye 312 and the partially cured elastomer 201 (see Scheme 3. 45, p. 113). The yellow colour of the ferrocene dye 312 can be seen inside the matrix of the elastomer, as well as on the surface of the elastomer. Photo 9 represents the reaction between the ferrocene dye 312 and the fully cured elastomer 201 (Scheme 3. 46, p. 116). The dark areas on the surface, between the artificially introduced lines represent the ferrocene dye 312 bound almost exclusively to the surface of elastomer 201.

It was then decided to almost fully cure elastomer **201** (the exposed surface was to be dry), then to add a suitable coupling reagent, i.e. isophorone diisocyanate (**200**), and then to add the ferrocene dye **312**. This was done to force the ferrocene dye **312** to only bind to the surface of elastomer **201**. The fully cured elastomer **201** was placed in a solution of isophorone diisocyanate (**200**). This produced an elastomer with pendent isocyanate groups, elastomer **314**, as shown in Scheme 3. 46, p. 116. The ferrocene dye **312** was then dissolved in a suitable solvent and the elastomer was placed in this mixture so that the ferrocene dye **312** could react with elastomer **314**. It was found that solvents such as diethyl ether and dichloromethane, caused the elastomer **201** to swell into a gel-like constitution, thus producing an elastomer with the ferrocene dye **312** not only on the surface of the elastomer but again in its interior as well (Figure 3. 12, p. 114, **photo 6**). In contrast, a solvent such as hexane did not cause elastomer **201** to swell into a gel and the ferrocene dye **312** was successfully anchored to the surface of elastomer **201**. **Photo 2** (Figure 3. 12, p. 114) and especially the cross-section shown in **photo 9** (Figure 3. 13, p. 115), clearly showed that the majority of the ferrocene dye **312** was bound to the surface of the casted elastomer when this method is followed. Following the correct procedure, the alcohol containing ferrocene dye **312** can thus anchored onto the surface of the solid support by the reaction between the hydroxy functionality of **312** and the isocyanate groups of the isophorone diisocyanate spacer on the surface of the cured elastomer **201**, as shown in Scheme 3. 46.



Scheme 3. 46. The reaction between previously cured elastomer 201 and isophorone diisocyanate (200) followed by the subsequent reaction between elastomer 314 and the ferrocene dye 312. In this manner the goal of surface bound ferrocene dye was achieved.

In order to determine if the bound ferrocene dye **312** was still chemically active, elastomer **315** was placed in a solution of the oxidising agent *p*-benzoquinone (**316**). It was found that the yellow ferrocene dye bound to the surface of elastomer **201** as shown in elastomer **315** (Scheme 3. 46) could still be oxidised to the blue ferrocenium species, elastomer **317**. This result was very important because it showed that the surface bound ferrocene on elastomer **315** did not lose any chemical activity as a result of being bonded to the surface of elastomer **201**. Since the ferrocenyl group of elastomer **315** did not lose any chemical activity, it was envisaged that when the crown ether derivatives is bound to elastomer **201**, they would also retain their capability to complex sodium cations.

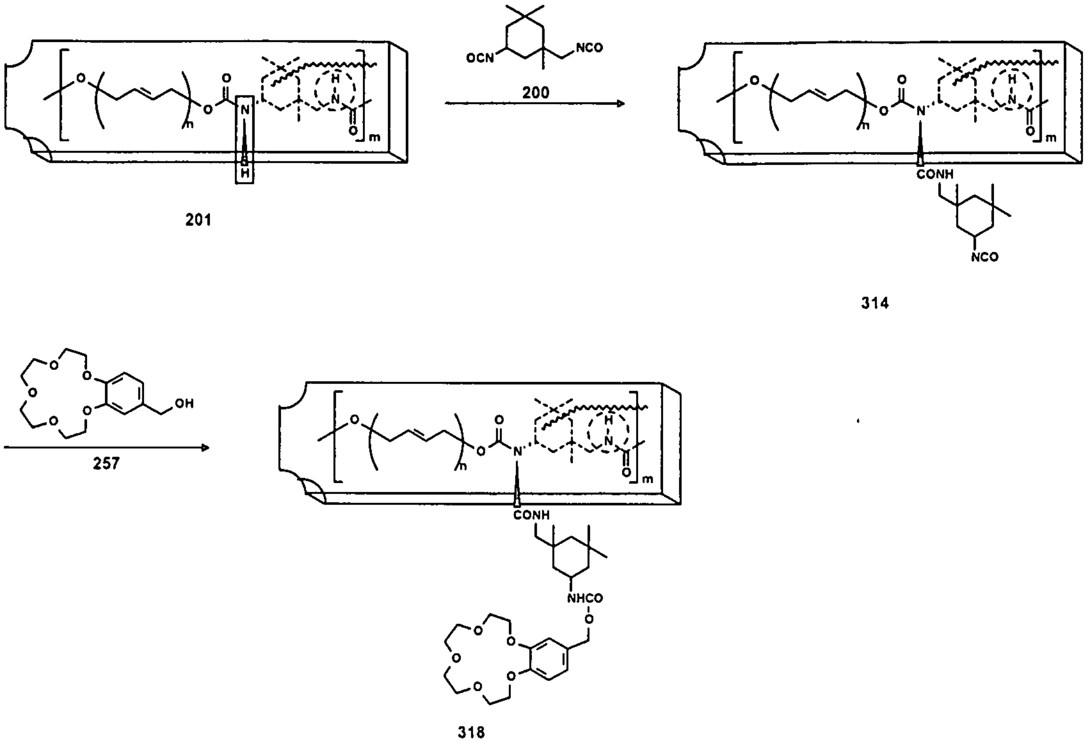


315 yellow

317 blue

Scheme 3. 47. The oxidising of the bound yellow ferrocene on the surface of elastomer 315 by the oxidising agent *p*-benzoquinone (316) proved that surface bound ferrocene anchored to the surface of the solid support retain its redox activity.

The alcohol derivative 4'-(hydroxymethyl)benzo-15-crown-5 (**257**) was subsequently bound to elastomer **201**, utilising the same experimental procedure as in the synthesis of elastomer **315**. The reaction is shown in Scheme 3. 48. A photograph of this product is shown in Figure 3. 12, p. 114, **photo 2**. It was also found that the alcohol derivative 4'-(hydroxymethyl)benzo-15-crown-5 (**257**) could be placed onto elastomer **201** without dissolving it in the solvent hexane simply by spreading a thin liquid film of 4'-(hydroxymethyl)benzo-15-crown-5 (**257**) over the surface of elastomer **314**, followed by washing the excess the crown ether from the surface of this elastomer.



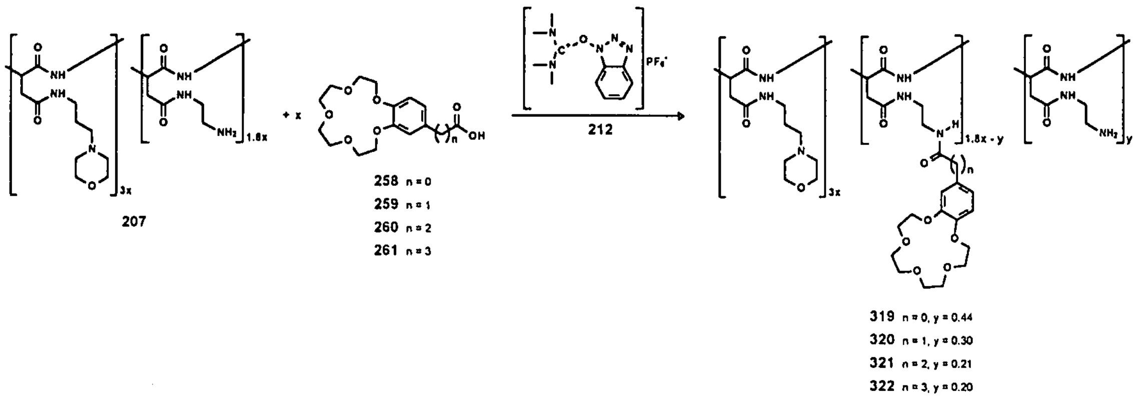
Scheme 3. 48. The anchoring of the alcohol derivative 4'-(hydroxymethyl)benzo-15-crown-5 (257) to the elastomer 201 with the use of the spacer isophorone diisocyanate (200).

The effectiveness of elastomers **318** to remove Na^+ from a standard sodium chloride solution was hereafter determined. This was done by dipping elastomer **318** into a solution containing 200 ppm Na^+. After the removal of the elastomer **318** from the solution, the amount of Na^+ that was removed from the solution was measured by standard flame photometric techniques. It was found that elastomer **318** could remove 0.044 g Na^+ / m^2 surface area of the sodium cation scavenging device. This is a very modest result, but it demonstrated the principle that the anchoring of a crown ether onto a solid support, to produce a sodium cation scavenging device, could work, provided that the crown ether scavenger is not immobilised directly onto a solid support. It needs to be separated from the solid support by a spacer, here the isophorone diisocyanate moiety. The next task was to try and improve the effectiveness of this sodium cation scavenging device.

In order to improve the effectiveness of Na^+ uptake by this insoluble elastomer **318**, it was decided to attach large spacers between the solid support and the crown ether so that the crown ether would be further separated from the surface of the elastomer, and to simultaneously add more active sites, where crown ethers can be anchored, to the same area of elastomer. Several methods of introducing this spacer were investigated.

3.6 ANCHORING OF BENZO-15-CROWN-5 DERIVATIVES ONTO THE WATER-SOLUBLE POLYMERIC CARRIERS

Having had established that the sodium cation scavenging device **318** can actually remove Na^+ from an aqueous solution, albeit with a low effectiveness, attention was turned to the water-soluble polymer series **207** and **302**. The reason behind this approach was that if crown ether derivatives can be anchored onto them, and if they in turn can then be anchored onto elastomer **201**, the resulting new device is envisaged to have a much larger crown ether content per square meter of the solid support **201**. The choice to impose water-solubility into the polymeric side chain that is to be anchored onto elastomer **201** is also well founded. It is a well-known fact that reactions that have to take place across any phase change, i.e. a heterogeneous process, are much slower and ineffective than those that takes place in a homogenous system. Although elastomer **201** is water insoluble, it was therefore argued that if the side chains that is anchored onto elastomer **201**, which contains the crown ethers, could be made hydrophilic, this will change the properties of the resulting device to have a faster and more effective cation scavenging action in wastewater, than would be the case if the side chains were incompatible with water. Towards this goal then, chemistry had first to be developed to bind functionalised crown ethers effectively onto the water-soluble carrier polymers **207** and **302**. In a first approach, borrowing from the techniques developed by biochemists, the carboxylic acid functionalised crown ether 4'-carboxybenzo-15-crown-5 (**258**), 4'-(ethanoic acid)benzo-15-crown-5 (**259**), 4'-(propanoic acid)benzo-15-crown-5 (**260**) and 4'-(butanoic acid)benzo-15-crown-5 (**261**) were anchored onto polymer **207**, with side chain ratios of 3:1.8, utilising the coupling reagent *O*-benzotriazolyl-*N,N,N',N'*-tetramethyluronium hexafluorophosphate (**212**) according to Scheme 3. 49, p. 120. After workup, which included dialysis in a 12 000 g/mol molecular mass cut-off dialysis tube and freeze drying, polymers **319** – **322** were isolated in ± 25 % yield.



Scheme 3. 49. The anchoring of the carboxylic acid functionalised crown ethers 258 – 261 onto the water-soluble polymer 207 with the coupling reagent *O*-benzotriazolyl-*N,N,N',N'*-tetramethyluronium hexafluorophosphate (212).

The efficiency of the coupling reaction between the carboxylic acid derivatives **258** – **261** and the water-soluble polymer **207** was determined by ^{1}H NMR spectroscopy. To illustrate this procedure the ^{1}H NMR spectrum of the water-soluble polymer **321** (Figure 3. 14, p. 122) may serve as an example. The starting polymer, according to Scheme 3. 49 had an average 3 *N*-(3-aminopropyl) morpholine side groups for every 1.8 ethylenediamine side chains. The water-soluble polymer **321** must have the same side chain distribution. The signal of the six (6) β-protons of the *N*-(3-aminopropyl)-morpholine side group are found at 1.28 – 1.52 ppm and has an integral value of 5.29. This corresponds to $\frac{5.29}{6} = 0.882$ integral units per proton. The signal of the three (3) aromatic protons of the crown ether moiety, protons $H_{a'}$, $H_{b'}$ and $H_{c'}$, are found at 6.41 – 6.72 ppm and has an integral value of 1.46 + 2.69 = 4.15 integral units. This integral value corresponds to $\frac{4.15}{0.882} = 4.71$ protons. Because there are 3 aromatic protons for each crown ether moiety, it follows that the water-soluble polymer **321** must have $\frac{4.71}{3} = 1.57$ crown ether moieties in its total repeating unit structure. Since the maximum amount of crown ether moieties that the water-soluble polymer **321** can have is 1.8, it follows that y = 1.8 – 1.57 = 0.23.

In an alternative approach to obtain the value of y, attention may be focussed on the four (4) $PhOC\underline{H_2}CH_2O$ protons of the crown ether moiety. The ^{1}H NMR signal of these protons may be found at 3.72 – 3.95 ppm. This signal has an integral value of 5.71 that correspond to $\frac{5.71}{0.882} = 6.47$ protons. The amount of crown ether moieties that led to this signal must therefore be $\frac{6.47}{4} = 1.62$, implying that y = 1.8 – 1.62 = 0.18. This is in fairly good agreement with the previously described determination of y = 0.23, utilising the aromatic protons.

In a third, more complicated, approach attention can be focussed on the combined ^{1}H NMR signals of the four (4) $PhOCH_2C\underline{H_2}O$ protons and the eight (8) $OC\underline{H_2}C\underline{H_2}O$ protons of the crown ether moiety, which can be found at 3.30 – 3.55 and 3.55 – 3.72 ppm respectively. These two signals must be treated simultaneously due to the poor resolution of these two peaks. A further complicating factor of these signals is due to the fact that the 4 x 3 = 12 ε-protons of the *N*-(3-aminopropyl)morpholine group are also found at 3.30 – 3.55 ppm. The total integral value found at the two peaks under discussion is 21.80 + 6.08 = 27.88 integral units. From this must be subtracted the integral value that is associated with the 12 ε-protons. The integral value associated with the 12 correct crown ether protons is therefor 27.88 – (12 x 0.882) = 17.30 integral values. Utilising the 12 $PhOCH_2C\underline{H_2}O$ and $OC\underline{H_2}C\underline{H_2}O$ protons of the crown ether moiety on the water-soluble polymer **321**, it follows that there must be $\frac{17.30}{12} = 1.44$ crown ether moieties on the water-soluble polymer **321**, and y = 1.8 – 1.44 = 0.36. This value is slightly larger than the previous two values, and the inaccuracy is attributed to the poor resolution of the multiple peaks in the ^{1}H NMR spectral region. But even so, the value of y = 0.36 is still in fairly to moderate agreement with the two first mentioned determinations of y.

In a fourth and final method to determine y, the combined spectral region of 1.93 – 3.12 ppm may be considered. The total integral count for this region is 5.79 + 13.61 + 3.84 + 7.32 + 10.99 = 41.55 integral units. The known protons that is found in this region is {[(6 α-protons) + (6 γ-protons) + (12 δ-protons)] from the *N*-(3-aminopropyl)morpholine side groups} + {[(1.8 x 2 α'-protons) + (1.8 x 2 β'-protons)] from the ethylenediamine side groups} + {(6 asp-CH_2 protons) from the main chain linked to the *N*-(3-aminopropyl)morpholine side groups} + {(1.8 x 2 asp-CH_2 protons) from the main chain linked to the ethylenediamine side group} = 40.80 protons. The integral value associated with these **KNOWN** protons is therefore 40.80 x 0.882 = 35.99 integral values. The unaccounted integral value is thus 41.55 – 35.99 = 5.56, and this corresponds to $\frac{5.56}{0.882} = 6.30$ protons. The only unaccounted protons, in this region, are the $PhC\underline{H}_2C\underline{H}_2CO$ protons that originates from the side chain that linked the crown ether **260** to the water-soluble carrier **207**. There are four (4) of these protons in each of the crown ether moieties in the water-soluble polymer **321**, which implies that the water-soluble polymer **321** contains $\frac{6.30}{4} = 1.58$ crown ether moieties, and that y = 1.80 – 1.58 = 0.22. This result is remarkably well in agreement with methods 1 and 2, as described above. Methods 1, 2 and 4 were considered as mutually consistent, giving an average y-value of 0.21x.

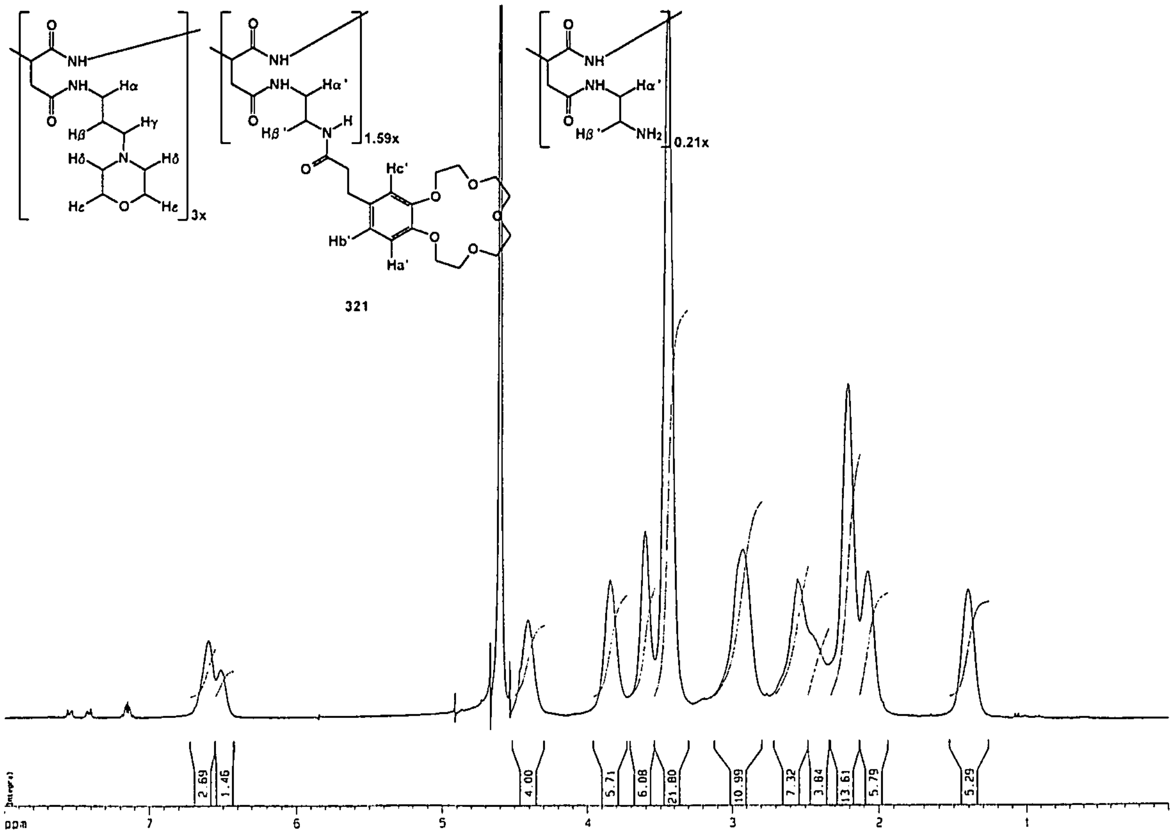


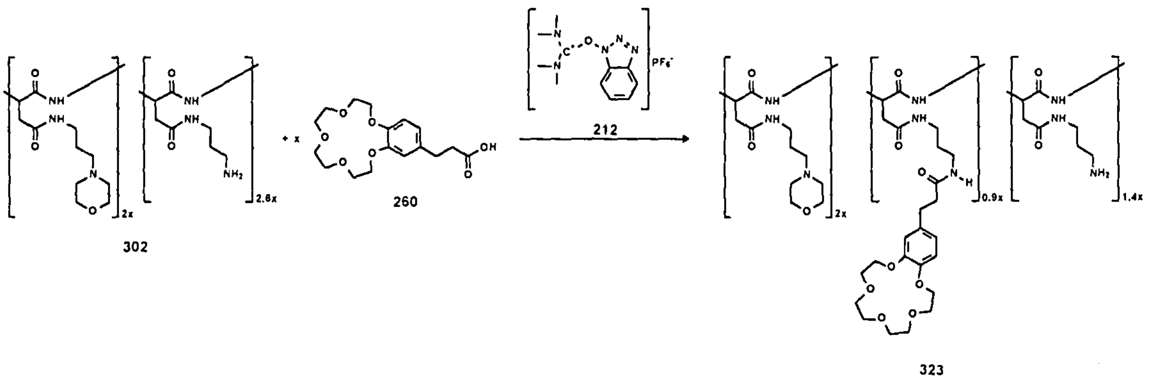
Figure 3. 14. ^1H NMR spectrum of the water-soluble polymer 321.

The carboxylic acid functionalised derivatives with one or more methylene groups in the side chain, that is the series **258** – **261** were successfully anchored, but the target ratios of the side chains could not be achieved. The actual ratios obtained are summarised in Table 3. 2.

Table 3. 2. The actual side chain ratios for the series of water-soluble polymers 319 – 322.

Polymer number	n	Target *N*-(3-aminopropyl)morpholine:crown ether ratio	Obtained *N*-(3-aminopropyl)morpholine:crown ether ratio
319	0	3:1	3:1.36
320	1	3:1	3:1.50
321	2	3:1	3:1.59
322	3	3:1	3:1.60

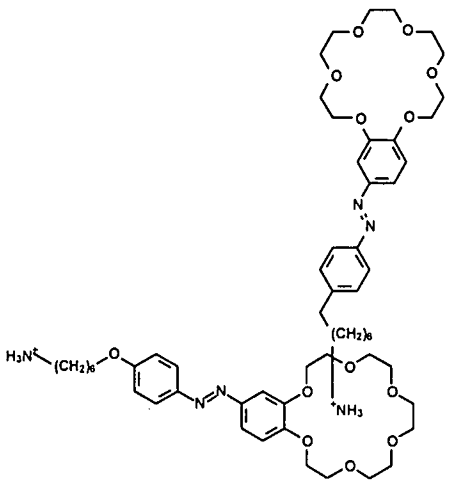
Having established a successful protocol of anchoring carboxylic acid derivatised crown ethers onto an amine functionalised water-soluble polymer, 4'-(propanoic acid)benzo-15-crown-5 (**260**) was anchored onto the water-soluble polymer **302**, according to Scheme 3. 50. This was done to obtain a handle, in the form of the free amines, to anchor the water-soluble polymer **323** onto the solid support **201**. This anchoring handle was not supposed to be available in the series of polymers **319** – **322** if crown ether anchoring was quantitative. The target ratio of solubilising morpholino groups to crown ether cation scavenger to free amines was chosen to be 2:1:1.3 in the water-soluble polymer **323**, but ^{1}H NMR study showed that in practise a ratio of 2:0.9:1.4 was actually obtained.



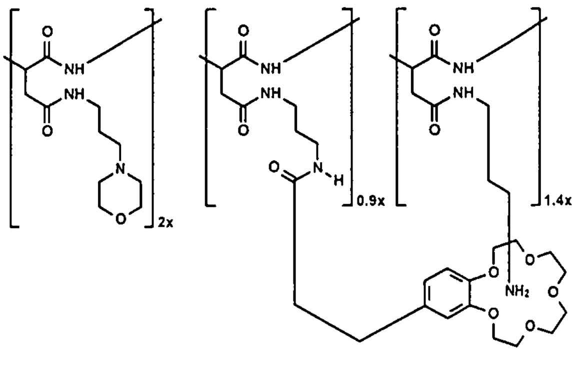
Scheme 3. 50. The anchoring of 4'-(propanoic acid)benzo-15-crown-5 (260) onto the water-soluble polymer 302.

A peculiar observation in the ^{1}H NMR spectrum of the water-soluble polymer **323** was made. There appeared to be two distinct sets of aromatic protons in this

^1H NMR spectrum. The one is the usual set observed at 6.35 – 6.71 ppm. A second set, however, was observed at 7.05 – 7.65 ppm. The latter set of signals was also observed in a few other ^1H NMR spectra, e.g. for the water-soluble polymer **321** (Figure 3. 14, p. 122), but in all these cases the second set of aromatic ^1H NMR signals was so small that it was ignored. For the water-soluble polymer **323** this set of signals constitutes almost 50 % of the total aromatic signals. The exact reason of this observation needs further research for clarification, but it was considered outside the boundaries of this study. However, it is known that amines may interact with an empty crown ether cavity, as shown in Figure 3. 15, p. 124.[178]



324



323

Figure 3. 15. The interaction between an amine and an empty crown ether cavity.

Water-soluble polymer **323** is the first made in this study that contains a large content of free amine side chains (ration crown ether:free amine groups is 0.9:1.4). The water-soluble polymer **321** have a ratio of crown ether:free amine groups of 1:0.21. It may well be that in the water-soluble polymer **323** a similar amine-crown ether interaction may take place, as shown in Figure 3. 15. This would result in a completely different environment around the phenyl group, which may explain the two sets of the aromatic ^1H NMR signals for this compound. To prove this hypothesis, in a follow-up study, various derivatives of the water-soluble polymer **323** should be prepared, containing different crown ether:free amine group ratios. If it is found that there is a direct relationship between the intensities of the two ^1H

NMR sets of signals at 6.35 – 6.71 and 7.05 – 7.65 ppm, and the crown ether/free amine content ratios, then the above hypothesis will be valid. If no such relation is found, a different explanation will have to be searched for.

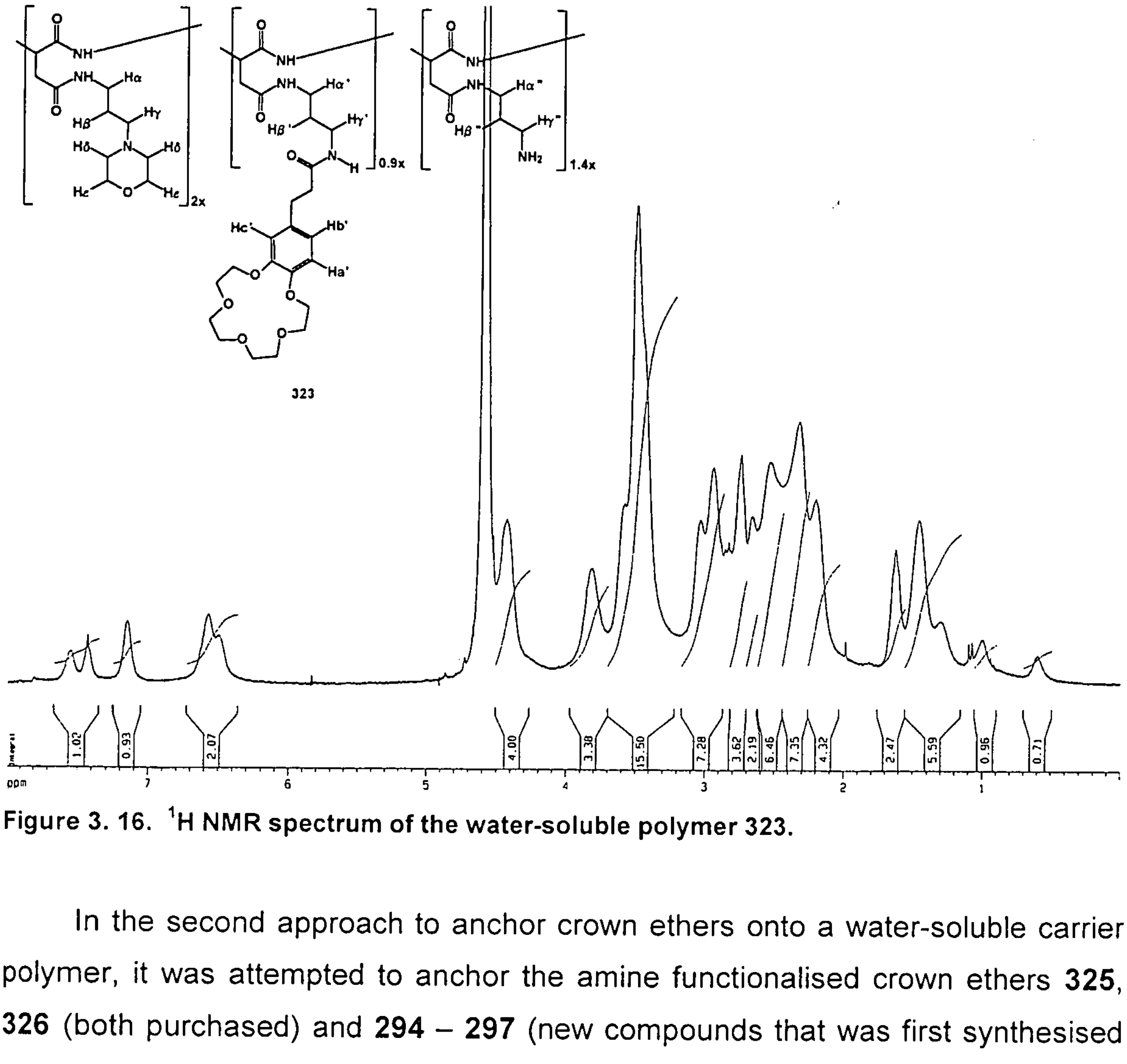
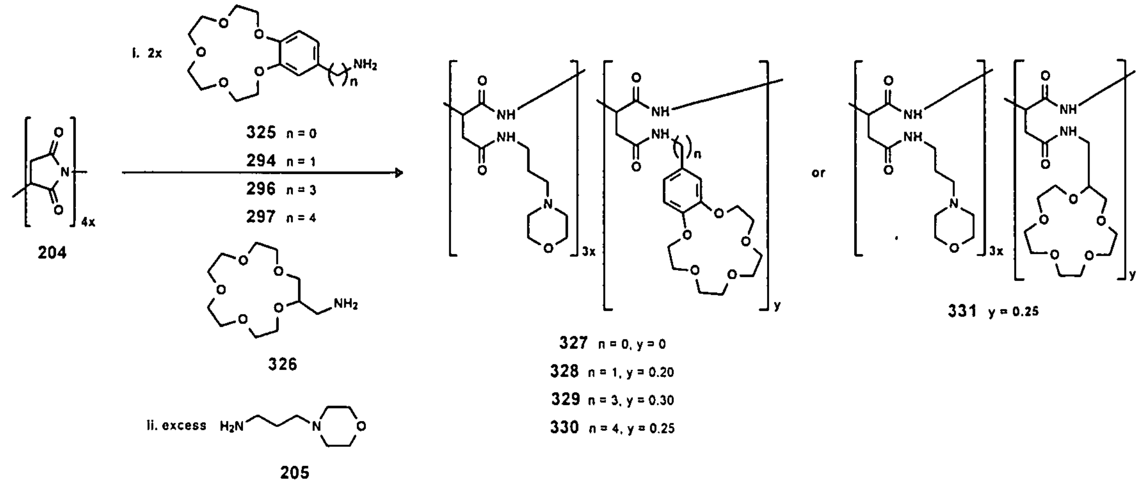


Figure 3. 16. ^{1}H NMR spectrum of the water-soluble polymer 323.

In the second approach to anchor crown ethers onto a water-soluble carrier polymer, it was attempted to anchor the amine functionalised crown ethers **325**, **326** (both purchased) and **294** – **297** (new compounds that was first synthesised during the course of this study) directly onto polysuccinimide (**204**), according to Scheme 3. 51, p. 126.

The target ratio of the water-soluble polymers **327** – **331** was 3x morpholino side groups for every x crown ether side group. Polymer **327** could not be obtained even under forcing (high temperatures, long reaction times) conditions. The reason for this synthetic failure is in part due to the fact that 4'-aminobenzo-15-crown-5 (**325**) is apparently a poor nucleophile. Steric hindrance, due to the fact that the amine group of 4'-aminobenzo-15-crown-5 (**325**) is so close to the benzo-crown moiety may, however, also play a part.



Scheme 3. 51. The synthesis of water-soluble polymers 327 – 331 from the amine functionalised crown ether derivatives 325, 294, 296, 297 and 326. The target y-value was y = 1.

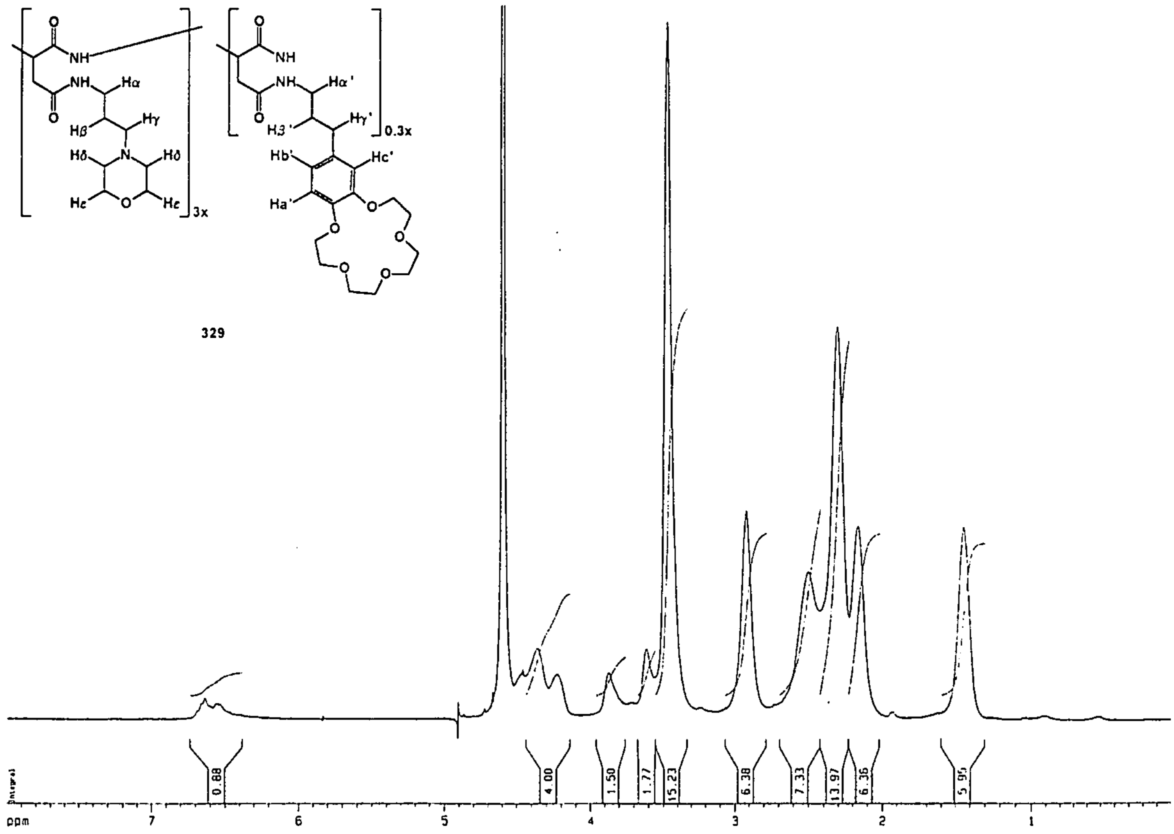


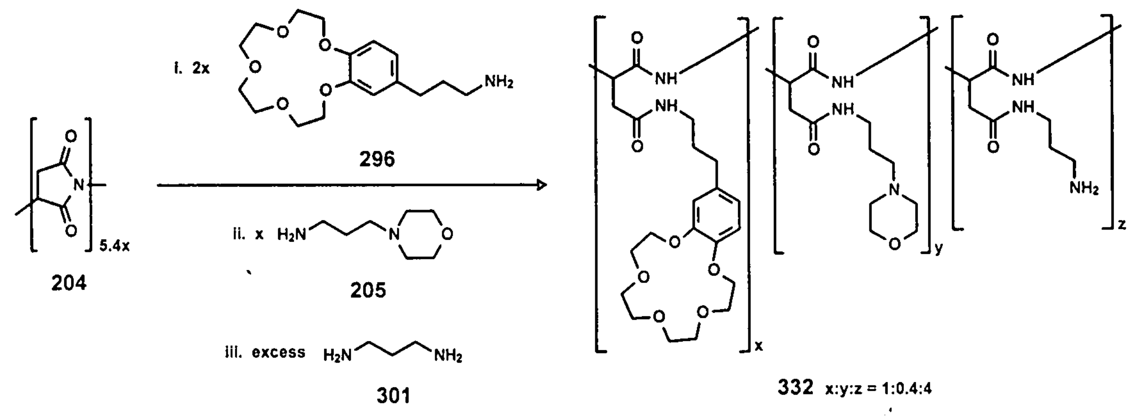
Figure 3. 17. The ^{1}H NMR spectrum of polymer 329.

The amine functionalised derivatives with one or more methylene groups in the side chain, that is the series **294** – **297** and **326**, were, however, successfully anchored, but the target ratios of the side chains could not be achieved. The actual ratios obtained is summarised in Table 3. 3 and Figure 3. 17, p. 126 represents the ^{1}H NMR spectrum of the water-soluble polymer **328**.

Table 3. 3. The actual side chain ratios for the series of water-soluble polymers 326 – 330.

Polymer number	n	Target morpholine:crown ether ratio	Obtained morpholine:crown ether ratio
327	0	3:1	—
328	1	3:1	3:0.20
329	3	3:1	3:0.30
330	4	3:1	3:0.25
331	—	3:1	3:0.25

To increase the amount of crown ethers on these water-soluble polymers by the interaction of aminated crown ether derivatives with polysuccinimide (**204**) and simultaneously obtain a free amine handle, on this polymer for future anchoring reactions, it was thought appropriate to synthesise polymer **332**, which possess the amine functionalised derivative 4'-(aminopropyl)benzo-15-crown-5 (**296**), as well as propylenediamine (**301**) as side chains. Again, the *N*-(3-aminopropyl)morpholine side group would increase the water solubility. This water-soluble polymer would then be heavily laden with crown ethers, and will also contain active amine sites for the ultimate anchoring of this water-soluble polymer onto elastomer **201**. The synthesis of this water-soluble polymer **331** is depicted in Scheme 3. 52, p. 128, and the side chain ratios was intended to be x:y:z = 2:1:1. In practice, however, the ratio of this water-soluble polymer **331** was determined by ^{1}H NMR spectroscopy as x:y:z = 1:0.4:4.



Scheme 3. 52. The synthesis of the water-soluble polymer 332.

In all the reactions involving the interaction between polysuccinimide (**204**) and the aminated crown ether derivatives, **325**, **294**, **296**, **297** and **326** (Scheme 3. 51, p. 126 and Scheme 3. 52) the actual binding success was consistently much lower than intended.

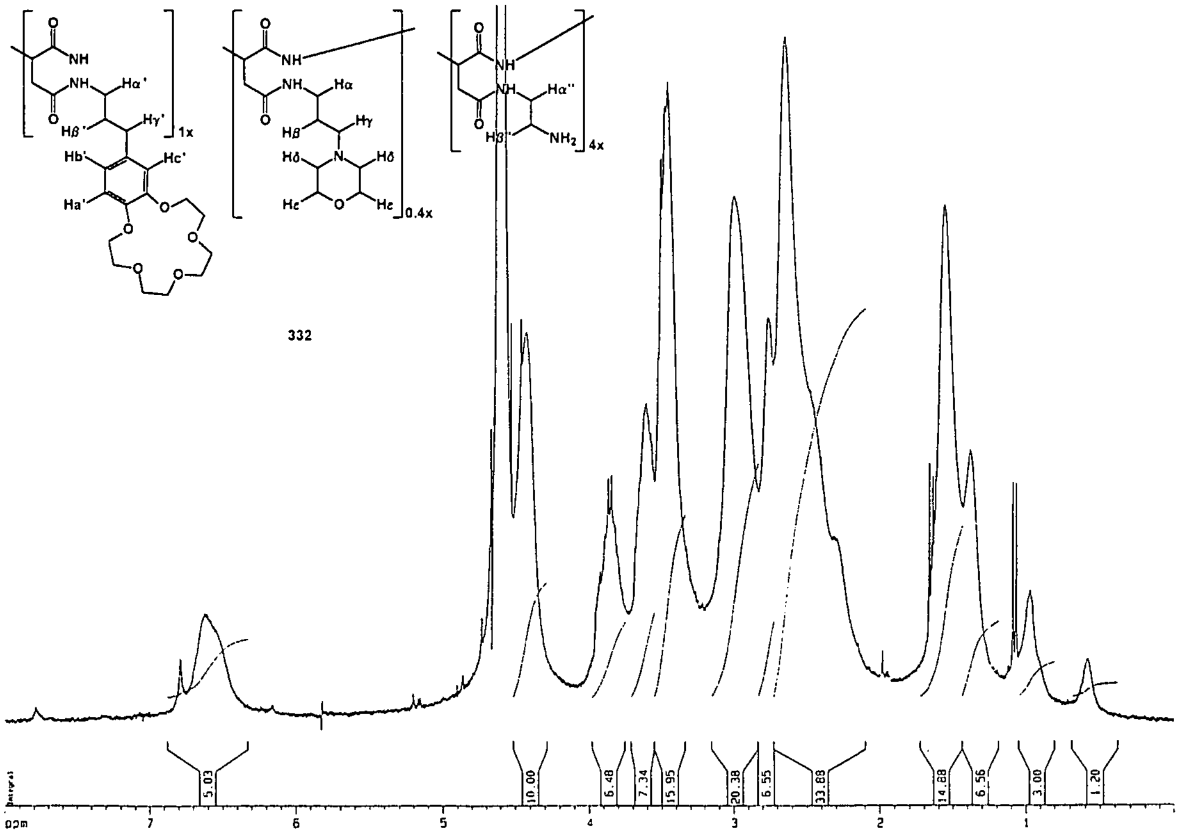


Figure 3. 18. ^{1}**H NMR spectrum of the water-soluble polymer 332.**

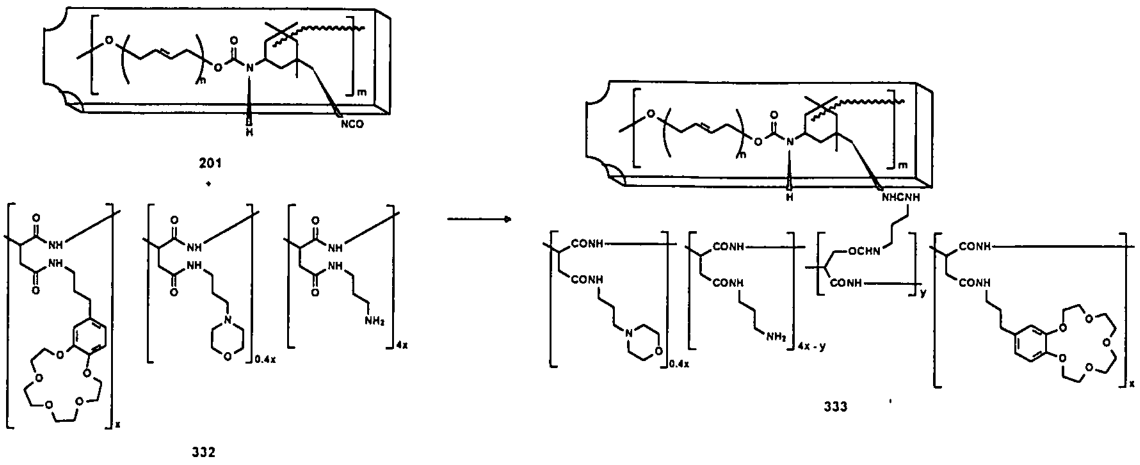
The failure of 4'-aminobenzo-15-crown-5 (**325**) to react with polysuccinimide (**204**, Scheme 3. 51, p. 126) could be explained in terms of the poor nucleophilic activity of **325**. It cannot, however, explain the poor anchoring success rate of **294**, **296**, **297** and **326**. It can be concluded that the bulk of the crown ether moiety prevent easy access to the reaction sites on polysuccinimide and that this method of anchoring the crown ether derivatives to polysuccinimide (**204**) is inferior compare to the anchoring of the carboxylated crown ether derivatives to aminated polymers as described in Scheme 3. 49, p. 120.

3.7 ANCHORING OF POLYMERIC CROWN ETHER DERIVATIVES ONTO THE SOLID SUPPORT

Having concluded the investigation of how to successfully anchor crown ether derivatives onto water-soluble polymers, attention was focussed on how to anchor these polymeric-crown ether systems to a solid support.

3.7.1 *Anchoring of the water-soluble polymer* ***332***

The availability of the crown ether/polyaspartamide conjugate **332**, initiated anchoring procedures of how to anchor the polymeric crown ether derivatives onto partially cured solid support. An adaptation of the procedure that was developed for device **318** (Scheme 3. 48, p. 118) was used. Although the fully cured support **201** have surface accessible amino groups as shown in Figure 3. 11, p. 112, the partially cured support **201** has surface accessible isocyanate groups and the free amines of the water-soluble polymer **332** can be used to react with these isocyanate groups, thereby anchoring it onto elastomer **201** *via* an urethane bond to form the sodium cation scavenging device **333** (Scheme 3. 53, p. 130).

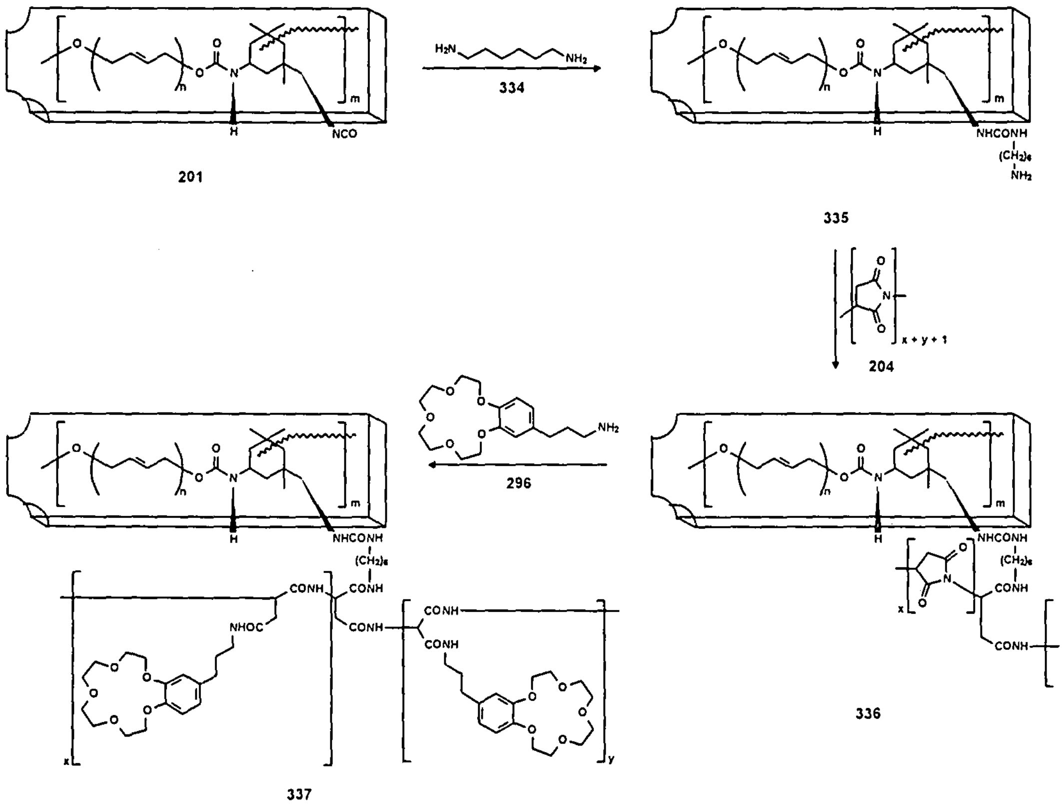


Scheme 3. 53. The synthesis of elastomer 333.

The effectiveness of elastomer **333** to remove Na^+ from a standard sodium chloride solution (50 ppm) was hereafter determined, utilising again the flame photometric method. It was found that elastomer **333** could remove 0.062 g Na^+ / m^2 surface area of the sodium cation scavenging device. This represents an improvement of 41 % over the sodium cation scavenging capabilities of device **318** of Scheme 3. 48, p. 118. This result is not particular good, and the reason for this can be ascribed to the presence of the large amount of free amine side chains in the water-soluble polymer **332**. Elastomer **333** is shown to only have bind to the water-soluble polymer **332** by y-amount of free amines on the water-soluble polymer **332**. In reality this is an idealised structure, and it is possible that more amine side groups can add to the surface of elastomer **201**, producing loop-like structures. The crown ether moieties on the water-soluble polymer **332** that is trapped underneath these loops, cannot take part in the complexation of Na^+, and the amount of available crown ether moieties for the ultimate complexation of Na^+ is thus diminished. This can also be the reason for the low complexation ability of the sodium cation scavenging device **333**.

*3.7.2 Polysuccinimide (**204**) as anchoring intermediate*

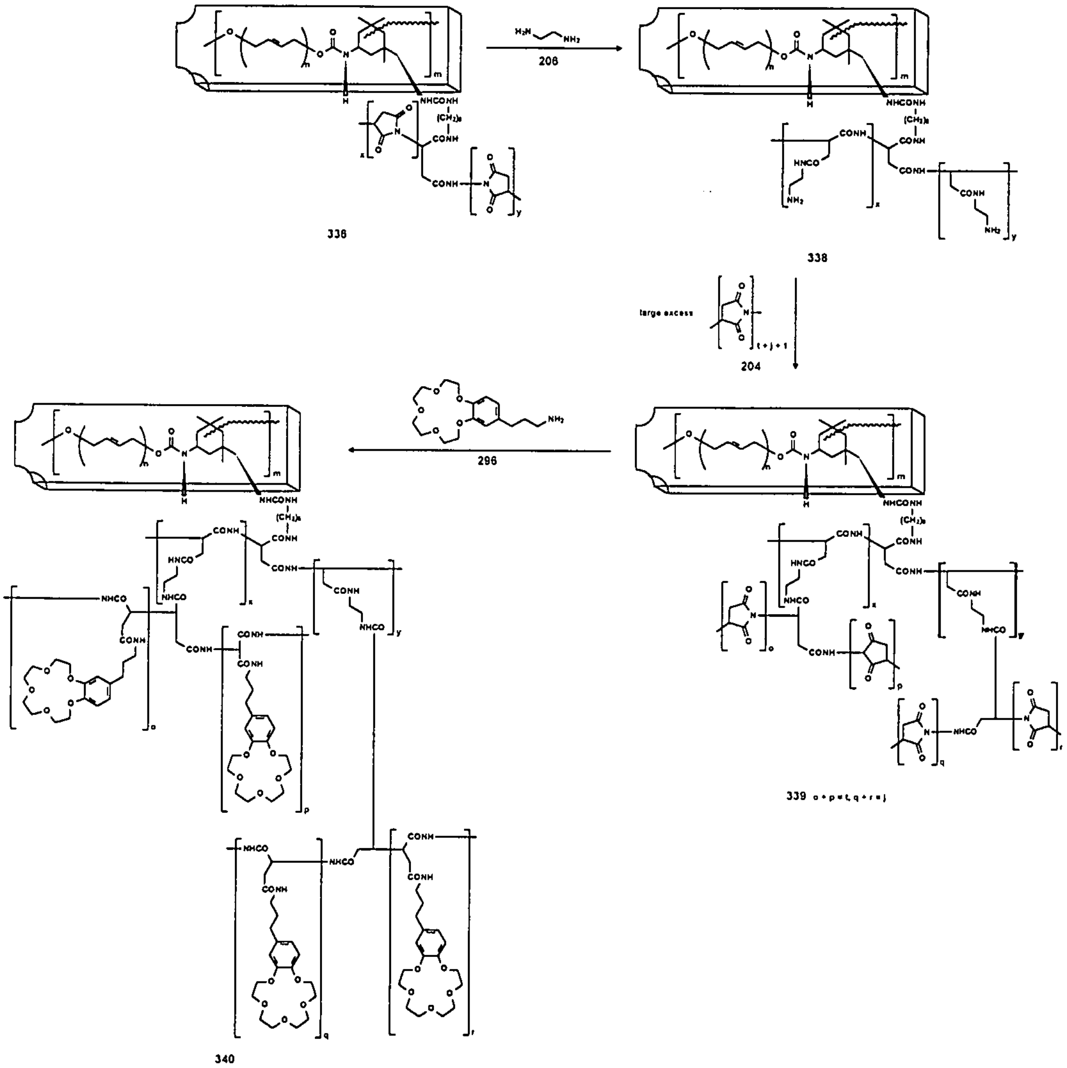
The improvement that elastomer **333** induced in sodium cation scavenging capabilities was really not what was anticipated. It was therefore attempted to bind polysuccinimide (**204**) directly onto elastomer **201** before the crown ether moieties were introduced into the system. This approach however implied that it was first necessary to anchor a diamine compound, such as hexamethylenediamine (**334**), on elastomer **201** before polysuccinimide (**204**) is attached to the solid support. Only after elastomer **201** was modified to have surface-bound amine nucleophiles (compound **335**) would polysuccinimide (**204**) successfully react to give the polysuccinimide coated device **336**. In the final step of this approach, the amine functionalised crown ether 4'-(aminopropyl)benzo-15-crown-5 (**296**) was given ample time to react with the surface bonded succinimide moieties on device **336**. The entire reaction sequence is shown in Scheme 3. 54. Although the final potential sodium cation scavenging device **337** shown in Scheme 3. 54, are shown to have reacted to completion with the amine 4'-(aminopropyl)benzo-15-crown-5 (**296**), this may in practise not have happened. Suffice it to say that the structure of elastomer **337** is idealised.



Scheme 3. 54. The synthesis of elastomer 337.

After the removal of any unreacted residues of the crown ethers from the surface of the potential sodium cation scavenging device **337** the effectiveness of elastomer to remove Na^+ from a standard sodium chloride solution (50 ppm) was determined. It was found that elastomer **337** could remove 0.065 g Na^+ / m^2 surface area of the sodium cation scavenging device. This value is mutually consistent with what was observed for device **333**. Now, to further improve the sodium cation scavenging properties of **337**, 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 **201**.

To achieve this the device **336** from Scheme 3. 54, was swamped with a large excess of ethylenediamine (**206**) to obtain the highly aminated surface **338** in Scheme 3. 55.



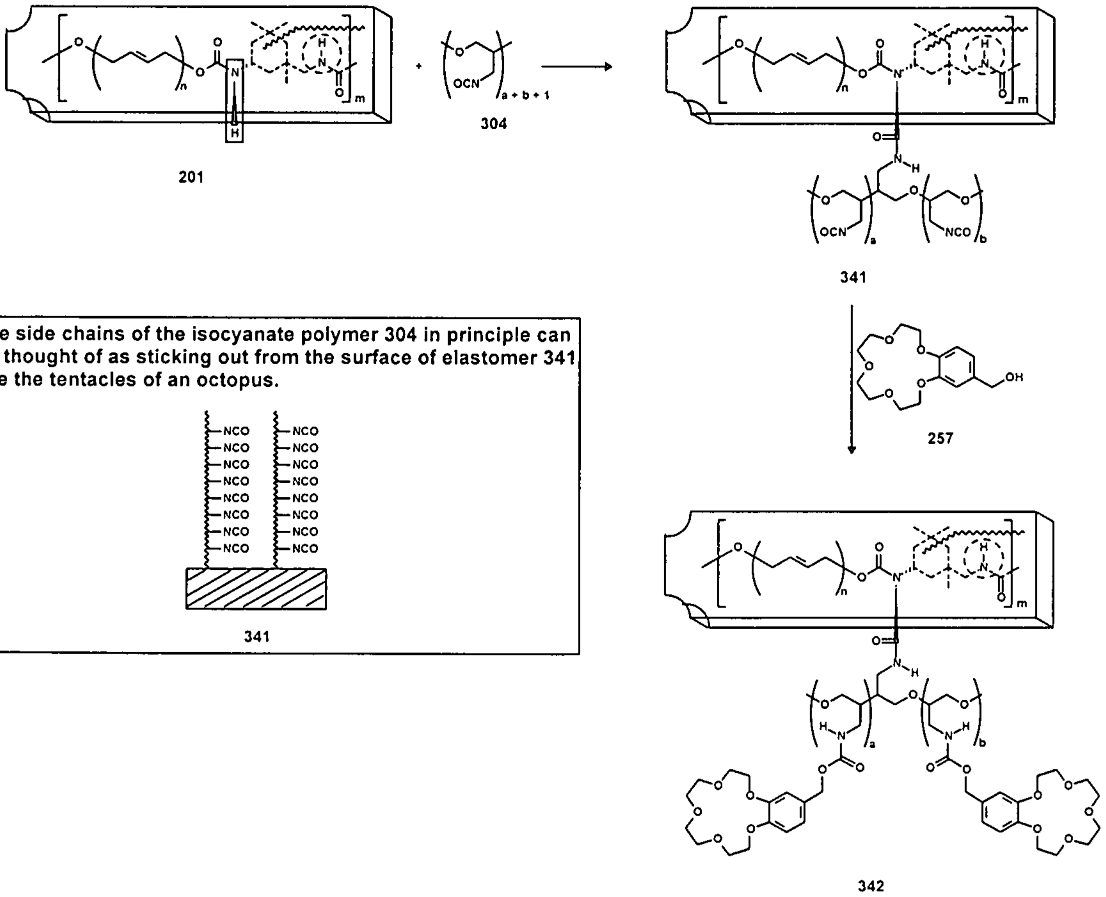
Scheme 3. 55. The synthesis of elastomer 340.

Structure **338** 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 (**206**) should have minimised this unwanted side reaction. The device **338** was then treated with a large excess of polysuccinimide (**204**) to liberate elastomer **339**. This procedure resulted in the solid support being much heavier laden with succinimide moieties than device **336**. The nucleophilic attachment of 4'-(aminopropyl)benzo-15-crown-5 (**296**) onto elastomer **339** then resulted in the idealised presentation of elastomer **340**.

The effectiveness of the sodium cation scavenging device **340** to remove Na^+ from a standard sodium chloride solution (50 ppm) was then determined. It was found that elastomer **340** could remove only 0.098 g Na^+ / m^2 surface area of the sodium cation scavenging device. This is an improvement of 123 % over the performances of the sodium cation scavenging device **318**, and 51 % over that of the sodium cation scavenging device **337**, but all in all still a disappointing result. It was concluded that polysuccinimide derivatised sodium cation scavengers are inherently not efficient enough to warrant further research on these complexes, probably because anchoring of aminated crown ether derivatives onto polysuccinimide (**204**) is not an efficient reaction. Attention was then focussed on more reactive polymeric side chains that could be used to anchor crown ethers more effectively on them. Within the scope of this study, attention, therefore, was turned to isocyanate containing polymers.

*3.7.3 The isocyanate polymer **304** as anchoring intermediate*

In order to improve the effectiveness of the anchoring of crown ethers onto the surface of elastomer **201**, it was decided to synthesis a solid support using the isocyanate polymer **304** as the spacer. The isocyanate group would react faster with alcohol and amine functionalised compounds than the imide rings of polysuccinimide (**204**). The synthesis of this elastomer can be seen in Scheme 3. 56, p. 134. The target of the polyisocyanate derivative **304** was either the surface accessible imino group of elastomer **201** (see Figure 3. 11, p. 112) or one of the hydroxy end-groups of the HTPB fragment of **201** that is accessible on the elastomer's surface. The hydroxy attacking site of elastomer **201** is not shown in Scheme 3. 56. For simplicity only the amino site will be shown throughout this thesis. After the removal of the unbound polymer **304** from the surface of elastomer **341**, 4'-(hydroxymethyl)benzo-15-crown-5 (**257**), was allowed to react with the isocyanate groups of the solid support **341** that may be envisaged to stick out from the surface of elastomer **341** as shown in the insert in Scheme 3. 56.



The side chains of the isocyanate polymer 304 in principle can be thought of as sticking out from the surface of elastomer 341 like the tentacles of an octopus.

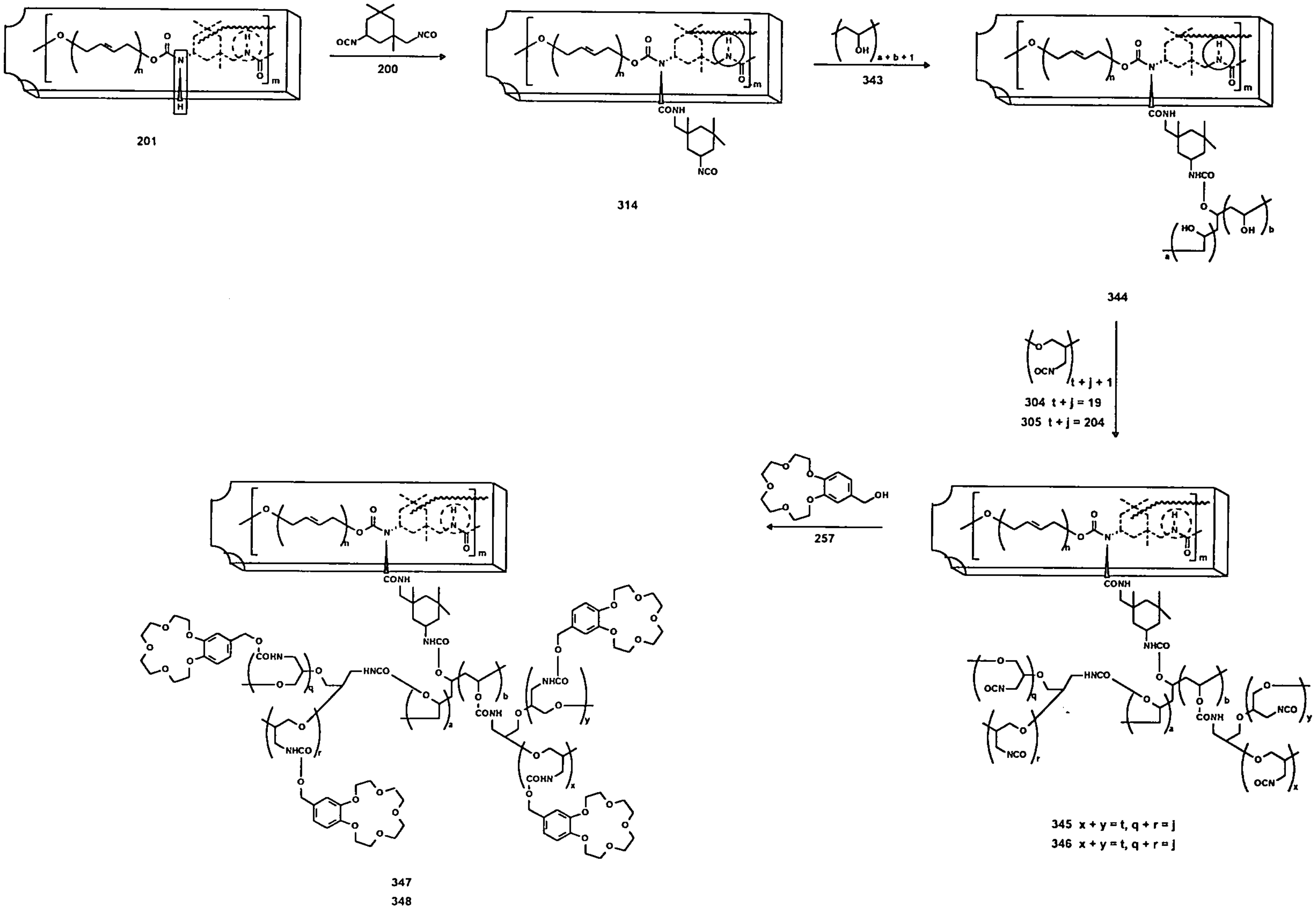
Scheme 3. 56. The synthesis of elastomer 342.

The effectiveness of elastomer **342** to remove Na^+ from a standard sodium chloride solution (200 ppm) was determined in the same manner as all the other sodium cation scavenging devices, and it was found that elastomer **342** removed 0.264 g Na^+ / m^2 surface area of the sodium cation scavenging device. This represents a quantum leap in the effectiveness of sodium cation scavenging devices discussed so far. In particular it represents an improvement of 500 %

over the sodium cation scavenging device **318** (Scheme 3. 48, p. 118) and 169 % over the best polysuccinimide derivative, i.e. device **342** (Scheme 3. 55, p. 132), in tests of sodium cation scavenging capabilities from aqueous solutions.

*3.7.4 Isophorone diisocyanate (**200**), polyvinyl alcohol (**343**) and the isocyanate polymers **304** and **305** as anchoring intermediates*

To further improve the sodium cation scavenging capabilities of devices resembling **342**, it is apparent that a method must be found to load elastomer **201** even heavier with crown ethers than device **342**. With this goal in mind, the devices **347** and **348** was prepared according to Scheme 3. 57, p. 136. In the first step the surface available imino groups of elastomer **201** was allowed to react with isophorone diisocyanate (**200**) to create a surface that is not swamped with a sea of isocyanate groups as was **341**. This mildly isocyanated surface was then reacted with an excess of commercially available polyvinyl alcohol (**343**) of molecular mass 72 000 g/mol. The mildly isocyanated surface of elastomer **314** limited cross-linking reactions more than would a surface like **341** when reacted with a large excess of multifunctionalised alcohols or amines. The newly generated surface during this reaction is heavily coated with hydroxy groups (device **344**). By totally swamping this alcohol surface with a large excess of the polyisocyanate polymers **304** or **305**, products with the idealised structures **345** and **346** were produced. For practical purposes no cross-linking is shown. Cross-linking was minimised by utilising a large excess of polymers **304** or **305** for these reactions. This new heavily isocyanate coated surface was then treated with the alcohol derivative 4'-(hydroxymethyl)benzo-15-crown-5 (**257**). The new sodium cation scavenging devices thus obtained, devices **347** and **348** represent the most heavily crown ether-coated devices prepared so far.



Scheme 3. 57. The synthesis of elastomers 347 and 348.

The effectiveness of these sodium cation scavenging devices **347** and **348** to remove Na^+ from a standard sodium chloride solution (200 ppm) was determined, and it was found that elastomer **347** and **348** could removed 0.76 and 1.28 g Na^+ / m^2 surface area of the sodium cation scavenging device, respectively. This is an improvement of more than 2 800 % over the effectiveness of the sodium cation scavenging device **318** (Scheme 3. 48, p. 118) and this represented the best performance of sodium cation scavenging from aqueous solutions found in this laboratory to date. A summary of all the sodium cation scavenging results by the devices prepared during the course of this study may be found in Table 3. 4.

Table 3. 4. A summary of all the sodium cation scavenging devices tested for Na^+ removal during this study.

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
318	0.044	200
333	0.062	50
337	0.065	50
340	0.098	50
342	0.264	200
347	0.760	200
348	1.280	200

Tests indicated that the exposure of the sodium cation scavenging device **348** to an aqueous sodium solution for times 30 seconds, 2 minutes and 10 minutes, did not influence the complexation ability of the bound ligands (here crown ethers), to complex Na^+. We thus concluded that the kinetics of the complexation of Na^+ is fast on the time scale required for industrial usage.

To further improve the Na^+ scavenging capabilities of the devices described in this study, it will be beneficial to increase the surface area of the solid support as in that of ion exchange resins, but it was considered outside the boundaries of this study to pursue this line of approach.

3.7.5 *Na^+ release from the sodium cation scavenging devices **318**, **333**, **337**, **340**, **342**, **347** and **348***

Having achieved a fair amount of success in removing Na^+ from water with the devices described in the preceding paragraphs, the next step in the development of this technology is to establish conditions by which the Na^+ can again be released from the solid support. The type of crown ethers utilised in this study only releases Na^+ from them under the influence of acids.

The release of Na^+ was therefore investigated utilising two different acid concentrations, namely 1 mol/dm^3 and 6 mol/dm^3 HCl. The effect of temperature and time for this release was also investigated. It was found that the acid concentration of 6 mol/dm^3 did not release more Na^+ from the sodium cation scavenging devices **318**, **333**, **337**, **340**, **342**, **347** or **348** than the 1 mol/dm^3 acid solutions. The time of exposure of the sodium cation scavenging devices to the acid media also did not influence the efficiency of Na^+ release. It was found that the sodium cation scavenging devices release the same amount of Na^+ after 2 minutes and after 10 minutes in the acid solution. The temperature of the acid solution does, however, play a role in the release of the Na^+ from these systems. Results of the temperature study are summarised in Figure 3. 19.

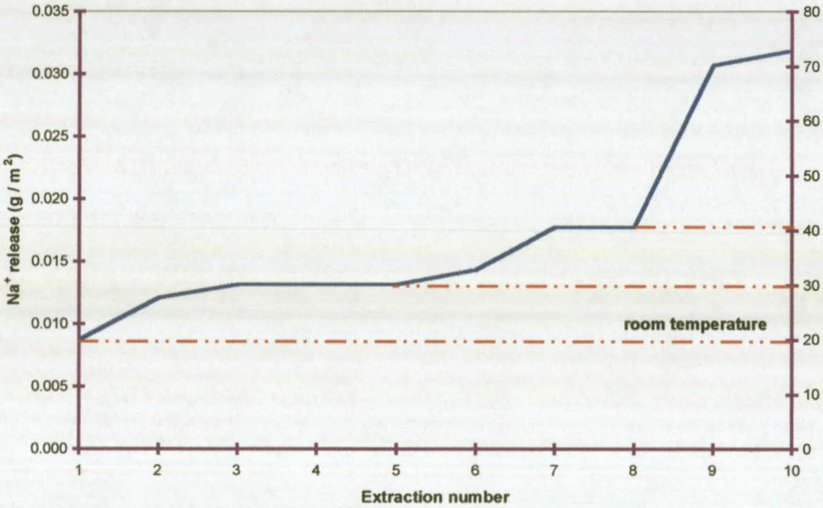


Figure 3. 19. The effect of temperature on the Na^+ release from the sodium cation scavenging device 333.

Figure 3. 19, p. 138, shows that the warmer the acid solution gets (extraction number 9 – 10) the more Na^+ is released from the sodium cation scavenging device. At 70 – 75 °C it was found that all the sodium cation scavenging devices tested in this study released about 50 % of the Na^+ that each device had trapped on its surface the sodium source phase. Results are summarised in Table 3. 5

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

Device	Na^+ released from the surface of the indicated devices 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
318	0.023	0.044
333	0.032	0.062
337	0.033	0.065
340	0.050	0.098
342	0.136	0.264
347	0.391	0.760
348	0.658	1.280

The sodium cation scavenging device **333** was cycled through a 10 cycle sequence. This sequence involved the complexation of Na^+ by device **333**, followed by the release of the trapped Na^+ from device **333** by acid. It was found that the complexation ability of this device did not alter throughout the duration of this test.

3.8 CONCLUSION

In Chapter 1, the problem surrounding removal of especially Na^+ from factory wastewater was described. To address this problem, it was proposed that a conveyor belt should be constructed to act as a solid support for surface-bound benzo-15-crown-5 derivatives, because benzo-15-crown-5 are good Na^+ co-ordinators. This conveyor belt should then be passed through a lake containing Na^+ contaminated factory wastewater. While passing through the contaminated lake, the conveyor belt should trap, or bind, Na^+ with its surface-bound crown ethers. The conveyor belt should then pass through a receiving reservoir, where the trapped Na^+ contaminants are released from the surface of the conveyor belt to regenerate the contaminant scavenging crown ethers. In a cyclic process this system should remove Na^+ contaminants from the lake and concentrate it in a reservoir. When the concentration of the contaminants in this reservoir gets high enough, it will begin to precipitate, allowing recovery of the waste material in a solid form. This will enable the industry to recycle the recovered material in an appropriate way.

This study has developed (but not optimised) the technology needed for this system. Shown below is a diagram of how this system should be operated based on the research results of this study. The conveyor belt, or elastomeric solid support, developed here is polymer **201** (see Figure 3. 20, p. 141).

The crown ether co-ordinators for Na^+ scavenging chosen in this study, had to be functionalised first to enable binding to this solid support. Several functional groups were introduced, notably amines, carboxylic acids and alcohols. Thereafter, the crown ethers were anchored onto the solid support to give *inter alia* the scavenging device **348**. Finally, it was demonstrated how the trapped Na^+ contaminants could again be released from the crown ethers anchored onto the solid support. This was accomplished by passing it through a 1 mol/dm^3 HCl solution.

What still remains to be done in follow-up research programs is the optimisation of this newly developed water-purification technique and extension of the ideas that was developed in this study to include other contaminants than just Na^+. These may also include heavy metals and anions.

CHAPTER 4

CONCLUSION AND FUTURE PERSPECTIVES

The aim of this study was to develop a new technique to clean the total ***factory*** generated wastewater as seen in the light of the background given in Chapter 1. It was decided to develop a material that would enable an industry to complex sodium cations from a contaminated source, and to release the complexed sodium cations, under controlled conditions, at a previously determined site, or receiving reservoir, in a cyclic manner. Such a system, for example, would be a "smart" conveyor belt that could remove Na^+ from a reservoir of contaminated water and could then also deposited this into a receiving phase to regenerate the ligands for subsequent cycles. For this purpose:

a) Crown ethers had to be functionalised.
b) Polymers had to be developed to anchor the crown ethers.
c) A solid support, insoluble in all solvents, had to be developed.

For the realisation of a), 32 different functionalised crown ether derivatives were synthesised to produce a series of 17 new crown ether derivatives, including 4 carboxylic acid, 4 amide, 4 alcohol and 4 amine crown ether derivatives, with spacers ranging from one to four carbon atoms in the side chain. During this study, experimental procedures had to be develop to produce the 17 new crown ether functionalised derivatives. Selected crown ether functionalised derivatives was anchored onto a polymeric solid support and its sodium cation complexation ability was determined.

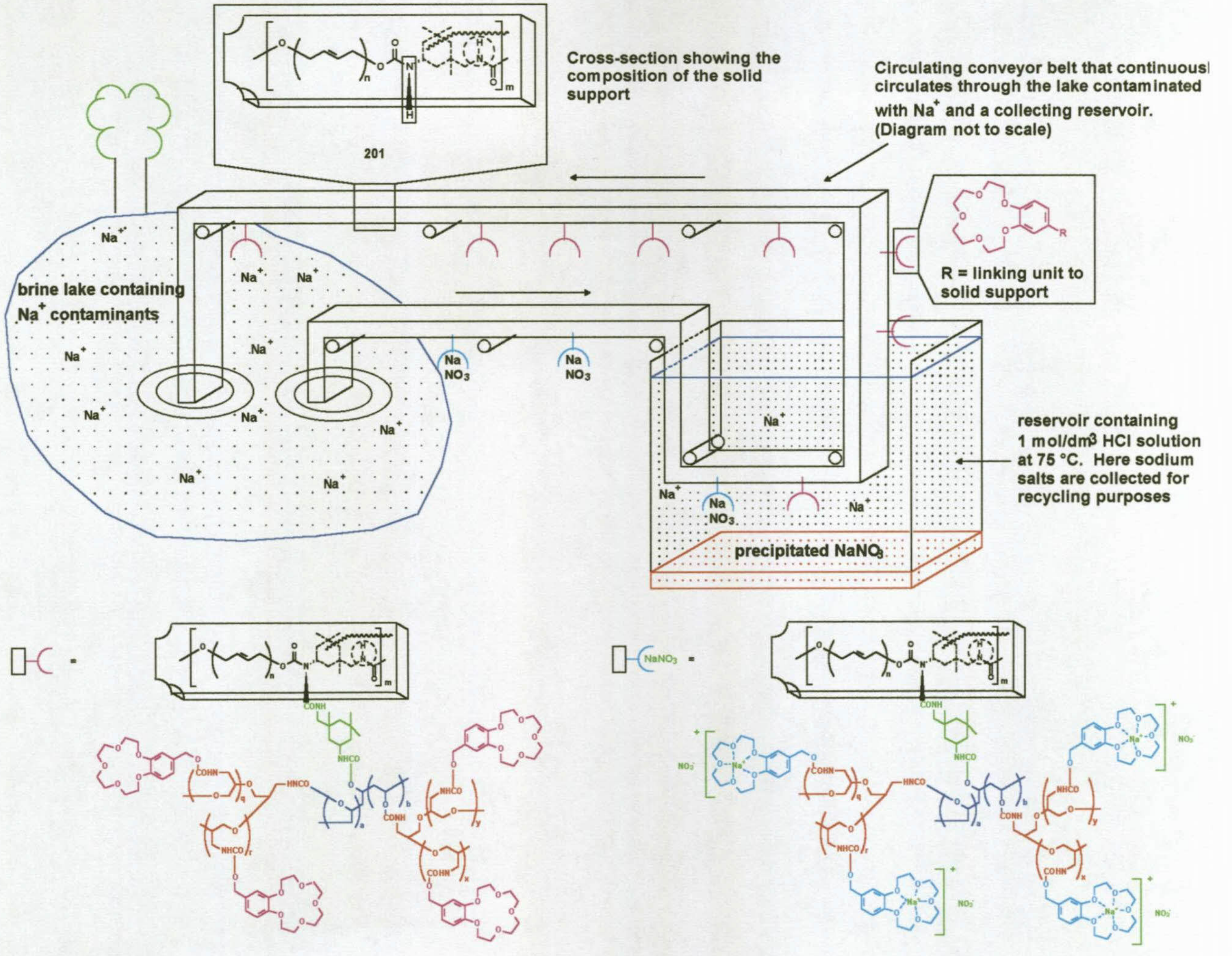
For the realisation of b), 20 polymeric carriers were synthesised. These include the synthesis of 12 new water-soluble polyaspartamide derivatives as well as 5 new polyepichlorohydrin water-insoluble derivatives. The experimental procedures for the synthesis of the water-soluble polymers could be tuned to achieve almost exact ratios between the crown ethers and several other functional groups. The carboxylic acid derivatives could be anchored to the water-soluble polymer and this reaction could be tuned to achieve almost 100 % coupling, with the use of the coupling reagent *O*-benzotriazolyl-*N,N,N',N'*-tetramethyluronium hexafluorophosphate. These polymeric crown ether derivatives are the first of their kind.

For the realisation of c), an elastomeric solid support was synthesised by the curing of hydroxy terminated polybutadiene with isophorone diisocyanate. It was also demonstrated that crown ether derivatives and/or polymeric carriers could be anchored onto this elastomeric solid support, with or without the use of a spacer between the elastomeric solid support and the crown ether. This was demonstrated in the synthesis of an elastomer where poly(vinyl alcohol) was the spacer between the elastomer, and the polymeric carrier, polyepichlorohydrin, and the crown ether, 4'-(hydroxymethyl)benzo-15-crown-5. The synthesis of the described 6 elastomeric solid supports containing crown ethers is the first of their kind.

Extraction studies of Na^+ from an aqueous phase onto the elastomeric solid supports just described were demonstrated, and it was found that it could remove 1.28 g Na^+ / m^2 surface area of the sodium cation scavenging device. Acid media was used to accomplish the release of the Na^+ from this elastomeric solid support. It was found that it could release 0.65 g Na^+ / m^2 surface area of the sodium cation scavenging device.

Results of this study are promising enough to warrant further investigation of this protocol. The most important issue to address is to further enhance the complexation ability of the elastomeric solid support. Towards this end, the crown ether moieties could be anchored onto a bead-like support that would increase the total surface area of the crown ethers on the bead-like support. During this study, acid media was used to release the Na^+ from the sodium cation scavenging devices, but as discussed in Chapter 2, paragraph 2.5, p. 28 – 37, other methods also exist that could be used to release the complexed cations. For a cost effective and very environmental friendly release of cations, from the cation scavenging devices, one can even use UV-light and heat. If this could be accomplished, the only cost involved in using this technology would be in the synthesis of the cation scavenging device.

Although this study shows how Na^+ could be complexed by a sodium cation scavenging device and the release of the complexed Na^+ from this device, sodium is not the only metal that must be removed from contaminated water. It is also possible to produce other metal cation scavenging devices, including exotic ones such as gold cation scavenging device, or even a silver cation scavenging device. One can then even remove gold or other rare earth metallic cations from the ocean. This technology can also be used to clean water for household use. Instead of producing a conveyor belt, one can produce bead-like compounds for the use in a filter system. This filter, unlike most commercially available water purification filters, could then be recycled. Although the initial cost of this filter would be higher than the conventional filters, this filter could be used indefinitely. This filter could be tuned to remove most, if not all of, the metal cations present in drinking water. It will also be possible to provide clean drinkable water to people living in remote areas, where the only water sources are usually not suitable to sustain life.



Cross-section showing the composition of the solid support

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

reservoir containing 1 mol/dm^3 HCl solution at 75 °C. Here sodium salts are collected for recycling purposes

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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 3. 20. A schematic representation of the process of transferring Na$^+$ from a sodium aqueous phase to a suitable reservoir.

CHAPTER 5

EXPERIMENTAL

5.1 STANDARD EXPERIMENTAL TECHNIQUES

Unless specified to the contrary, the following techniques were applied throughout the course of this study. Pressure units are torr (1 torr = 133.34 Pa = 1.316×10^{-3} atm), while volumes are given in cm^3 (1 cm^3 = 1 ml).

5.1.1 Chromatography

5.1.1.1 Thin layer chromatography (TLC)

Qualitative TLC was conducted on "Merck TLC-aluminium sheets: Silica Gel 60 F_{254}" (0.2-mm layer) divided into strips of 3 x 5 cm. R_f values are those observed in these qualitative assessments using benzene:acetone in an 8:2 ratio by volume.

5.1.1.2 Column chromatography

100 g of "Merck Kieselgel 60 (70 – 230 mesh ASTM) for column chromatography" for every 1 g of crude product was stirred with the appropriate solvent system. This mixture was poured in a glass tube (5 cm in diameter). The top was covered with a layer (*ca.* 1 cm) of acid washed sand. The crude product was dissolved in a minimum of the solvent system, and this was added, carefully, on top, followed by elution with the appropriate eluting mixture at atmospheric pressure.

5.1.2 Spectroscopy methods

5.1.2.1 Nuclear magnetic resonance spectroscopy (NMR)

NMR spectroscopy was performed on a Bruker AM 300 FT-spectrometer at 296 K. The deuterated solvent peaks (Table 5. 1) were used as internal standard for reference purpose.

Table 5. 1. Deuterated Solvents.

Solvent	**δ (ppm)**
Acetone-d_6	2.04 (5)
Chloroform-d	7.24 (1)
Deuterium oxide	4.63
Dimethylformamide-d_7	8.05 (br) 2.91 (5) 2.74 (5)

Chemical shifts are reported in parts per million (ppm) on the δ-scale and coupling constants are given in hertz (Hz), following the format expected for *J. Am. Chem. Soc.*

5.1.2.2 Infrared spectroscopy (IR)

IR spectroscopy was conducted on a Hitachi 270-50 spectrometer. All solid samples were recorded in KBr pellets, while liquid samples were recorded as thin films between two KBr discs.

5.1.2.3 pH determinations

All pH determinations were done with a "Metrohm 704 pH Meter". This pH meter was calibrated with "Merck Buffer – Titrisol for 500 cm^3 – Buffer solution pH 4.00" and with "Merck Buffer – Titrisol for 500 cm^3 – Buffer solution pH 10.00".

5.1.3 Flame photometry for the determinations of sodium cations

The Na^+ were determined on a Flame Photometer, PFP7, Jenway Ltd. A Na^+ stock solution was prepared by dissolving 508 mg NaCl (200 mg Na^+ content) in a 1 000 cm^3 volumetric flask. Five dilutions from the Na^+ stock solution were made, having a Na^+ content of 150 mg, 100 mg, 75 mg, 50 mg and 10 mg respectively. The atomic absorption of these Na^+ stock solutions was measured and a calibration curve was constructed from these measurements. The atomic absorption of the unknown sample was measured and the Na^+ content was directly read from the calibration curve. The percentage Na^+ content was calculated from the mass of the sample originally weighed.

5.1.4 Determinations of melting points (m.p.)

Melting points were determined with a Reichet Thermopan microscope, with a Koffler hot-stage and are uncorrected. This instrument can only detect melting points lower than 250 °C.

5.1.5 Synthesis of diazomethane (285)

EXPLOSION WARNING: The synthesis of diazomethane is extremely explosive. The wearing of safety gear is essential. This reaction should be carried out in a well-ventilated fume cupboard. All glassware should have polished (**NOT GROUND**) joints. Diazald (**288**, 22.00 g) were placed in a 500 cm^3 flask, and washed down with ether (100 cm^3). Ether (100 cm^3) was added to the flask, followed by the careful addition of ethanolic potassium hydroxide (50 cm^3). The flask sides were again washed with ether (100 cm^3). The reaction vessel was then placed in a heating mantle and the ether/diazomethane mixture was distilled until the yellow colour of the distillate becomes colourless. This yellow solution contains about 6.96 g of diazomethane (**285**).

5.1.6 Synthesis of silver oxide

To an aqueous solution of $AgNO_3$ (10 % (m/v), 5 g in 50 cm^3 water) was gradually added diluted NaOH solution (8.00 g in 400 cm^3 water) until precipitation was just complete. The solution was filtered and the precipitate washed with distilled water, to give the product as a brownish solid; yield 5.94 g.

5.2 SYNTHESIS AND FUNCTIONALISATION OF CROWN ETHERS

5.2.1 Synthesis of 1,11-dichloro-3,6,9-trioxaundecane (230)[2]

Tetraethylene glycol (**229**, 120 cm^3, 134.40 g, 0.6920 mol) was added to benzene[‡] (600 cm^3) and pyridine (122.9 cm^3, 120.42 g, 1.522 mol), and heated to *ca.* 86 °C. Thionyl chloride (110.4 cm^3, 181.07 g, 1.522 mol) was added, over a 3 h period. The colour changed to a dark-brown colour, and heating was continued overnight (16 h). After this mixture was cooled to room temperature, hydrochloric acid [15 cm^3 concentrated HCl, diluted with 60 cm^3 water] was slowly added, to protonate the excess pyridine. The organic layer was separated, dried ($MgSO_4$) and removed under reduced pressure, to give the final product as a brown-yellow liquid; yield 151.80 g (94.92 %).

NMR ($CDCl_3$, Figure 6. 1): ^1H (300 MHz), δ = 3.63 – 3.81 (m, 16 H, $OC\underline{H_2}C\underline{H_2}O$) ppm.

[‡] <u>CAUTION</u>: Benzene is a carcinogen and all reactions with it were conducted in an efficient fume hood, using gloves.

5.2.2 Synthesis of benzo-15-crown-5 (11)[2]

Catechol (**234**, 64.71 g, 0.5877 mol) was added to 1-butanol (600 cm^3), and this mixture was degassed under a nitrogen atmosphere. NaOH (51.72 g, 1.293 mol) was added and the mixture was allowed to stir for 5 min, after which 1,11-dichloro-3,6,9-trioxaundecane (**230**, 135.82 g, 0.5877 mol) was added and the mixture heated for 30 h at 117 °C. The reaction mixture was acidified with conc. hydrochloric acid (100 cm^3), cooled, filtered and the solid washed with methanol (200 cm^3). The combined filtrates were concentrated under reduced pressure and the residue was continuously extracted using a soxhlet with hexane as the solvent. This gave the final product, after recrystallisation from hexane, as a white solid; yield 67.61 g (42.88 %, R_f = 0.692, m.p. 75 – 78 °C).

NMR ($CDCl_3$, Figure 6. 2): ^1H (300 MHz), δ = 3.72 – 3.76 (s, 8 H, $OC\underline{H}_2C\underline{H}_2O$), 3.86 – 3.92 (m, 4 H, $PhOCH_2C\underline{H}_2O$), 4.08 – 4.15 (m, 4 H, $PhOC\underline{H}_2CH_2O$), 6.84 – 6.88 (m, 4 H, $Ar\underline{H}$) ppm.

IR (KBr discs): 1077 – 1239 (C-O-C), 1458 – 1593 (Ar), 2872 – 2914 (ArH) cm^{-1}.

5.2.3 Synthesis of 4'-formylbenzo-15-crown-5 (255)[54]

Phosphoryl chloride (45.72 g, 0.2982 mol) was added to *N*-methylformanilide (**254**, 40.31 g, 0.2982 mol) and the resulting mixture was put aside for 20 min. Benzo-15-crown-5 (**11**, 20.00 g, 0.07454 mol) was added and the mixture heated to *ca.* 90 °C for 4 h. The resulting dark-brown mixture was cooled, added to water (120 cm^3), and the crude product extracted into chloroform (6 x 50 cm^3). The organic layer was dried ($MgSO_4$) and removed under reduced pressure, and the residual brown oil was continuously extracted using hexane. This gave the final product, after recrystallisation from hexane, as a white solid; yield 14.51 g (65.70 %, R_f = 0.180, m.p. 79 – 81 °C).

NMR ($CDCl_3$, Figure 6. 3): ^1H (300 MHz), δ = 3.72 – 3.77 (s, 8 H, $OC\underline{H}_2C\underline{H}_2O$), 3.87 – 3.95 (m, 4 H, $PhOCH_2C\underline{H}_2O$), 4.14 – 4.21 (m, 4 H, $PhOC\underline{H}_2CH_2O$), 6.89 – 6.94 (d, $J_{a'b'}$ = 8 Hz, 1 H, $Ar\underline{H}_{a'}$), 7.35 – 7.38 (d,

$J_{b'c'}$ = 2 Hz, 1 H, Ar$\underline{H}_{c'}$), 7.39 – 7.45 (dd, $J_{a'b'}$ = 8 Hz, $J_{b'c'}$ = 2 Hz, 1 H, Ar$\underline{H}_{b'}$), 9.80 – 9.82 (s, 1 H, C$\underline{H}$O) ppm.

IR (KBr discs): 1050 – 1131 (C-O-C), 1509 – 1599 (Ar), 1686 (C=O), 2872 – 2932 (ArH) cm^{-1}.

5.2.4 Synthesis of 4'-(hydroxymethyl)benzo-15-crown-5 (257)

4'-Formylbenzo-15-crown-5 (**255**, 5.34 g, 0.01802 mol) in a 1:4 THF:ethanol (10 cm^3 THF:40 cm^3 ethanol) solution was added dropwise to a freshly prepared, ice cooled, suspension of sodium borohydride (1.36 g, 0.03604 mol) in THF (2 cm^3) and ethanol (8 cm^3). The reaction was stirred at room temperature (< 30 °C) for 5 h. This solution was added to ice (100 g), and filtered. The product was extracted with chloroform (6 x 50 cm^3) from the filtrate. The organic layer was dried ($MgSO_4$) and removed under reduced pressure, to give the product as a white solid; yield 4.97 g (92.45 %, R_f = 0.220, m.p. 45 – 47 °C).

NMR ($CDCl_3$, Figure 6. 4): ^1H (300 MHz), δ = 3.71 – 3.74 (s, 8 H, $OC\underline{H}_2C\underline{H}_2O$), 3.83 – 3.90 (m, 4 H, $PhOCH_2C\underline{H}_2O$), 4.05 – 4.12 (m, 4 H, $PhOC\underline{H}_2CH_2O$), 4.52 – 4.57 (s, 2 H, $PhC\underline{H}_2OH$), 6.76 – 6.88 (m, 3 H, Ar$\underline{H}$) ppm.

IR (KBr discs): 1044 – 1122 (C-O-C), 1458 – 1596 (Ar), 2878 (ArH), 3328 – 3430 (O-H) cm^{-1}.

5.2.5 Synthesis of 4'-(oximinomethyl)benzo-15-crown-5 (263)

To a solution of 4'-formylbenzo-15-crown-5 (**255**, 2.00 g, 0.006750 mol) in ethanol (20 cm^3) was added sequentially a solution of hydroxylamine hydrochloride (2.31 g, 0.03375 mol), in water (50 cm^3), and NaOH (1.35 g, 0.3375 mol). This mixture was allowed to refluxed, with stirring, for 4 h. After this mixture was cooled, it was extracted with $CHCl_3$ (6 x 50 cm^3). The organic layer was dried ($MgSO_4$) and removed under reduced pressure, to give the product as a white solid; yield 2.08 g (98.89 %, m.p. 61 – 64 °C).

NMR ($CDCl_3$, Figure 6. 5): ^1H (300 MHz), δ = 3.71 – 3.75 (s, 8 H, $OC\underline{H}_2C\underline{H}_2O$), 3.85 – 3.93 (m, 4 H, $PhOCH_2C\underline{H}_2O$), 4.08 – 4.16 (m, 4 H, $PhOC\underline{H}_2CH_2O$), 6.76 – 6.81 (d, $J_{a'b'}$ = 8 Hz, 1 H, $Ar\underline{H}_{a'}$), 6.91 – 6.96 (dd, $J_{a'b'}$ = 8 Hz, $J_{b'c'}$ = 2 Hz, 1 H, $Ar\underline{H}_{b'}$), 7.11 – 7.16 (d, $J_{b'c'}$ = 2 Hz, 1 H, $Ar\underline{H}_{c'}$), 7.95 – 7.99 (s, 1 H, $CN(OH)\underline{H}$) ppm.

5.2.6 Synthesis of 4'-cyanobenzo-15-crown-5 (265)

4'-(Oximinomethyl)benzo-15-crown-5 (**263**, 2.23 g, 0.007163 mol) in acetic anhydride (**264** , 20.00 g, 0.1959 mol) was refluxed, with stirring, at 160 °C for 4 h. This mixture was poured onto an ice water mixture and this was stirred until all the acetic anhydride was hydrolysed (*ca.* 1 h). This mixture was extracted with chloroform. The organic layer was dried ($MgSO_4$) and removed under reduced pressure, to give the product as a white solid; yield 2.09 g (99.48 %, m.p. 81 – 84 °C).

NMR ($CDCl_3$, Figure 6. 6): ^1H (300 MHz), δ = 3.69 – 3.75 (s, 8 H, $OC\underline{H}_2C\underline{H}_2O$), 3.85 – 3.92 (m, 4 H, $PhOCH_2C\underline{H}_2O$), 4.07 – 4.16 (m, 4 H, $PhOC\underline{H}_2CH_2O$), 6.81 – 6.85 (d, $J_{a'b'}$ = 8 Hz, 1 H, $Ar\underline{H}_{a'}$), 7.02 – 7.05 (d, $J_{b'c'}$ = 2 Hz, 1 H, $Ar\underline{H}_{c'}$), 7.19 – 7.22 (dd, $J_{a'b'}$ = 8 Hz, $J_{b'c'}$ = 2 Hz, 1 H, $Ar\underline{H}_{b'}$) ppm.

5.2.7 Synthesis of 4'-carboxybenzo-15-crown-5 (258)

4'-Cyanobenzo-15-crown-5 (**265**, 2.09 g, 0.007125 mol) in diluted HCl (150 cm^3 concentrated HCl diluted with 50 cm^3 water) was refluxed, with stirring, at 110 °C for 4 h. The aqueous layer was removed under reduced pressure, and the resulting residue was dissolved in chloroform. The organic layer was filtered and the precipitated washed with chloroform. The combined filtrates was dried ($MgSO_4$) and removed under reduced pressure, to give the product, after recrystallisation from a 10 % ethanol solution, as a white solid; yield 1.79 g (79.99 %, m.p. 188 – 191 °C).

NMR ($CDCl_3$, Figure 6. 7): ^{1}H (300 MHz), δ = 3.77 – 3.82 (s, 8 H, $OC\underline{H}_2C\underline{H}_2O$), 3.91 – 4.00 (m, 4 H, $PhOCH_2C\underline{H}_2O$), 4.18 – 4.25 (m, 4 H, $PhOC\underline{H}_2CH_2O$), 6.85 – 6.92 (d, $J_{a'b'}$ = 8 Hz, 1 H, $Ar\underline{H}_{a'}$), 7.55 – 7.59 (d, $J_{b'c'}$ = 2 Hz, 1 H, $Ar\underline{H}_{c'}$), 7.69 – 7.77 (dd, $J_{a'b'}$ = 8 Hz, $J_{b'c'}$ = 2 Hz, 1 H, $Ar\underline{H}_{b'}$) ppm.

IR (KBr discs): 1104 (C-O-C), 1515 – 1593 (Ar), 1686 (C=O), 2872 (ArH), 2550 – 3322 (O-H) cm^{-1}.

5.2.8 Synthesis of 4'-(acrylic acid)benzo-15-crown-5 (267)[179]

4'-Formylbenzo-15-crown-5 (**255**, 3.18 g, 0.01073 mol), malonic acid (**266**, 2.79 g, 0.02683 mol) and piperidine (0.65 cm^3) were dissolved in pyridine (50 cm^3), and heated, under a nitrogen atmosphere, at 100 °C for 2 h. After cooling, the solution was diluted with water, and HCl (50 cm^3 in 50 cm^3 H_2O) was added. The product was extracted with chloroform (6 x 50 cm^3). The chloroform extract was washed with water (6 x 50 cm^3), dried ($MgSO_4$) and removed under reduced pressure to give the final product as a white solid; 3.21 g (88.42 %, R_f = 0.441).

NMR ($CDCl_3$, Figure 6. 8): ^{1}H (300 MHz), δ = 3.76 – 3.81 (s, 8 H, $OC\underline{H}_2C\underline{H}_2O$), 3.91 – 3.98 (m, 4 H, $PhOCH_2C\underline{H}_2O$), 4.15 – 4.22 (m, 4 H, $PhOC\underline{H}_2CH_2O$), 6.26 – 6.34 (d, J_{CHCH} = 16 Hz, 1 H, $PhC\underline{H}CHCOOH$), 6.84 – 6.90 (d, $J_{a'b'}$ = 8 Hz, 1 H, $Ar\underline{H}_{a'}$), 7.06 – 7.10 (d, $J_{b'c'}$ = 2 Hz, 1 H, $Ar\underline{H}_{c'}$), 7.10 – 7.16 (dd, $J_{a'b'}$ = 8 Hz, $J_{b'c'}$ = 2 Hz, 1 H, $Ar\underline{H}_{b'}$), 7.66 – 7.74 (d, J_{CHCH} = 16 Hz, 1 H, $PhCHC\underline{H}COOH$) ppm.

5.2.9 Synthesis of 4'-(propanoic acid)benzo-15-crown-5 (260)[179]

4'-(Acrylic acid)-benzo-15-crown-5 (**267**, 4.49 g, 0.01327 mol) was dissolved in ethanol (150 cm^3) and to this solution was added palladium-on-carbon (20 mg, 10 % Pd). This solution was stirred under a hydrogen atmosphere for 4 h. The mixture was filtered through Celite and removed under reduced pressure, to give the final product as a white solid; yield 4.52 g (99.99 %, R_f = 0.085, m.p. 82 – 84 °C).

NMR ($CDCl_3$, Figure 6. 9): ^1H (300 MHz), δ = 2.56 – 2.64 (t, 2 H, $PhC\underline{H_2}CH_2COOH$), 2.80 – 2.88 (m, 2 H, $PhCH_2C\underline{H_2}COOH$), 3.71 – 3.76 (s, 8 H, $OC\underline{H_2}C\underline{H_2}O$), 3.85 – 3.92 (m, 4 H, $PhOCH_2C\underline{H_2}O$), 4.06 – 4.14 (m, 4 H, $PhOC\underline{H_2}CH_2O$), 6.68 – 6.80 (m, 3 H, $Ar\underline{H}$) ppm.

IR (KBr discs): 1044 – 1228 (C-O-C), 1519 – 1593 (Ar), 1725 (C=O), 2873 – 2944 (ArH), 2593 – 3364 (O-H) cm^{-1}.

5.2.10 Synthesis of methyl succinate (274)

A mixture of succinic anhydride (**271**, 100.00 g, 0.9993 mol) and methanol (38.42 g, 1.199 mol) was refluxed at 80 °C for 2 h. The excess methanol was removed under reduced pressure, to give the product as a white solid; yield 126.49 g (95.81 %, m.p = 54 – 57 °C).

NMR ($CDCl_3$, Figure 6. 10): ^1H (300 MHz), δ = 2.61 – 2.75 (m, 4 H, $COC\underline{H_2}C\underline{H_2}COOH$), 3.70 – 3.74 (s, 3 H, $OC\underline{H_3}$) ppm.

5.2.11 Synthesis of methyl succinyl chloride (272)

Methyl hydrogen succinate (**274**, 20.00 g, 0.1514 mol) and $SOCl_2$ (23.7 cm^3, 36.02 g, 0.3028 mol) was placed in a flask bearing a refluxed condenser and this mixture was allowed to stir at 30 – 40 °C for 3 h. The excess thionyl chloride was removed under reduced pressure, to give the product as a yellow liquid, yield 22.18 g (97.29 %)

NMR ($CDCl_3$, Figure 6. 11): ^1H (300 MHz), δ = 2.64 – 2.72 (t, 2 H, $COC\underline{H_2}CH_2COCl$), 3.18 – 3.25 (t, 2 H, $COCH_2C\underline{H_2}COCl$), 3.68 – 3.72 (s, 3 H, $OC\underline{H_3}$) ppm.

5.2.12 The attempted synthesis of crown ether 273

5.2.12.1 The synthesis of crown ether **273** with succinic anhydride (**271**)

A solution of succinic anhydride (**271**, 0.37 g, 0.003697 mol) in oxygen free dichloromethane (25 cm^3) was added to a mixture of benzo-15-crown-5 (**11**, 1.00 g, 0.003727 mol) and $AlCl_3$ (0.50 g, 0.003727 mol) in oxygen free dichloromethane (25 cm^3). This colourless mixture was refluxed for 2 h, after which it was poured onto ice water (60 cm^3). The aqueous layer was washed with dichloromethane (6 x 50 cm^3). The organic layer was extracted with a 2 M LiOH (6 x 50 cm^3) solution, acidified with 1 M HCl solution and extracted into dichloromethane (6 x 50 cm^3). The organic layer was dried ($MgSO_4$) and removed under reduced pressure. No desired product was obtained.

5.2.12.2 The synthesis of crown ether **273** with methyl succinyl chloride (**272**)

Benzo-15-crown-5 (**11**, 2.00 g, 0.007454 mol) was dissolved in chloroform (10 cm^3) and added to a flask containing methyl succinyl chloride (**272**, 1.12 g, 0.007454 mol). To this mixture was slowly added finely powdered $AlCl_3$ (1.49 g, 0.01118 mol). This reddish mixture was then heated at 50 °C for 1 h. This mixture was added to a flask containing ice water (50 cm^3). The organic layer was removed, and the aqueous layer was washed with chloroform (6 x 50 cm^3). The organic layer was dried ($MgSO_4$) and removed under reduced pressure. No desired product was obtained.

5.2.13 Synthesis of oxetane 277

Catechol (**234**, 5.00 g, 0.04541 mol) in a solution of pyridine (4 cm^3) and acetone (20 cm^3) was added to a solution of diphenyldichloromethane (**275**, 10.77 g, 0.04541 mol) in acetone (10 cm^3). This mixture was stirred for 12 h at room temperature. A solution of NaOH (3.63 g, 0.09082 mol) in water (10 cm^3) was added slowly to this mixture. The temperature rose and reached the boiling point of the mixture, after 2 h, the whole was added to water (200 cm^3). The brown oily material was separated and dissolved in ether (50 cm^3), and washed with aqueous Na_2CO_3 and then with aqueous NaOH. The methyl ester precipitated from the latter extract on acidification, filtered and crystallised form benzene as a white solid; yield 10.87 g (87.23 %).

NMR ($CDCl_3$, Figure 6. 12): ^{1}H (300 MHz), δ = 6.78 – 3.91 (m, 4 H, Ar$\underline{H}_{a'}$), 7.32 – 7.39 (m, 6 H, Ar$\underline{H}_{c'}$), 7.54 – 7.61 (m, 4 H, Ar$\underline{H}_{b'}$) ppm.

5.2.14 Synthesis of the diester 278 from acetic anhydride (264)

Catechol (**234**, 20.00 g, 0.1816 mol) and acetic anhydride (**264**, 40 cm^3) was refluxed at 100 °C for 16 h. After this mixture was cooled to room temperature, water (100 cm^3) was added and the product extracted into chloroform (6 x 50 cm^3). The organic layer was dried ($MgSO_4$) and removed under reduced pressure, to give the product as a white solid; yield 33.75 g (95.65 %, m.p. 62 – 63 °C).

5.2.15 Synthesis of the diester 278 from acetyl chloride (276)

Catechol (**234**, 20.00 g, 0.1816 mol) and acetyl chloride (**276**, 31.36 g, 0.3995 mol) was refluxed at 100 °C for 16 h. After the addition of the acetyl chloride there occurred a violent frothing. After 5 min this frothing stopped and the flask was placed in the oil bath. The mixture was cooled and added to water (100 cm^3). The aqueous layer was extracted with chloroform (6 x 50 cm^3). The organic layer was dried ($MgSO_4$) and removed under reduced pressure, to give the product as a white solid; yield 32.91 g (93.34 %, m.p. = 62 – 63 °C).

NMR (Acetone-d_6, Figure 6. 13): ^{1}H (300 MHz), δ = 2.25 – 2.28 (s, 6 H, CO$C\underline{H}_3$), 7.21 – 7.32 (m, 4 H, Ar$\underline{H}$) ppm.

5.2.16 Synthesis of compound 279

The oxetane **277** (2.00 g, 0.007291 mol), succinic anhydride (**271**, 0.73 g, 0.007291 mol) and finely powdered $AlCl_3$ (1.46 g, 0.01094 mol) was refluxed at 100 °C for 18 h. After this mixture was cooled, water (100 cm^3) was added. The aqueous layer was extracted with chloroform (6 x 50 cm^3). The organic layer was dried ($MgSO_4$) and removed under reduced pressure. No desired product was obtained.

5.2.17 Synthesis of compound 280

The diester **278** (13.10 g, 0.06745 mol) was added to a solution of finely powdered $AlCl_3$ (9.89 g, 0.07419 mol) in chloroform (50 cm^3). To this solution was added methyl succinyl chloride (**272**, 11.17 g, 0.07419 mol) over a 30 min period. This mixture was refluxed at 50 °C for 24 h. After the solution was cooled, water (100 cm^3) was added. The organic layer was removed and washed with water (6 x 50 cm^3), followed by 0.1 M NaOH (6 x 50 cm^3) and again with water (6 x 50 cm^3). The organic layer was dried ($MgSO_4$) and removed under reduced pressure, to give the product as a black liquid; yield 11.34 g (54.53 %).

5.2.18 Synthesis of compound 282

Compound **280** (2.00 g, 0.006488 mol) was added to 10 % (m/v) ethanoic NaOH (50 cm^3) and refluxed at 80 °C for 18 h. After it was dissolved, water (50 cm^3) was added. The aqueous layer was extracted with chloroform (6 x 50 cm^3). The organic layer was dried ($MgSO_4$) and removed under reduced pressure, to give the product as a brown liquid; yield 1.20 g (88.00 %).

NMR ($CDCl_3$, Figure 6. 14): ^{1}H (300 MHz), δ = 3.64 – 3.70 (t, 2 H, $COCH_2C\underline{H_2}COOH$), 3.76 – 3.83 (t, 2 H, $CO\underline{CH_2}CH_2COOH$), 6.81 – 6.7 (m, 3 H, Ar$\underline{H}$) ppm.

5.2.19 Synthesis of 4'-(carbonyl chloride)benzo-15-crown-5 (283)

4'-Carboxybenzo-15-crown-5 (**258**, 1.00 g, 0.003202 mol) was added to thionyl chloride (0.84 g, 0.007061 mol), and this mixture was allowed to stir for 3 h at 50 °C. The excess thionyl chloride was removed by reduced pressure, to give the product as a yellow liquid; yield 1.06 g (99.99 %).

5.2.20 Synthesis of 4'-(propanoyl chloride)benzo-15-crown-5 (284)

4'-(Propanoic acid)benzo-15-crown-5 (**260**, 1.00 g, 0.002938 mol) was added to thionyl chloride (1.05 g, 0.008826 mol), and this mixture was allowed to stir for 3 h at 50 °C. The excess thionyl chloride was removed by reduced pressure, to give the product as a yellow liquid; yield 1.05 g (99.99 %).

NMR ($CDCl_3$, Figure 6. 15): ^1H (300 MHz), δ = 2.91 – 3.00 (t, 2 H, $PhC\underline{H_2}CH_2COCl$), 3.15 – 3.22 (t, 2 H, $PhCH_2C\underline{H_2}COCl$), 3.75 – 3.80 (s, 8 H, $OC\underline{H_2}C\underline{H_2}O$), 3.89 – 3.97 (m, 4 H, $PhOCH_2C\underline{H_2}O$), 4.09 – 4.18 (m, 4 H, $PhOC\underline{H_2}CH_2O$), 6.70 – 6.85 (m, 3 H, Ar$\underline{H}$) ppm.

5.2.21 Synthesis of 4'-(ethanoic acid)benzo-15-crown-5 (259)

4'-(Carbonyl chloride)benzo-15-crown-5 (**283**, 1.06 g, 0.003202 mol) in THF (5 cm^3) was added to an ethereal solution of diazomethane (**285**, about 1.5 times the amount synthesised in paragraph 5.1.5, p. 150). This solution was allowed to stand for 48 h in a freezer. The excess reagent, together with the ether, was removed under reduced pressure. The resultant yellow liquid was dissolved in warm 1,4-dioxane (20 cm^3) and added to a solution of freshly precipitated Ag_2O (1.25 g, 0.005380 mol) in water (50 cm^3), containing sodium thiosulphate pentahydrate (2.67 g, 0.01076 mol) at 75 °C. A brisk evolution of nitrogen occurred. After 1.5 h at 75 °C, the solution was filtered and the filtrate was acidified with nitric acid, and extracted with chloroform (6 x 50 cm^3). The organic layer was dried ($MgSO_4$) and removed under reduced pressure to give the product as a yellow liquid, which solidified upon standing; yield 0.64 g (61.24 %, m.p. 95 – 98 °C).

NMR ($CDCl_3$): ^1H (300 MHz), δ = 3.55 – 3.59 (s, 2 H, PhC$\underline{H_2}$COOH), 3.75 – 3.80 (s, 8 H, OC$\underline{H_2}$C$\underline{H_2}$O), 3.89 – 3.95 (m, 4 H, PhOCH$_2$C$\underline{H_2}$O), 4.10 – 4.17 (m, 4 H, PhOC$\underline{H_2}$CH$_2$O), 6.80 – 6.84 (s, 3 H, Ar$\underline{H}$) ppm.

IR (KBr discs): 1077 – 1239 (C-O-C), 1458 – 1593 (Ar), 2872 – 2914 (ArH), 2600 – 3425 (O-H) cm^{-1}.

5.2.22 Synthesis of 4'-(butanoic acid)benzo-15-crown-5 (261)

4'-(Propanoyl chloride)benzo-15-crown-5 (**284**, 1.05 g, 0.002926 mol) in THF (5 cm^3) was added to an ethereal solution of diazomethane (**285**, about 1.5 times the amount synthesised in paragraph 5.1.5, p. 150). This solution was allowed to stand for 48 h in a freezer. The excess reagent, together with the ether, was removed under reduced pressure. The resultant yellow liquid was dissolved in warm 1,4-dioxane (20 cm^3) and added to a solution of freshly precipitated Ag_2O (1.17 g, 0.005050 mol) in water (50 cm^3), containing sodium thiosulphate pentahydrate (2.51 g, 0.01010 mol) at 75 °C. A brisk evolution of nitrogen occurred. After 1.5 h at 75 °C, the solution was filtered and the filtrate was acidified with nitric acid, and extracted with chloroform (6 x 50 cm^3). The organic layer was dried ($MgSO_4$) and removed under reduced pressure, to give the product as a yellow liquid, which solidified upon standing; yield 0.64 g (61.47 %, m.p. 78 – 81 °C).

NMR ($CDCl_3$): ^1H (300 MHz), δ = 1.88 – 2.01 (m, 2 H, PhCH$_2$C$\underline{H_2}$CH$_2$COOH), 2.31 – 2.39 (t, 2 H, PhC$\underline{H_2}$CH$_2$CH$_2$COOH), 2.57 – 2.64 (t, 2 H, PhCH$_2$CH$_2$C$\underline{H_2}$COOH), 3.74 – 3.80 (s, 8 H, OC$\underline{H_2}$C$\underline{H_2}$O), 3.88 – 3.96 (m, 4 H, PhOCH$_2$C$\underline{H_2}$O), 4.10 – 4.18 (m, 4 H, PhOC$\underline{H_2}$CH$_2$O), 6.68 – 6.83 (m, 3 H, Ar$\underline{H}$) ppm.

IR (KBr discs): 1040 – 1131 (C-O-C), 1455 – 1617 (Ar), 1725 (C=O), 2926 (ArH), 3412 (O-H) cm^{-1}.

5.2.23 Synthesis of 4'-amidobenzo-15-crown-5 (290)

To a solution of 4'-(carbonyl chloride)benzo-15-crown-5 (**283**, 0.52 g, 0.001585 mol) in dichloromethane (25 cm^3) was added aqueous ammonium hydroxide (25 cm^3) and this mixture was stirred vigorously for 1 h. The organic layer was separated and the aqueous layer was extracted with dichloromethane (6 x 50 cm^3). The organic layer was dried ($MgSO_4$) and removed under reduced pressure, to give the product as a white solid; yield 0.41 g (83.09 %, m.p. 188 – 189 °C).

NMR ($CDCl_3$, Figure 6. 16): ^1H (300 MHz), δ = 3.71 – 3.77 (s, 8 H, $OC\underline{H}_2C\underline{H}_2O$), 3.85 – 3.94 (m, 4 H, $PhOCH_2C\underline{H}_2O$), 4.12 – 4.20 (m, 4 H, $PhOC\underline{H}_2OCH_2O$), 6.78 – 6.85 (d, $J_{a'b'}$ = 8 Hz, 1 H, $Ar\underline{H}_{a'}$), 7.26 – 7.30 (dd, $J_{a'b'}$ = 8 Hz, $J_{b'c'}$ = 2 Hz, 1 H, $Ar\underline{H}_{b'}$), 7.36 – 7.41 (d, $J_{b'c'}$ = 2 Hz, 1 H, $Ar\underline{H}_{c'}$) ppm.

IR (KBr discs): 1047 – 1125 (C-O-C), 1443 – 1518 (Ar), 1581 (amide 2, $C(O)NH_2$), 1644 (amide 1, C=O), 2872 – 2920 (ArH), 3160 – 3364 (N-H) cm^{-1}.

5.2.24 Synthesis of 4'-(propylamide)benzo-15-crown-5 (292)

To a solution of 4'-(propanoyl chloride)benzo-15-crown-5 (**284**, 2.00 g, 0.005574 mol) in dichloromethane (25 cm^3) was added aqueous ammonium hydroxide (25 cm^3) and this mixture was stirred vigorously for 1 h. The organic layer was separated and the aqueous layer was extracted with dichloromethane (6 x 50 cm^3). The organic layer was dried ($MgSO_4$) and removed under reduced pressure, to give the product as a white solid; yield 1.51 g (79.82 %, m.p. 119 – 120 °C).

NMR ($CDCl_3$, Figure 6. 17): ^1H (300 MHz), δ = 2.36 – 2.46 (m, 2 H, $PhC\underline{H}_2CH_2CONH_2$), 2.78 – 2.88 (m, 2 H, $PhCH_2C\underline{H}_2CONH_2$), 3.66 – 3.74 (s, 8 H, $OC\underline{H}_2C\underline{H}_2O$), 3.81 – 3.90 (m, 4 H, $PhOCH_2C\underline{H}_2O$), 4.01 – 4.09 (m, 4 H, $PhOC\underline{H}_2CH_2O$), 6.65 – 6.73 (m, 3 H, $Ar\underline{H}$) ppm.

IR (KBr discs): 1047 – 1131 (C-O-C), 1446 – 1515 (Ar), 1617 (amide 2, $C(O)NH_2$), 1665 (amide 1, C=O), 2875 – 2920 (ArH), 3400 (N-H) cm^{-1}.

5.2.25 Synthesis of 4'-(ethylamide)benzo-15-crown-5 (291)

4'-(Carbonyl chloride)benzo-15-crown-5 (**283**, 1.00 g, 0.003023 mol) in THF (5 cm^3) was added to an ethereal solution of diazomethane (**285**, about 1.5 times the amount synthesised in paragraph 5.1.5, p. 150). This solution was allowed to stand for 48 h in a freezer. The excess reagent, together with the ether, was removed under reduced pressure. The resultant yellow liquid was dissolved in warm 1,4-dioxane (20 cm^3) and added to a solution of 25 % aqueous ammonium hydroxide (15 cm^3) solution and 10 % (m/v) aqueous $AgNO_3$ (1 cm^3), and this mixture was refluxed for 1 h. This solution was filtered hot and the filtrate cooled, and the aqueous layer was with chloroform (6 x 50 cm^3). The organic layer was dried ($MgSO_4$) and removed under reduced pressure. No desired product was obtained.

5.2.26 Synthesis of 4'-(butylamide)benzo-15-crown-5 (293)

4'-(Propanoyl chloride)benzo-15-crown-5 (**284**, 1.05 g, 0.002960 mol) in THF (5 cm^3) was added to an ethereal solution of diazomethane (**285**, about 1.5 times the amount synthesised in paragraph 5.1.5, p. 150). This solution was allowed to stand for 48 h in a freezer. The excess reagent, together with the ether, was removed under reduced pressure. The resultant yellow liquid was dissolved in warm 1,4-dioxane (20 cm^3) and added to a solution of 25 % aqueous ammonium hydroxide (15 cm^3) solution and 10 % (m/v) aqueous $AgNO_3$ (1 cm^3), and this mixture was refluxed for 1 h. This solution was filtered hot and the filtrate cooled, and the aqueous layer was with chloroform (6 x 50 cm^3). The organic layer was dried ($MgSO_4$) and removed under reduced pressure, to give the product as a yellow solid; yield 0.89 g (88.63 %, m.p. 113 – 115 °C).

NMR ($CDCl_3$): ^{1}H (300 MHz), δ = 1.84 – 1.97 (m, 2 H, $PhCH_2C\underline{H_2}CH_2CONH_2$), 2.11 – 2.20 (t, 2 H, $PhC\underline{H_2}CH_2CH_2CONH_2$), 2.52 – 2.61 (t, 2 H, $PhCH_2CH_2C\underline{H_2}CONH_2$), 3.70 – 3.76 (s, 8 H, $OC\underline{H_2}C\underline{H_2}O$), 3.84 – 3.92 (m, 4 H, $PhOCH_2C\underline{H_2}O$), 4.05 – 4.13 (m, 4 H, $PhOC\underline{H_2}CH_2O$), 6.63 – 6.79 (m, 3 H, $Ar\underline{H}$) ppm.

IR (KBr discs): 1040 – 1122 (C-O-C), 1515 (Ar), 1622 (amide 2, C(O)NH_2), 1653 (amide 1, C=O), 2872 – 2920 (ArH), 3196 – 3400 (N-H) cm^{-1}.

5.2.27 Synthesis of 4'-(aminomethyl)benzo-15-crown-5 (294)

4'-Amidobenzo-15-crown-5 (**290**, 1.03 g, 0.003308 mol) in dry THF (25 cm^3) was added to a suspension of $LiAlH_4$ (0.38 g, 0.009924 mol) in dry THF (25 cm^3), and this mixture was allowed to refluxed, with stirring, at 50 °C for 24 h. After cooling it to room temperature, ice water was added to destroy the excess $LiAlH_4$. This solution was filtered and the filtrate extracted with chloroform (6 x 50 cm^3). The organic layer was dried ($MgSO_4$) and removed under reduced pressure, to give the product as a yellow solid; yield 0.83 g (83.88 %, m.p. 85 – 88 °C).

NMR ($CDCl_3$, Figure 6. 18): ^{1}H (300 MHz), δ = 3.67 – 3.72 (s, 8 H, $OC\underline{H}_2C\underline{H}_2O$), 3.72 – 3.75 (s, 2 H, $PhC\underline{H}_2NH_2$), 3.82 – 3.90 (m, 4 H, $PhOCH_2C\underline{H}_2O$), 4.03 – 4.13 (m, 4 H, $PhOC\underline{H}_2CH_2O$), 6.75 – 6.83 (m, 3 H, $Ar\underline{H}$) ppm.

IR (KBr discs): 1044 – 1104 (C-O-C), 1455 – 1512 (Ar), 1590 (N-H), 2850 – 2920 (ArH), 3352 (N-H) cm^{-1}.

5.2.28 Synthesis of 4'-(aminopropyl)benzo-15-crown-5 (296)

4'-(Propylamide)benzo-15-crown-5 (**291**, 1.00 g, 0.002947 mol) in dry THF (25 cm^3) was added to a solution of $LiAlH_4$ (0.34 g, 0.008840 mol) in dry THF (25 cm^3) and this mixture was allowed to refluxed, with stirring, at 50 °C for 24 h. After cooling it to room temperature, ice water was added to destroy the excess $LiAlH_4$. This solution was filtered and the filtrate extracted with chloroform (6 x 50 cm^3). The organic layer was dried ($MgSO_4$) and removed under reduced pressure, to give the product as a yellow liquid; yield 0.81 g (83.97 %).

NMR ($CDCl_3$): ^{1}H (300 MHz), δ = 1.64 – 1.77 (m, 2 H, $PhCH_2C\underline{H}_2CH_2NH_2$), 2.49 – 2.59 (t, 2 H, $PhC\underline{H}_2CH_2CH_2NH_2$), 2.64 – 2.72 (t, 2 H, $PhCH_2CH_2C\underline{H}_2NH_2$), 3.69 – 3.75 (s, 8 H, $OC\underline{H}_2C\underline{H}_2O$), 3.83 – 3.91 (m, 4 H,

$PhOCH_2C\underline{H_2}O$), 4.03 – 4.13 (m, 4 H, $PhOC\underline{H_2}CH_2O$), 6.63 – 6.79 (m, 3 H, $Ar\underline{H}$) ppm.

IR (KBr discs): 1030 – 1122 (C-O-C), 1465 – 1512 (Ar), 1590 (N-H), 2878 – 2914 (ArH), 3436 (N-H) cm^{-1}.

5.2.29 Synthesis of 4'-(aminobutyl)benzo-15-crown-5 (297)

4'-(Butylamide)benzo-15-crown-5 (**293**, 1.00 g, 0.002830 mol) in dry THF (25 cm^3) was added to a solution of $LiAlH_4$ (0.32 g, 0.008489 mol) in dry THF (25 cm^3) and this mixture was allowed to refluxed, with stirring, at 50 °C for 24 h. After cooling it to room temperature, ice water was added to destroy the excess $LiAlH_4$. This solution was filtered and the filtrate extracted with chloroform (6 x 50 cm^3). The organic layer was dried ($MgSO_4$) and removed under reduced pressure, to give the product as a yellow liquid; yield 0.80 g (83.76 %,).

NMR ($CDCl_3$): ^{1}H (300 MHz), δ = 1.37 – 1.65 (m, 4 H, $PhCH_2C\underline{H_2}C\underline{H_2}CH_2NH_2$), 2.46 – 2.56 (t, 2 H, $PhC\underline{H_2}CH_2CH_2CH_2NH_2$), 2.63 – 2.72 (t, 2 H, $PhCH_2CH_2CH_2C\underline{H_2}NH_2$), 3.70 – 3.75 (s, 8 H, $OC\underline{H_2}C\underline{H_2}O$), 3.83 – 3.91 (m, 4 H, $PhOCH_2C\underline{H_2}O$), 4.04 – 4.14 (m, 4 H, $PhOC\underline{H_2}CH_2O$), 6.62 – 6.78 (m, 3 H, $Ar\underline{H}$) ppm.

IR (KBr discs): 1047 – 1119 (C-O-C), 1458 – 1509 (Ar), 1584 (N-H), 2872 – 2920 (ArH), 3244 – 3472 (N-H) cm^{-1}.

5.2.30 Synthesis of 4'-(hydroxyethyl)benzo-15-crown-5 (298)

4'-(Ethanoic acid)benzo-15-crown-5 (**259**, 0.07 g, 0.0002144 mol) in dry THF (10 cm^3) was added to a solution of $LiAlH_4$ (0.02 g, 0.0006432 mol) in dry THF (10 cm^3) and this mixture was allowed to refluxed, with stirring, at 50 °C for 24 h. After cooling it to room temperature, ice water was added to destroy the excess $LiAlH_4$. This solution was filtered and the filtrate extracted with chloroform (6 x 50 cm^3). The organic layer was dried ($MgSO_4$) and removed under reduced pressure, to give the product as a yellow liquid; yield 0.05 g (79.36 %).

NMR ($CDCl_3$): ^{1}**H (300 MHz),** δ = 1.16 – 1.25 (t, 2 H, $PhC\underline{H_2}CH_2OH$), 2.71 – 2.78 (t, 2 H, $PhCH_2C\underline{H_2}OH$), 3.68 – 3.74 (s, 8 H, $OC\underline{H_2}C\underline{H_2}O$), 3.84 – 3.91 (m, 4 H, $PhOCH_2C\underline{H_2}O$), 4.05 – 4.14 (m, 4 H, $PhOC\underline{H_2}CH_2O$), 6.68 – 6.87 (m, 3 H, $Ar\underline{H}$) ppm.

5.2.31 Synthesis of 4'-(hydroxypropyl)benzo-15-crown-5 (299)

4'-(Propanoic acid)benzo-15-crown-5 (**260**, 1.03 g, 0.003026 mol) in dry THF (25 cm^3) was added to a solution of $LiAlH_4$ (0.34 g, 0.009078 mol) in dry THF (25 cm^3) and this mixture was allowed to refluxed, with stirring, at 50 °C for 24 h. After cooling it to room temperature, ice water was added to destroy the excess $LiAlH_4$. This solution was filtered and the filtrate extracted with chloroform (6 x 50 cm^3). The organic layer was dried ($MgSO_4$) and removed under reduced pressure, to give the product as a yellow liquid; yield 0.85 g (85.79 %,).

NMR ($CDCl_3$, Figure 6. 19): ^{1}**H (300 MHz),** δ = 1.74 – 1.87 (m, 2 H, $PhCH_2C\underline{H_2}CH_2OH$), 2.54– 2.64 (t, 2 H, $PhC\underline{H_2}CH_2CH_2OH$), 3.57 – 3.66 (t, 2 H, $PhCH_2CH_2C\underline{H_2}OH$), 3.68 – 3.75 (s, 8 H, $OC\underline{H_2}C\underline{H_2}O$), 3.83 – 3.91 (m, 4 H, $PhOCH_2C\underline{H_2}O$), 4.04 – 4.13 (m, 4 H, $PhOC\underline{H_2}CH_2O$), 6.65 – 6.78 (m, 3 H, $Ar\underline{H}$) ppm.

5.2.32 Synthesis of 4'-(hydroxybutyl)benzo-15-crown-5 (300)

4'-(Butanoic acid)benzo-15-crown-5 (**261**, 1.00 g, 0.002822 mol) in dry THF (25 cm^3) was added to a solution of $LiAlH_4$ (0.31 g, 0.008466 mol) in dry THF (25 cm^3) and this mixture was allowed to refluxed, with stirring, at 50 °C for 24 h. After cooling it to room temperature, ice water was added to destroy the excess $LiAlH_4$. This solution was filtered and the filtrate extracted with chloroform (6 x 50 cm^3). The organic layer was dried ($MgSO_4$) and removed under reduced pressure, to give the product as a yellow liquid; yield 0.77 g (80.65 %,).

NMR ($CDCl_3$): ^{1}**H (300 MHz),** δ = 1.46 – 1.69 (m, 4 H, $PhCH_2C\underline{H_2}C\underline{H_2}CH_2OH$), 2.44 – 2.5 (m, 4 H, $PhC\underline{H_2}CH_2CH_2C\underline{H_2}OH$), 3.70 –

3.75 (s, 8 H, OC$\underline{H}_2$C$\underline{H}_2$O), 3.83 – 3.91 (m, 4 H, PhOCH$_2$C$\underline{H}_2$O), 4.02 – 4.15 (m, 4 H, PhOC$\underline{H}_2$CH$_2$O), 6.62 – 6.84 (m, 3 H, Ar$\underline{H}$) ppm.

5.2.33 Attempted synthesis of 4'-(aminoethyl)benzo-15-crown-5 (295)

5.2.33.1 Synthesis of 4'-(aminoethyl)benzo-15-crown-5 (**295**) from 4'-(propylamide)benzo-15-crown-5 (**292**)

A cold NaOBr solution was prepared from Br_2 (1.56 g, 0.009784 mol) and NaOH (0.39 g, 0.009784 mol) in water (10 cm^3). The 4'-(propylamide)benzo-15-crown-5 (**292**, 0.83 g, 0.002446 mol) was poured into this NaOBr solution and stirred for 15 min. The solution was then warmed to 75 °C and stirred for a further 45 min. The crude product was extracted with chloroform (6 x 50 cm^3). The organic layer was dried ($MgSO_4$) and removed under reduced pressure. No desired product was obtained.

5.2.33.2 Synthesis of 4'-(aminoethyl)benzo-15-crown-5 (**295**) from 4'-(hydroxymethyl)benzo-15-crown-5 (**257**)

4'-(Hydroxymethyl)benzo-15-crown-5 (**257**, 0.50 g, 0.001676 mol) and red phosphorus (0.05 g, 0.001676 mol) was added to 1,4-dioxane (10 cm^3). This mixture was heated to 100 °C and the Br_2 (0.27 g, 0.001676 mol) was slowly added to this mixture. The rate of addition was such that there was little to no Br_2 vapour above the surface of the reaction mixture. This mixture was refluxed for a further 1 h. This mixture was filtered and washed with 1,4-dioxane (50 cm^3). The organic layer was washed with water (6 x 50 cm^3). The organic layer was dried ($MgSO_4$) and removed under reduced pressure. No desired product was obtained.

5.3 SYNTHESIS OF BENZOAZA-15-CROWN-5 (241)

5.3.1 Synthesis of benzoaza-15-crown-5 (241)[2]

Aminophenol (**240**, 23.03 g, 0.2110 mol) was added to 1-butanol (320 cm^3), and this mixture was degassed under a nitrogen atmosphere. NaOH (17.97 g, 0.4494 mol) was added and the mixture was allowed to stir for 5 min, after which 1,11-dichloro-3,6,9-trioxaundecane (**230**, 48.77 g, 0.2110 mol) was added and the mixture heated for 30 h at 117 °C. The reaction mixture was acidified with conc. hydrochloric acid (2 cm^3), cooled, filtered and the solid washed with methanol (85 cm^3). The combined filtrates were concentrated under reduced pressure and the residue was continuously extracted using hexane. This gave the final product, after recrystallisation from hexane, as a white solid; yield 25.47 g (45.16 %, m.p. 95 – 98 °C).

NMR ($CDCl_3$, Figure 6. 20): ^1H (300 MHz), δ = 3.24 – 3.31 (t, 2 H, $PhNHCH_2C\underline{H_2}O$), 3.68 – 3.70 (s, 4 H, $OC\underline{H_2}CH_2O$), 3.71 – 3.74 (d, 4 H, $OCH_2C\underline{H_2}O$), 3.78 – 3.83 (t, 2 H, $PhNHC\underline{H_2}CH_2O$), 3.84 – 3.89 (m, 2 H, $PhOCH_2C\underline{H_2}O$), 4.09 – 4.15 (m, 2 H, $PhOC\underline{H_2}CH_2O$), 6.58 – 6.68 (m, 2 H, $Ar\underline{H_{b'}}$), 6.75 – 6.80 (dd, 1 H, $Ar\underline{H_{c'}}$), 6.85 – 6.93 (t, 1 H, $Ar\underline{H_{a'}}$) ppm.

5.3.2 Synthesis of *N*-methylbenzoaza-15-crown-5 (244)

Benzoaza-15-crown-5 (**241**, 3.26 g, 0.01219 mol) was added to a solution of methyl iodide (8 cm^3). This solution was stirred for 16 h at room temperature. This solution was placed in an oven to remove all the unreacted methyl iodide. After all the methyl iodide was removed, the product was dissolved in chloroform (10 cm^3) and the organic layer was washed with 1 mol/dm^3 LiOH solution (6 x 25 cm^3). The organic layer was dried ($MgSO_4$) and removed under reduced pressure, to give the product as a yellow liquid; yield 3.13 g (91.22 %).

NMR ($CDCl_3$, Figure 6. 21): ^1H (300 MHz), δ = 2.83 – 2.86 (s, 3 H, $C\underline{H_3}$), 3.18 – 3.27 (t, 2 H, $PhNHCH_2C\underline{H_2}O$), 3.70 – 3.76 (d, 8 H, $OC\underline{H_2}C\underline{H_2}O$), 3.90 –

3.98 (m, 4 H, PhO(NH)$CH_2C\underline{H}_2O$), 4.14 – 4.21 (PhO$C\underline{H}_2CH_2O$), 6.79 – 6.97 (Ar$\underline{H}$) ppm.

5.4 SYNTHESIS AND FUNCTIONALISATION OF AZA-15-CROWN-5 (253)

5.4.1 Synthesis of *N*-*p*-tolylsulphonyldiethanolamine (247)

To a solution of diethanolamine (**245**, 21.03 g, 0.2000 mol) in a 1 M Na_2CO_3 solution (500 cm^3), maintained between 65 – 70 °C, is slowly added *p*-toluenesulphonyl chloride (**246**, 38.13 g, 0.2000 mol). This mixture is stirred for a further 1 h at 95 °C. As this mixture cooled the product crystallised as a white solid. The product was filtered and the precipitate was washed with water (100 cm^3) and dried to give the product as a white solid; yield 37.28 g (71.88 %, m.p. 129 – 131 °C).

NMR ($CDCl_3$, Figure 6. 22): ^1H (300 MHz), δ = 2.38 – 2.42 (s, 3 H, Ph$C\underline{H}_3$), 3.22 – 3.30 (t, 4 H, $NC\underline{H}_2CH_2OH$), 3.70 – 3.77 (t, 4 H, $NCH_2C\underline{H}_2OH$), 7.25 – 7.30 (d, $J_{a'b'}$ = 8 Hz, 2 H, Ar$\underline{H}_{a'}$), 7.63 – 7.70 (d, $J_{a'b'}$ = 8 Hz, 2 H, Ar$\underline{H}_{b'}$) ppm.

5.4.2 Synthesis of *N*-tolylsulphonyl-aza-15-crown-5 (250) from 1,8-dichloro-3,6-dioxaoctane (249)

N-*p*-Tolylsulphonyldiethanolamine (**247**, 1.30 g, 0.005013 mol) in dry THF (10 cm^3) was added dropwise, over a period of 1.5 h, to a stirred, cooled, suspension of NaH (0.36 g, 0.01504 mol) in dry THF (35 cm^3). This mixture was stirred for 2.5 h at room temperature (N_2 atmosphere). 1,8-dichloro-3,6-dioxaoctane (**249**, 0.94 g, 0.005013 mol) in dry THF (10 cm^3) was added to this solution, and this mixture was allow to stir for 48 h at room temperature (N_2 atmosphere). Water was added to this mixture, the THF removed, and the product extracted into chloroform (6 x 50 cm^3). The organic layer was dried ($MgSO_4$) and removed under reduced pressure. No desired product was obtained. Paragraph 5.4.4, p. 170, describes an alternative successful synthesis.

5.4.3 Synthesis of triethylene glycol bis-toluene-*p*-sulphonate (252)

To flask equipped with a thermometer was added triethylene glycol (**251**, 4.27 g, 0.02843 mol) and pyridine (14 cm^3). This was allowed to cool down to about 4 °C, and then toluene-*p*-sulphonyl chloride (**246**, 13.55 g, 0.07108 mol) was added at such a rate that the temperature did not rise above 10 °C. This mixture was stirred at 4 °C for 3 h. Concentrated hydrochloric acid (50 cm^3) diluted with water (100 cm^3) was added to this solution. The product crystallised as a white solid and was obtained by means of filtration. The product was washed with cold water (50 cm^3), to give the product as a white solid; yield 8.10 g, (72.69 %, m.p. 78 – 81 °C).

NMR ($CDCl_3$, Figure 6. 23): ^{1}H (300 MHz), δ = 2.45 – 2.49 (s, 6 H, PhC$\underline{H}_3$), 3.51 – 3.55 (s, 4 H, OC$\underline{H}_2$C$\underline{H}_2$O), 3.64 – 3.69 (t, 4 H, TsOCH$_2$C$\underline{H}_2$O), 4.12 – 4.16 (t, 4 H, TsOC$\underline{H}_2$CH$_2$O), 7.31 – 7.37 (d, $J_{a'b'}$ = 8 Hz, 4 H, Ar$\underline{H}_{a'}$), 7.78 – 7.83 (d, $J_{a'b'}$ = 8 Hz, 4 H, Ar$\underline{H}_{b'}$) ppm.

5.4.4 Synthesis of *N*-tolylsulphonyl-aza-15-crown-5 (250)

N-*p*-Tolylsulphonyldiethanolamine (**247**, 12.97 g, 0.05001 mol) in dry THF (50 cm^3) was added dropwise, over a period of 1.5 h, to a stirred, cooled, suspension of NaH (3.60 g, 0.1500 mol) in dry THF (140 cm^3). This mixture was stirred for 2.5 h at room temperature (N_2 atmosphere). Triethylene glycol bis-toluene-*p*-sulphonate (**252**, 22.93 g, 0.05001 mol) in dry THF (50 cm^3) was added to this solution, and this mixture was allow to stir for 48 h at room temperature (N_2 atmosphere). Water was added to this mixture, the THF removed, and the product extracted into chloroform (6 x 100 cm^3). The organic layer was dried ($MgSO_4$) and removed under reduced pressure, to give the product as a brownish liquid; yield 7.62 g (40.79 %).

NMR ($CDCl_3$, Figure 6. 24): ^{1}H (300 MHz), δ = 2.37 – 2.41 (s, 3 H, PhC$\underline{H}_3$), 3.22 – 3.30 (t, 4 H, NCH$_2$C$\underline{H}_2$O), 3.58 – 3.65 (s, 12 H, OC$\underline{H}_2$C$\underline{H}_2$O), 3.68 – 3.77 (t, 4 H, NC$\underline{H}_2$CH$_2$O), 7.25 – 7.30 (d, 2 H, $J_{a'b'}$ = 8 Hz, Ar$\underline{H}_{a'}$), 7.65 – 7.70 (d, 2 H, $J_{a'b'}$ = 8 Hz, Ar$\underline{H}_{b'}$) ppm.

5.4.5 Synthesis of aza-15-crown-5 (253)

N-tolylsulphonyl-aza-15-crown-5 (**250**, 1.50 g, 0.004016 mol) in dry THF (25 cm^3) was added to a suspension of $LiAlH_4$ (0.46 g, 0.01205 mol) in dry THF (25 cm^3) and this mixture was stirred for 24 h at room temperature (N_2 atmosphere). Water was added to this mixture and extracted with chloroform (6 x 50 cm^3). The organic layer was dried ($MgSO_4$) and removed under reduced pressure, to give the product as a white solid; yield 0.58 g (65.32 %, m.p. 36 – 39 °C).

NMR ($CDCl_3$, Figure 6. 25): ^{1}H (300 MHz), δ = 2.75 – 2.83 (t, 4 H, $NHC\underline{H_2}CH_2O$), 3.63 – 3.70 (d, 16 H, $NHCH_2C\underline{H_2}OC\underline{H_2}C\underline{H_2}O$) ppm.

5.5 SYNTHESIS AND FUCNTIONALISATION OF POLYMERIC CARRIERS

5.5.1 Polymerisation of aspartic acid (203) to produce polysuccinimide (204)

Finely powdered DL-aspartic acid (**203**, 15.00 g, 0.1127 mol) and phosphoric acid (15.00 g) were thoroughly mixed in a 1 000 cm^3 round-bottomed flask. The flask was submerged into an oil bath at 200 °C, with slow rotation. Care was taken that the reaction mixture does not froth out. After 5 min, the temperature was lowered and maintained at 170 – 190 °C for 2.5 h, while the pressure was reduced to below 2 torr. After the reaction was cooled to about 50 °C, DMF (100 cm^3) was poured onto the warm reaction mixture. This mixture was slowly stirred overnight (16 h) at room temperature. This light brown solution was poured, with vigorous stirring, into a beaker containing water (1 000 cm^3). The polymer precipitated as a white solid. The polymer was removed by filtration and washed with water (100 cm^3). The solid was ground under liquid N_2 and dried at 56 °C under reduced pressure over P_2O_5 in an Abderhalden drying tube, using boiling acetone as the heat source. The polysuccinimide (**204**) was obtained as a white solid; yield 12.33 g (99.99 %, m.p. < 200 °C).

NMR (DMF-d_7, Figure 6. 26): ^{1}H (300 MHz), δ = 3.28 – 3.51 (s, 1 H, C$\underline{H}$), 3.78 – 3.93 (s, 2 H, C$\underline{H}_2$), 5.36 – 5.62 (s, 1 H, C$\underline{H}$) ppm.

5.5.2 Synthesis of water-soluble polymer 207

To a solution of polysuccinimide (**204**, 4.00 g, 0.04121 mol) in anhydrous DMF (60 cm^3) was added *N*-(3-aminopropyl)morpholine (**205**, 4.46 g, 0.03091 mol) in DMF (15 cm^3), over a period of 10 min at 0 °C. This solution was stirred for 25 min at 0 °C, and then for a further 5 h at room temperature. After cooling the solution to 0 °C, ethylenediamine (**206**, 2.48 g, 0.04121 mol) in DMF (15 cm^3) was slowly added over a period of 20 min. The reaction mixture was stirred for 20 min at 0 °C, and then for a further 5 h at room temperature. This mixture was diluted with water (90 cm^3) and dialysed for 16 h in a 12 000 molecular mass cut-off membrane tubing. The product was obtained after freeze-drying as a white solid; yield 7.83 g (21.57 %).

NMR (D_2O): ^{1}H (300 MHz), δ = 1.35 – 1.56 (s 6 H, $\underline{H}_{\beta}$), 2.10 – 2.20 (s, 6 H, $\underline{H}_{\gamma}$), 2.20 – 2.36 (s, 12 H, $\underline{H}_{\delta}$), 2.83 – 3.06 (s, 6 H, $\underline{H}_{\alpha}$), 3.40 – 3.59 (s, 12 H, $\underline{H}_{\varepsilon}$), 4.30 – 4.51 (s, 4 H, C$\underline{H}$) ppm.

5.5.3 Synthesis of the water-soluble polymer 302

To a solution of polysuccinimide (**204**, 3.00 g, 0.03090 mol) in anhydrous DMF (50 cm^3) was added *N*-(3-aminopropyl)morpholine (**205**, 2.23 g, 0.01545 mol) in DMF (10 cm^3), over a period of 10 min at 0 °C. This solution was stirred for 25 min at 0 °C, and then for a further 5 h at room temperature. After cooling the solution to 0 °C, propylenediamine (**301**, 2.29 g, 0.03090 mol) in DMF (10 cm^3) was slowly added over a period of 20 min. The reaction mixture was stirred for 20 min at 0 °C, and then for a further 5 h at room temperature. This mixture was diluted with water (70 cm^3) and dialysed for 16 h in a 12 000 molecular mass cut-off membrane tubing. The product was obtained after freeze-drying as a white solid; yield 5.70 g (22.36 %).

NMR (D_2O): ^1H (300 MHz), δ = 1.29 – 1.69 (s, 8 H, $\underline{H}_{\beta}$), 2.02 – 2.20 (s, 4 H, $\underline{H}_{\gamma}$), 2.20 – 2.35 (m, 8 H, $\underline{H}_{\delta}$), 2.85 – 3.05 (s, 8 H, $\underline{H}_{\alpha}$), 3.39 – 3.60 (s, 8 H, $\underline{H}_{\varepsilon}$), 4.30 – 4.50 (s, 4 H, $C\underline{H}$) ppm.

5.5.4 Synthesis of polyepichlorohydrin (215) with Mr = 2 000 g/mol

Hexane-1,6-diol (**214**, 11.82 g, 0.1000 mol) was added to a mixture of pentane (100 cm^3) and hexane (100 cm^3). Epichlorohydrin (**213**, 188.38 g, 2.036 mol) was mixed with hexane (400 cm^3) and was added to a dropping funnel. About 5 cm^3 of this solution was added to the reaction mixture. The temperature of the reaction mixture was set to 25 °C. Fresh distilled $BF_3\cdot O(C_2H_6)_2$ complex (0.8 cm^3) was added with stirring. The contents of the dropping funnel was added over a 24 h period, ensuring that the temperature remain between 24 – 27 °C. After the contents was added the reaction mixture was stirred for a further 30 min. The hexane was decanted and water (400 cm^3) was added. This was done to terminate the reaction and to destroy the $BF_3\cdot O(C_2H_6)_2$ complex. After 30 min the water was decanted and the colourless product dissolved in dichloromethane (300 cm^3). The organic layer was thoroughly washed with water (6 x 100 cm^3). The organic layer was dried ($MgSO_4$) and removed under reduced pressure, to give the product as a colourless liquid; yield 183.65 g.

NMR ($CDCl_3$): ^1H (300 MHz), δ = 1.30 – 1.65 (d, 8 H, $OCH_2C\underline{H}_2C\underline{H}_2C\underline{H}_2C\underline{H}_2CH_2O$), 3.35 – 4.05 (m, 5 H, $C\underline{H}_2O$, $C\underline{H}$, $C\underline{H}_2Cl$ and $OCH_2C\underline{H}_2C\underline{H}_2C\underline{H}_2C\underline{H}_2CH_2O$) ppm.

5.5.5 Synthesis of polyepichlorohydrin (303) with Mr = 20 000 g/mol

Hexane-1,6-diol (**214**, 1.18 g, 0.009985 mol) was added to a mixture of pentane (100 cm^3) and hexane (100 cm^3). Epichlorohydrin (**213**, 188.38 g, 2.036 mol) was mixed with hexane (400 cm^3) and was added to a dropping funnel. About 5 cm^3 of this solution was added to the reaction mixture. The temperature of the reaction mixture was set to 25 °C. Fresh distilled $BF_3\cdot O(C_2H_6)_2$ complex (0.8 cm^3) was added with stirring. The contents of the dropping funnel was added over a 24 h period, ensuring that the temperature remain between 24 – 27 °C.

After the contents was added the reaction mixture was stirred for a further 30 min. The hexane was decanted and water (400 cm^3) was added. This was done to terminate the reaction and to destroy the $BF_3{\cdot}O(C_2H_6)_2$ complex. After 30 min the water was decanted and the colourless product dissolved in dichloromethane (300 cm^3). The organic layer was thoroughly washed with water (6 x 100 cm^3). The organic layer was dried ($MgSO_4$) and removed under reduced pressure, to give the product as a colourless liquid; yield 182.86 g.

NMR ($CDCl_3$, Figure 6. 27): ^1H (300 MHz), δ = 1.15 – 1.23 (m, 8 H, $OCH_2C\underline{H_2}C\underline{H_2}C\underline{H_2}C\underline{H_2}CH_2O$), 3.28 – 4.05 (m, 5 H, $C\underline{H_2}O$, $C\underline{H}$ and $C\underline{H_2}Cl$) ppm.

5.5.6 Synthesis of the isocyanate polymer 304

A number of methods was investigated, see p 107. Here only the method producing the best result was given. Polyepichlorohydrin (**215**, 5.00 g, 0.002542 mol), K_2CO_3 (3.51 g, 0.02542 mol), tetrabuthylammoniumbromide (0.16 g, 0.0005084 mol) and KNCO (4.12 g, 0.05084 mol) was added to a flask containing DMF (100 cm^3). This solution was refluxed at 100 °C for 16 h. The solution was cooled to room temperature and filtered. The filtrate was added to hexane (500 cm^3) and this solution was stirred for 16 h at room temperature. The hexane layer was decanted and the colourless polymer **304** was obtained; yield 4.25 g (89.94 %).

5.5.7 Synthesis of polyepichlorohydrin (307) with Mr = 1 850 g/mol

tert-Butanol (**306**, 7.41 g, 0.1000 mol) was added to a mixture of pentane (100 cm^3) and hexane (100 cm^3). Epichlorohydrin (**213**, 188.38 g, 2.036 mol) was mixed with hexane (400 cm^3) and was added to a dropping funnel. About 5 cm^3 of this solution was added to the reaction mixture. The temperature of the reaction mixture was set to 25 °C. Fresh distilled $BF_3{\cdot}O(C_2H_6)_2$ complex (0.8 cm^3) was added with stirring. The contents of the dropping funnel was added over a 24 h period, ensuring that the temperature remain between 24 – 27 °C. After the contents was added the reaction mixture was stirred for a further 30 min. The hexane was decanted and water (400 cm^3) was added. This was done to terminate the reaction and to destroy the $BF_3 \cdot O(C_2H_6)_2$ complex. After 30 min the water was decanted and the colourless product dissolved in dichloromethane (300 cm^3). The organic layer was thoroughly washed with water (6 x 100 cm^3). The organic layer was dried ($MgSO_4$) and removed under reduced pressure, to give the product as a colourless liquid; yield 185.68 g.

NMR ($CDCl_3$, Figure 6. 28): ^1H (300 MHz), δ = 1.78 – 1.88 (m, 9 H, $C(C\underline{H}_3)_3$), 3.51 – 4.05 (m, 5 H, $C\underline{H}_2O$, $C\underline{H}$ and $C\underline{H}_2Cl$) ppm.

5.5.8 Synthesis of the isocyanate polymer 308

Polyepichlorohydrin (**307**, 5.00 g, 0.002599 mol), K_2CO_3 (3.59 g, 0.02599 mol), tetrabuthylammoniumbromide (0.17 g, 0.0005198 mol) and KNCO (4.22 g, 0.05198 mol) was added to a flask containing DMF (100 cm^3). This solution was refluxed at 100 °C for 16 h. The solution was cooled to room temperature and filtered. The filtrate was added to hexane (500 cm^3) and this solution was stirred for 16 h at room temperature. The hexane layer was decanted and the colourless polymer **307** was obtained; yield 4.18 g (88.56 %).

NMR ($CDCl_3$): ^1H (300 MHz), δ = 3.19 – 3.40 (t, 2 H, $C\underline{H}_2NCO$), 3.40 – 4.01 ($C\underline{H}_2O$, $C\underline{H}$ and $C\underline{H}_2Cl$) ppm.

IR (between two KBr discs): 2104 – 2140 (-NCO).

5.5.9 Synthesis of elastomer 201

HTPB (**199**, 45.15 g, 0.01530 mol) and isophorone diisocyanate (**200**, 3.49 g, 0.01570 mol) was thoroughly stirred with an overhead stirrer fitted with a propeller shaft blade, and added to the mould. The mould was placed in an oven at a temperature of 78 °C for 24 h. The mould was then taken out of the oven and allowed to reach room temperature. The fully cured elastomer was then taken out of the mould.

5.6 ANCHORING OF BENZO-15-CROWN-5 DERIVATIVES ONTO THE WATER-SOLUBLE POLYMERIC CARRIERS

5.6.1 Anchoring of carboxylic acid functionalised crown ethers onto the water-soluble polymers 207 and 302

5.6.1.1 Synthesis of the water-soluble polymer **319**

To a solution of 4'-carboxybenzo-15-crown-5 (**258**, 0.11 g, 0.0003404 mol) in DMF (5 cm^3) was added triethylamine (0.06 g, 0.0005674 mol) and *O*-benzotriazolyl-*N*,*N*,*N'*,*N'*-tetramethyluronium hexafluorophosphate (**212**, 0.22 g, 0.0005674 mol). This mixture was allowed to stir for 10 min, after which polymer **207** (0.25 g, 0.0002837 mol) was added. This mixture was allowed to stir for 30 min. If the entire solid did not dissolve, add DMF (5 cm^3) portion over 30 min periods. This mixture was stirred for 24 h at room temperature. The mixture was diluted with water (20 cm^3) and dialysed for 16 h in a 12 000 molecular mass cut-off membrane tubing. The product was obtained after freeze-drying as a white solid; yield 0.30 g (90.56 %).

NMR (D_2O): ^{1}H (300 MHz), δ = 1.35 – 1.56 (s 6 H, $\underline{H}_{\beta}$), 1.85 – 2.36 (s, 20 H, $\underline{H}_{\gamma}$, $\underline{H}_{\delta}$ and $\underline{H}_{\beta'}$), 2.70 – 3.00 (s, 6 H, $\underline{H}_{\alpha}$), 3.30 – 3.50 (s, 20 H, $\underline{H}_{\varepsilon}$ and $OC\underline{H}_2OC\underline{H}_2$), 3.50 – 3.75 (s, 4 H, $PhOCH_2C\underline{H}_2O$), 3.75 – 3.95 (s, 4 H, $PhOC\underline{H}_2CH_2O$), 4.25 – 4.51 (s, 4 H, $C\underline{H}$), 6.55 – 6.80 (s, 1 H, $Ar\underline{H}_{b'}$), 6.85 – 7.15 (s, 2 H, $Ar\underline{H}_{a'}$) ppm.

5.6.1.2 Synthesis of the water-soluble polymer **320**

To a solution of 4'-(ethanoic acid)benzo-15-crown-5 (**259**, 0.11 g, 0.0003404 mol) in DMF (5 cm^3) was added triethylamine (0.06 g, 0.0005674 mol) and *O*-benzotriazolyl-*N*,*N*,*N'*,*N'*-tetramethyluronium hexafluorophosphate (**212**, 0.22 g, 0.0005674 mol). This mixture was allowed to stir for 10 min, after which polymer **207** (0.25 g, 0.0002837 mol) was added. This mixture was allowed to stir for 30 min. If the entire solid did not dissolve, add DMF (5 cm^3) portion over 30 min periods. This mixture was stirred for 24 h at room temperature. The mixture was diluted with water (20 cm^3) and dialysed for 16 h in a 12 000 molecular mass cut-off membrane tubing. The product was obtained after freeze-drying as a white solid; yield 0.31 g (90.45 %).

NMR (D_2O): ^1H (300 MHz), δ = 1.25 – 1.56 (s 6 H, $\underline{H}_{\beta}$), 1.99 – 2.33 (s, 20 H, $\underline{H}_{\gamma}$, $\underline{H}_{\delta}$ and $\underline{H}_{\beta'}$), 2.59 – 2.75 (s, 2 H, $PhC\underline{H}_2COOH$), 2.75 – 3.00 (s, 6 H, $\underline{H}_{\alpha}$), 3.30 – 3.52 (s, 20 H, $\underline{H}_{\varepsilon}$ and $OC\underline{H}_2OC\underline{H}_2$), 3.52 – 3.70 (s, 4 H, $PhOCH_2C\underline{H}_2O$), 3.70 – 4.00 (s, 4 H, $PhOC\underline{H}_2CH_2O$), 4.25 – 4.51 (s, 4 H, $C\underline{H}$), 6.40 – 6.70 (s, 3 H, $Ar\underline{H}$) ppm.

5.6.1.3 Synthesis of the water-soluble polymer **321**

To a solution of 4'-(propanoic acid)benzo-15-crown-5 (**260**, 0.12 g, 0.0003404 mol) in DMF (5 cm^3) was added triethylamine (0.06 g, 0.0005674 mol) and *O*-benzotriazolyl-*N*,*N*,*N'*,*N'*-tetramethyluronium hexafluorophosphate (**212**, 0.22 g, 0.0005674 mol). This mixture was allowed to stir for 10 min, after which polymer **207** (0.25 g, 0.0002837 mol) was added. This mixture was allowed to stir for 30 min. If the entire solid did not dissolve, add DMF (5 cm^3) portion over 30 min periods. This mixture was stirred for 24 h at room temperature. The mixture was diluted with water (20 cm^3) and dialysed for 16 h in a 12 000 molecular mass cut-off membrane tubing. The product was obtained after freeze-drying as a white solid; yield 0.31 g (90.34 %).

NMR (D_2O): ^1H (300 MHz), δ = 1.35 – 1.56 (s 6 H, $\underline{H}_{\beta}$), 1.95 – 2.30 (s, 20 H, $\underline{H}_{\gamma}$, $\underline{H}_{\delta}$ and $\underline{H}_{\beta'}$), 2.45 – 2.70 (s, 4 H, $PhC\underline{H}_2C\underline{H}_2COOH$), 2.75 – 3.05 (s, 6 H, $\underline{H}_{\alpha}$), 3.30 – 3.50 (s, 20 H, $\underline{H}_{\varepsilon}$ and $OC\underline{H}_2OC\underline{H}_2$), 3.50 – 3.70 (s, 4 H, $PhOCH_2C\underline{H}_2O$), 3.70 – 3.95 (s, 4 H, $PhOC\underline{H}_2CH_2O$), 4.25 – 4.51 (s, 4 H, $C\underline{H}$), 6.39 – 6.70 (s, 3 H, $Ar\underline{H}$) ppm.

5.6.1.4 Synthesis of the water-soluble polymer **322**

To a solution of 4'-(butanoic acid)benzo-15-crown-5 (**261**, 0.12 g, 0.0003404 mol) in DMF (5 cm^3) was added triethylamine (0.06 g, 0.0005674 mol) and *O*-benzotriazolyl-*N*,*N*,*N'*,*N'*-tetramethyluronium hexafluorophosphate (**212**, 0.22 g, 0.0005674 mol). This mixture was allowed to stir for 10 min, after which polymer **207** (0.25 g, 0.0002837 mol) was added. This mixture was allowed to stir for 30 min. If the entire solid did not dissolve, add DMF (5 cm^3) portion over 30 min periods. This mixture was stirred for 24 h at room temperature. The mixture was diluted with water (20 cm^3) and dialysed for 16 h in a 12 000 molecular mass cut-off membrane tubing. The product was obtained after freeze-drying as a white solid; yield 0.31 g (90.75 %).

NMR (D_2O): ^{1}H (300 MHz), δ = 1.25 – 1.46 (s 6 H, $\underline{H}_\beta$), 1.46 – 1.66 (s, 2 H, $PhCH_2C\underline{H}_2CH_2COOH$), 1.85 – 2.30 (s, 22 H, $\underline{H}_\gamma$, $\underline{H}_\delta$, $\underline{H}_{\beta'}$ and $PhC\underline{H}_2CH_2CH_2COOH$), 2.80 – 3.15 (s, 8 H, $\underline{H}_\alpha$ and $PhCH_2CH_2C\underline{H}_2COOH$), 3.30 – 3.55 (s, 20 H, $\underline{H}_\varepsilon$ and $OC\underline{H}_2OC\underline{H}_2$), 3.55 – 3.70 (s, 4 H, $PhOCH_2C\underline{H}_2O$), 3.70 – 3.95 (s, 4 H, $PhOC\underline{H}_2CH_2O$), 4.25 – 4.51 (s, 4 H, $C\underline{H}$), 6.40 – 6.71 (s, 3 H, $Ar\underline{H}$) ppm.

5.6.1.5 Synthesis of the water-soluble polymer **323**

To a solution of 4'-(propanoic acid)benzo-15-crown-5 (**260**, 0.99 g, 0.002921 mol) in DMF (5 cm^3) was added triethylamine (0.44 g, 0.004382 mol) and *O*-benzotriazolyl-*N*,*N*,*N'*,*N'*-tetramethyluronium hexafluorophosphate (**212**, 1.11 g, 0.002921 mol). This mixture was allowed to stir for 10 min, after which polymer **302** (1.00 g, 0.001212 mol) was added. This mixture was allowed to stir for 30 min. If the entire solid did not dissolve, add DMF (5 cm^3) portion over 30 min periods. This mixture was stirred for 24 h at room temperature. The mixture was diluted with water (20 cm^3) and dialysed for 16 h in a 12 000 molecular mass cut-off membrane tubing. The product was obtained after freeze-drying as a white solid; yield 1.27 g (91.26 %).

NMR (D_2O): ^{1}H (300 MHz), δ = 1.30 – 1.55 (s, 8 H, $\underline{H}_\beta$), 1.55 – 75 (s, 2 H, $PhCH_2C\underline{H}_2COOH$), 3.30 – 3.65 (s, 20 H, $\underline{H}_\varepsilon$, $OC\underline{H}_2C\underline{H}_2O$ and $PhOCH_2C\underline{H}_2O$), 3.65 – 3.95 (s, 4 H, $PhOC\underline{H}_2CH_2O$), 4.25 – 4.50 (s, 4 H, $C\underline{H}$), 6.30 – 6.65 (m, 3 H, $Ar\underline{H}$) ppm.

5.6.2 Reaction between polysuccinimide (204) and amine functionalised crown ethers 294, 296, 297, 325 and 326

5.6.2.1 Attempted synthesis of water-soluble polymer **327**

To a solution of polysuccinimide (**204**, 0.34 g, 0.003530 mol) in anhydrous DMF (5 cm^3) was added 4'-aminobenzo-15-crown-5 (**325**, 0.25 g, 0.0008825 mol) in DMF (2.5 cm^3), over a period of 10 min at 0 °C. This solution was stirred for 25 min at 0 °C, and then for a further 24 h at room temperature. After cooling the solution to 0 °C, *N*-(3-aminopropyl)morpholine (**205**, 0.51 g, 0.003530 mol) in DMF (2.5 cm^3) was slowly added over a period of 20 min. The reaction mixture was stirred for 20 min at 0 °C, and then for a further 24 h at room temperature. This mixture was diluted with water (10 cm^3) and dialysed for 16 h in a 12 000 molecular mass cut-off membrane tubing. The product was obtained after freeze-drying as a white solid. However, the product contained no crown ether moieties, presumably because 4'-aminobenzo-15-crown-5 (**325**) is to sterically hindered.

5.6.2.2 Synthesis of water-soluble polymer **328**

To a solution of polysuccinimide (**204**, 0.13 g, 0.001345 mol) in anhydrous DMF (5 cm^3) was added 4'-(aminomethyl)benzo-15-crown-5 (**294**, 0.10 g, 0.0003362 mol) in DMF (2.5 cm^3), over a period of 10 min at 0 °C. This solution was stirred for 25 min at 0 °C, and then for a further 24 h at room temperature. After cooling the solution to 0 °C, *N*-(3-aminopropyl)morpholine (**205**, 0.19 g, 0.001345 mol) in DMF (2.5 cm^3) was slowly added over a period of 20 min. The reaction mixture was stirred for 20 min at 0 °C, and then for a further 24 h at room temperature. This mixture was diluted with water (10 cm^3) and dialysed for 16 h in a 12 000 molecular mass cut-off membrane tubing. The product was obtained after freeze-drying as a white solid; yield 0.24 g (22.36 %).

NMR (D_2O): ^{1}H (300 MHz), δ = 1.29 – 1.55 (s, 6 H, $\underline{H}_\beta$), 3.32 – 3.59 (s, 20 H, $\underline{H}_\varepsilon$, $OC\underline{H_2}C\underline{H_2}O$), 3.59 – 3.70 (s, 4 H, $PhOCH_2C\underline{H_2}O$), 3.78 – 3.98 (s, 4 H, $PhOC\underline{H_2}CH_2O$), 4.11 – 4.43 (s, 4 H, $C\underline{H}$), 6.49 – 6.75 (m, 3 H, $Ar\underline{H}$) ppm.

5.6.2.3 Synthesis of water-soluble polymer **329**

To a solution of polysuccinimide (**204**, 0.24 g, 0.002458 mol) in anhydrous DMF (5 cm^3) was added 4'-(aminopropyl)benzo-15-crown-5 (**296**, 0.20 g, 0.0006145 mol) in DMF (2.5 cm^3), over a period of 10 min at 0 °C. This solution was stirred for 25 min at 0 °C, and then for a further 24 h at room temperature. After cooling the solution to 0 °C, *N*-(3-aminopropyl)morpholine (**205**, 0.35 g, 0.002458 mol) in DMF (2.5 cm^3) was slowly added over a period of 20 min. The reaction mixture was stirred for 20 min at 0 °C, and then for a further 24 h at room temperature. This mixture was diluted with water (10 cm^3) and dialysed for 16 h in a 12 000 molecular mass cut-off membrane tubing. The product was obtained after freeze-drying as a white solid; yield 0.48 g (22.89 %).

NMR (D_2O): ^1H (300 MHz), δ = 1.29 – 1.60 (s, 8 H, $\underline{H}_{\beta}$ and $PhCH_2C\underline{H}_2CH_2NH_2$), 3.32 – 3.55 (s, 20 H, $\underline{H}_{\varepsilon}$, $OC\underline{H}_2C\underline{H}_2O$), 3.55 – 3.68 (s, 4 H, $PhOCH_2C\underline{H}_2O$), 3.78 – 3.98 (s, 4 H, $PhOC\underline{H}_2CH_2O$), 4.13 – 4.43 (s, 4 H, $C\underline{H}$), 6.35 – 6.72 (m, 3 H, $Ar\underline{H}$) ppm.

5.6.2.4 Synthesis of water-soluble polymer **330**

To a solution of polysuccinimide (**204**, 0.11 g, 0.001178 mol) in anhydrous DMF (5 cm^3) was added 4'-(aminobutyl)benzo-15-crown-5 (**297**, 0.10 g, 0.0002945 mol) in DMF (2.5 cm^3), over a period of 10 min at 0 °C. This solution was stirred for 25 min at 0 °C, and then for a further 24 h at room temperature. After cooling the solution to 0 °C, *N*-(3-aminopropyl)morpholine (**205**, 0.17 g, 0.001178 mol) in DMF (2.5 cm^3) was slowly added over a period of 20 min. The reaction mixture was stirred for 20 min at 0 °C, and then for a further 24 h at room temperature. This mixture was diluted with water (10 cm^3) and dialysed for 16 h in a 12 000 molecular mass cut-off membrane tubing. The product was obtained after freeze-drying as a white solid; yield 0.45 g (22.19 %).

NMR (D_2O): ^1H (300 MHz), δ = 1.10 – 1.32 (s, 2 H, $PhCH_2C\underline{H}_2C\underline{H}_2CH_2NH_2$), 1.32 – 1.55 (s, 6 H, $\underline{H}_{\beta}$), 3.35 – 3.55 (s, 20 H, $\underline{H}_{\varepsilon}$, $OC\underline{H}_2C\underline{H}_2O$), 3.56 – 3.69 (s, 4 H, $PhOCH_2C\underline{H}_2O$), 3.75 – 3.95 (s, 4 H, $PhOC\underline{H}_2CH_2O$), 4.12 – 4.43 (s, 4 H, $C\underline{H}$), 6.43 – 6.71 (m, 3 H, $Ar\underline{H}$) ppm.

5.6.2.5 Synthesis of water-soluble polymer **331**

To a solution of polysuccinimide (**204**, 0.39 g, 0.004012 mol) in anhydrous DMF (5 cm^3) was added 2-aminomethyl-15-crown-5 (**326**, 0.25 g, 0.001003 mol) in DMF (2.5 cm^3), over a period of 10 min at 0 °C. This solution was stirred for 25 min at 0 °C, and then for a further 24 h at room temperature. After cooling the solution to 0 °C, *N*-(3-aminopropyl)morpholine (**205**, 0.58 g, 0.004012 mol) in DMF (2.5 cm^3) was slowly added over a period of 20 min. The reaction mixture was stirred for 20 min at 0 °C, and then for a further 24 h at room temperature. This mixture was diluted with water (10 cm^3) and dialysed for 16 h in a 12 000 molecular mass cut-off membrane tubing. The product was obtained after freeze-drying as a white solid; yield 0.74 g (23.01 %).

NMR (D_2O): ^1H (300 MHz), δ = 1.35 – 1.60 (s, 6 H, $\underline{H}_{\beta}$), 3.35 – 3.51 (d, 31 H, $\underline{H}_{\varepsilon}$, $OC\underline{H}_2C\underline{H}_2O$ and $OC\underline{H}_2C\underline{H}O$), 4.12 – 4.50 (s, 4 H, $C\underline{H}$) ppm.

5.6.2.6 Synthesis of water-soluble polymer **332**

To a solution of polysuccinimide (**204**, 0.81 g, 0.008315 mol) in anhydrous DMF (5 cm^3) was added 4'-(aminopropyl)benzo-15-crown-5 (**296**, 0.54 g, 0.001663 mol) in DMF (2.5 cm^3), over a period of 10 min at 0 °C. This solution was stirred for 25 min at 0 °C, and then for a further 24 h at room temperature. After cooling the solution to 0 °C, *N*-(3-aminopropyl)morpholine (**205**, 0.12 g, 0.0008315 mol) in DMF (2.5 cm^3) was slowly added over a period of 20 min. The reaction mixture was stirred for 20 min at 0 °C, and then for a further 24 h at room temperature. After cooling the solution to 0 °C, propylenediamine (**301**, 0.62 g, 0.008315 mol) in DMF (2.5 cm^3) was slowly added over a period of 20 min. The reaction mixture was stirred for 20 min at 0 °C, and then for a further 24 h at room temperature. This mixture was diluted with water (20 cm^3) and dialysed for 16 h in a 12 000 molecular mass cut-off membrane tubing. The product was obtained after freeze-drying as a white solid; yield 1.52 g (20.95 %).

NMR (D_2O): ^1H (300 MHz), δ = 1.25 – 1.45 (s, 8 H, $\underline{H}_{\beta}$), 1.45 – 7.70 (s, 2 H, $PhCH_2C\underline{H}_2COOH$), 3.25 – 3.70 (s, 20 H, $\underline{H}_{\varepsilon}$, $OC\underline{H}_2C\underline{H}_2O$ and $PhOCH_2C\underline{H}_2O$), 3.70 – 3.95 (s, 4 H, PhOC$\underline{H}_2$CH$_2$O), 4.25 – 4.50 (s, 4 H, C$\underline{H}$), 6.30 – 6.65 (m, 3 H, Ar$\underline{H}$) ppm.

5.7 ANCHORING OF BENZO-15-CROWN-5 DERIVATIVES ONTO ELASTOMER 201

GENERAL REMARK: Due to the insolubility of these compounds, characterisation by NMR, etc. was not possible. For the purpose of this study, the compound was only considered as successful by virtue of its sodium cation scavenging properties, as describe in paragraph 5.8, p. 187.

5.7.1 Synthesis of elastomer 313

HTPB (**199**, 45.15 g, 0.01530 mol), isophorone diisocyanate (**200**, 3.49 g, 0.01570 mol) and 1-hydroxyethylferrocene (**312**, 1.00 g, 0.004346 mol) was thoroughly stirred and added to the mould. The mould was placed in an oven at a temperature of 78 °C for 24 h. The mould was then taken out of the oven and allowed to reach room temperature. The fully cured elastomer was then taken out of the mould. See Figure 3. 11, p. 112 and **photo 1**, Figure 3. 12, p. 114.

5.7.2 Synthesis of elastomer 314

Elastomer **201** was synthesised according to paragraph 5.5.9, p. 175. After 16 h, the mould was taken from the oven and allowed to reach room temperature. The elastomer was removed from the mould and cut lengthwise to produce to identical halves of thickness approximately half that of the original. This was done to expose a still sticky surface. This sticky surface is not fully cured. This cut elastomer **201** was placed into a solution of isophorone diisocyanate (**200**, 10 cm^3). After 24 h at room temperature this elastomer was thoroughly washed with, sequentially, water and acetone. To produce an elastomer with limited isocyanate groups on the surface of the elastomer.

5.7.3 Synthesis of elastomer 315

Elastomer **314** was synthesised according to paragraph 5.7.2, p. 182. After 16 h, the mould was taken from the oven and allowed to reach room temperature. The elastomer was removed from the mould and cut lengthwise to produce to identical halves of thickness approximately half that of the original. This was done to expose a still sticky surface. This sticky surface is still not fully cured. This cut elastomer **201** was placed in a solution of 1-hydroxyethylferrocene (**312**, 1.00 g, 0.004346 mol) in hexane (5 cm^3). After 24 h at room temperature this elastomer was taken out from the solution and thoroughly washed with hexane. This elastomer had ferrocene mainly bound to the surface, see **photo 2** (Figure 3. 12, p. 114) and **photo 9** (Figure 3. 13, p. 115).

5.7.4 Reduction of elastomer 315

To a solution of *p*-benzoquinone (**316**, 0.70 g, 0.006476 mol) in acetone (10 cm^3) at room temperature was added NH_4PF_6 (3.36 g, 0.02690 mol). Elastomer **315** was placed in this solution for 10 min. The yellow ferrocenyl of elastomer **315** was reduced to the blue ferrocenium moiety.

5.7.5 Synthesis of elastomer 318

Elastomer **314** was synthesised according to paragraph 5.7.2, p. 182. 4'-(Hydroxymethyl)benzo-15-crown-5 (**257**, 1.00 g, 0.003352 mol) was placed, without any solvent, on top of elastomer **314**. After 24 h at room temperature this elastomer was thoroughly washed with acetone.

5.7.6 Synthesis of elastomer 333

Elastomer **201** was synthesised according to paragraph 5.5.9, p. 175. After 16 h, the mould was taken from the oven and allowed to reach room temperature.

The elastomer was removed from the mould and cut lengthwise to produce to identical halves of thickness approximately half that of the original. This was done to expose a still sticky surface. This sticky surface is not fully cured. The water-soluble polymer **332** (1.00 g, 0.001052 mol) was placed, without any solvent, on top of this cut elastomer **201**. After 24 h at room temperature this elastomer was thoroughly washed with water.

5.7.7 Synthesis of elastomer 337

5.7.7.1 Synthesis of elastomer **335**

Elastomer **201** was synthesised according to paragraph 5.5.9, p. 175. After 16 h, the mould was taken from the oven and allowed to reach room temperature. The elastomer was removed from the mould and cut lengthwise to produce to identical halves of thickness approximately half that of the original. This was done to expose a still sticky surface. This sticky surface is not fully cured. This cut elastomer **201** was placed in a solution of hexamethylenediamine (**334**, 10 cm^3). After 24 h at room temperature this elastomer was thoroughly washed with, sequentially, water and acetone.

5.7.7.2 Synthesis of elastomer **336**

Polysuccinimide (**204**, 1.00 g, 0.01030 mol) was placed on top of the elastomer produced in paragraph 5.7.7.1. After 24 h, at room temperature this elastomer was thoroughly washed with, sequentially, DMF, water and acetone.

5.7.7.3 Synthesis of elastomer **337**

4'-(Aminopropyl)benzo-15-crown-5 (**296**, 3.00 g, 0.009219 mol) was placed on top of the elastomer produced in paragraph 5.7.7.2. After 24 h at room temperature this elastomer was thoroughly washed with, sequentially, acetone and water.

5.7.8 Synthesis of elastomer 340

5.7.8.1 Synthesis of elastomer **338**

The elastomer **336** synthesised according to paragraph 5.7.7.2, p. 184, was placed in a solution of ethylenediamine (**206**, 10 cm^3). After 24 h at room temperature this elastomer was thoroughly washed with, sequentially, water and acetone.

5.7.8.2 Synthesis of elastomer **339**

Polysuccinimide (**204**, 2.00 g, 0.02060 mol) was placed on top of the elastomer synthesised in paragraph 5.7.8.1. After 24 h at room temperature this elastomer was thoroughly washed with DMF, water and acetone.

5.7.8.3 Synthesis of elastomer **340**

4'-(Aminopropyl)benzo-15-crown-5 (**296**, 3.00 g, 0.009219 mol) was placed on top of the elastomer synthesised in paragraph 5.7.8.2. After 24 h at room temperature this elastomer was thoroughly washed with, sequentially, acetone, water and acetone.

5.7.9 Synthesis of elastomer 342

5.7.9.1 Synthesis of elastomer **341**

Elastomer **201** was synthesised according to paragraph 5.5.9, p. 175. After 16 h, the mould was taken from the oven and allowed to reach room temperature. The elastomer was removed from the mould and cut lengthwise to produce to identical halves of thickness approximately half that of the original. This was done to expose a still sticky surface. This sticky surface is not fully cured. The isocyanate polymer **304** (1.00 g, 0.0005382 mol) was placed on top of the cut elastomer **201**. After 24 h at room temperature this elastomer was thoroughly washed with acetone.

5.7.9.2 Synthesis of elastomer **342**

4'-(Hydroxymethyl)benzo-15-crown-5 (**257**, 3.00 g, 0.01006 mol) was placed on top of the elastomer synthesised in paragraph 5.7.9.1, p. 185. After 24 h at room temperature this elastomer (**337**) was thoroughly washed with acetone.

5.7.10 Synthesis of elastomer 347 and 348

5.7.10.1 Synthesis of elastomer **344**

Polyvinyl alcohol (**343**, 2.00 g, 0.00002857 mol) was placed on top of the elastomer **314** synthesised in paragraph 5.7.2, p. 182. After 24 h at room temperature this elastomer was thoroughly washed, sequentially, with water and acetone.

5.7.10.2 Synthesis of elastomer **345** and **346**

The isocyanate polymer **304** (2.00 g, 0.001077 mol) was placed on top of the elastomer **334** synthesised in paragraph 5.7.10.1. After 24 h at room temperature this elastomer was thoroughly washed with acetone.

The same was done with the isocyanate polymer **305**.

5.7.10.3 Synthesis of elastomer **347** and **348**

4'-(Hydroxymethyl)benzo-15-crown-5 (**257**, 3.00 g, 0.01006 mol) was placed on top of the elastomers **345** and **346** synthesised in paragraph 5.7.10.2. After 24 h at room temperature this elastomer was thoroughly washed with acetone.

5.8 DETERMINATION OF THE SODIUM CATION UPTAKE ABILITY OF THE ELASTOMERS 318, 333, 337, 340, 342, 347 AND 348

All the elastomers, **318**, **333**, **337**, **340**, **342**, **347** and **348**, thus produced (see paragraphs 5.7.5 – 5.7.10) was placed into a standard Na^+ solution (10 cm^3) containing 200 ppm (or 50 ppm) Na^+. This solution was shaken for 2 min. The water was then analysed for Na^+ as described in 5.1.3, p. 150, to see how much Na^+ was still left in the solution. The amount of Na^+ cations that was missing was taken as the amount that was removed by the sodium cation scavenging device. The surface area of the sodium cation scavenging device was determined by the use of graph paper. An example of the calculations performed, to determine the amount of Na^+ bound to the surface of the sodium cation scavenging device **348**, was as follows:

1. $[Na^+]$ before any Na^+ was removed: 200 ppm Na^+
2. $[Na^+]$ after Na^+ was removed: 40 ppm Na^+
3. Mass Na^+ removed from the solution: $(200-40)\,\text{ppm}\,Na^+ = 160\,\text{ppm}\,Na^+$
4. The surface are that removed this amount of Na^+: 0.00125 m^2 surface area of the sodium cation scavenging device
5. The capacity of the sodium cation scavenging device **348**, is therefore: $\left\{\frac{[(160 \times 10/1000)/0.00125]}{1000}\right\} = 1.28\,\text{g}$ Na^+ / m^2 surface area of the sodium cation scavenging device

5.9 DETERMINATION OF THE SODIUM CATION RELEASE ABILITY OF THE ELASTOMERS 318, 333, 337, 340, 342, 347 AND 348

The sodium cation scavenging devices tested in paragraph 5.8 was then placed in 10 cm^3 of a 1 mol/dm^3 (or 6 mol/dm^3) HCl solution at 20, 30, 40, 70 and 75 °C . The water was then analysed for Na^+ as described in 5.1.3, p. 150.

CHAPTER 6

^{1}H NMR SPECTRA

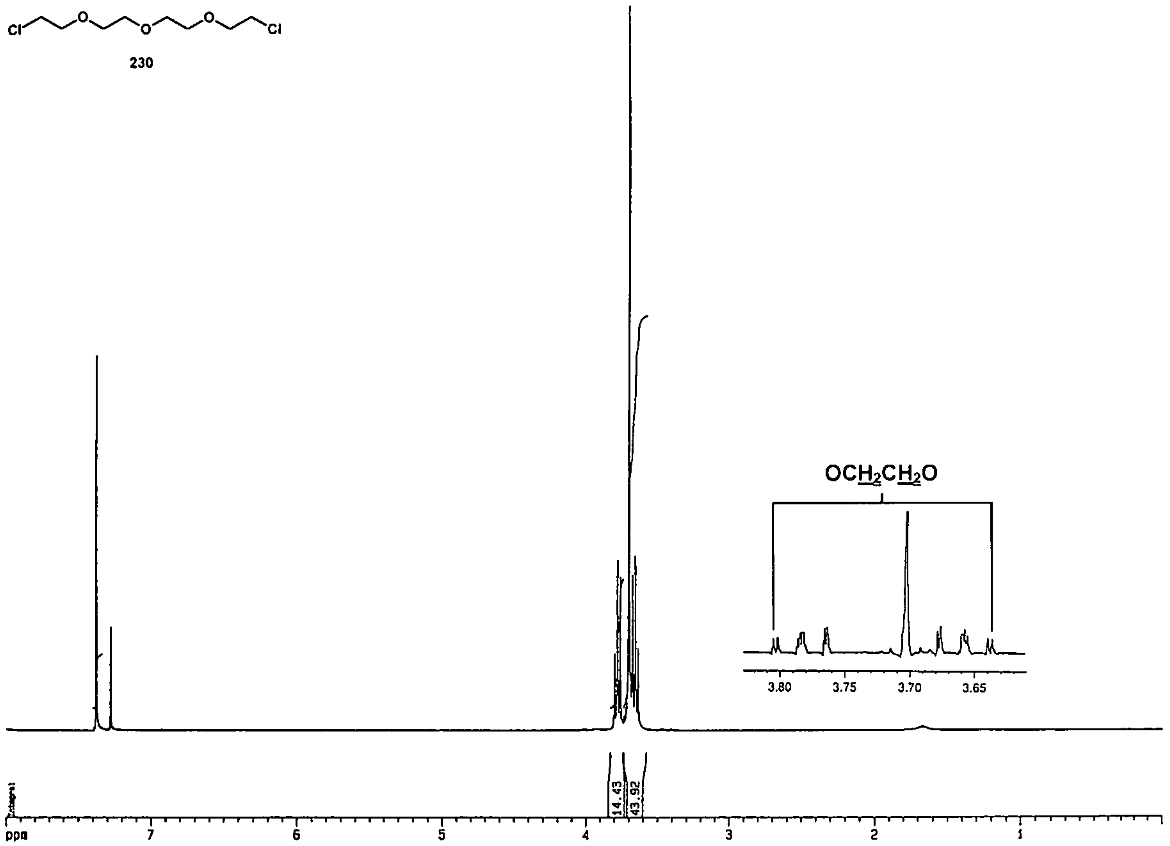

Figure 6. 1. ^{1}H NMR spectrum of 1,11-dichloro-3,6,9-trioxaundecane (230).

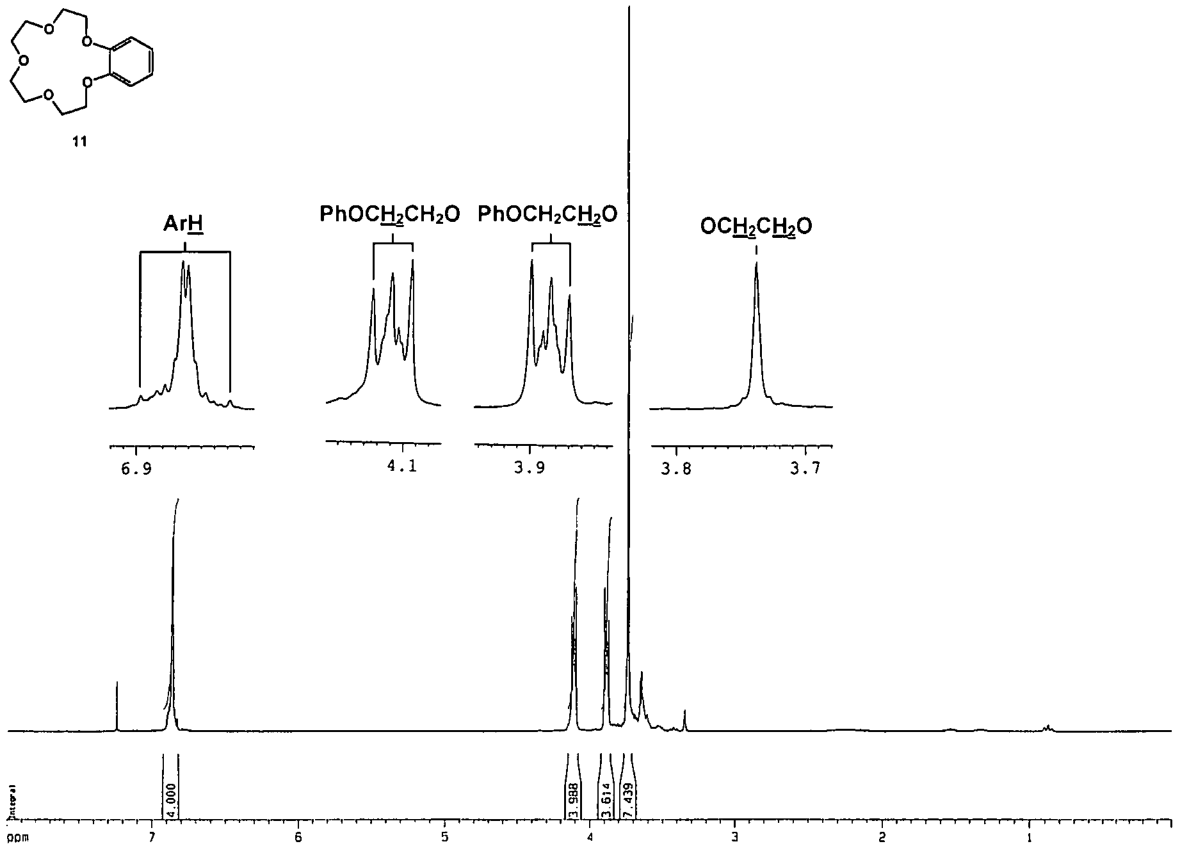

Figure 6. 2. ^{1}H NMR spectrum of benzo-15-crown-5 (11).

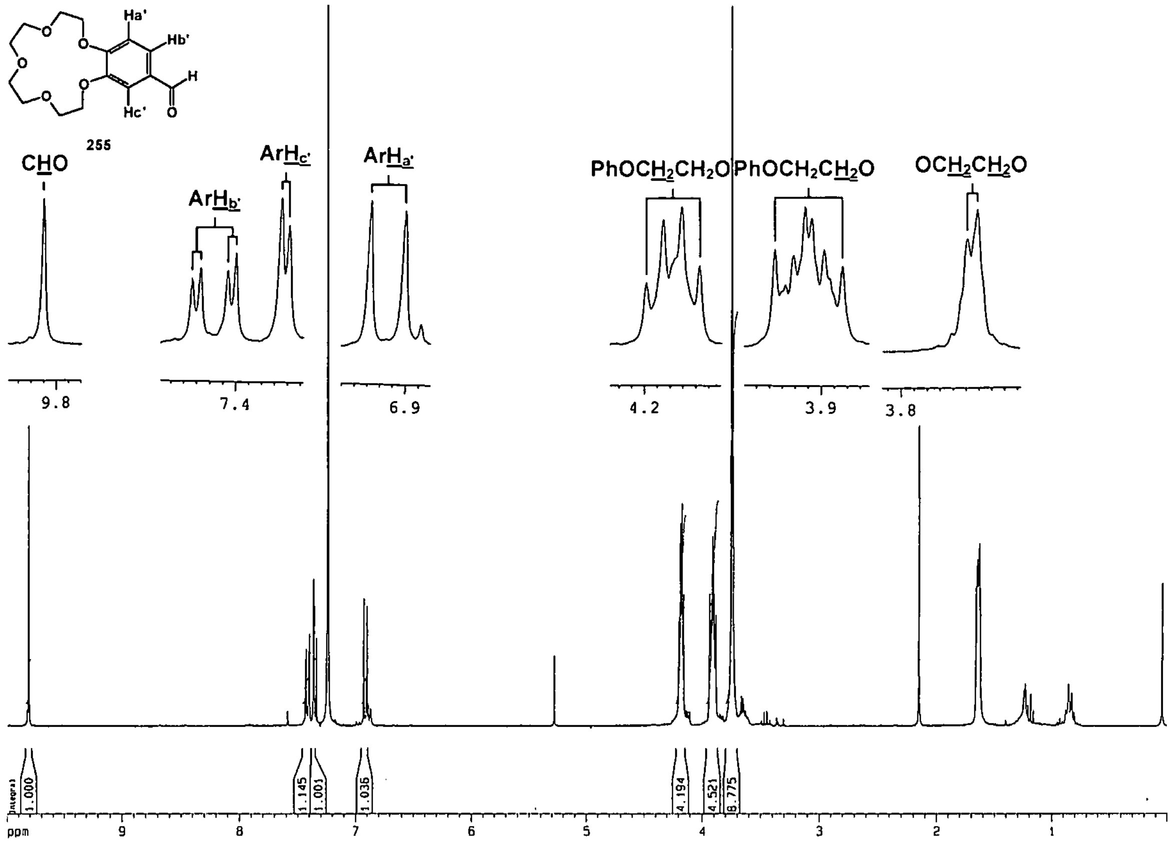

Figure 6. 3. ^{1}H NMR spectrum of 4'-formylbenzo-15-crown-5 (255).

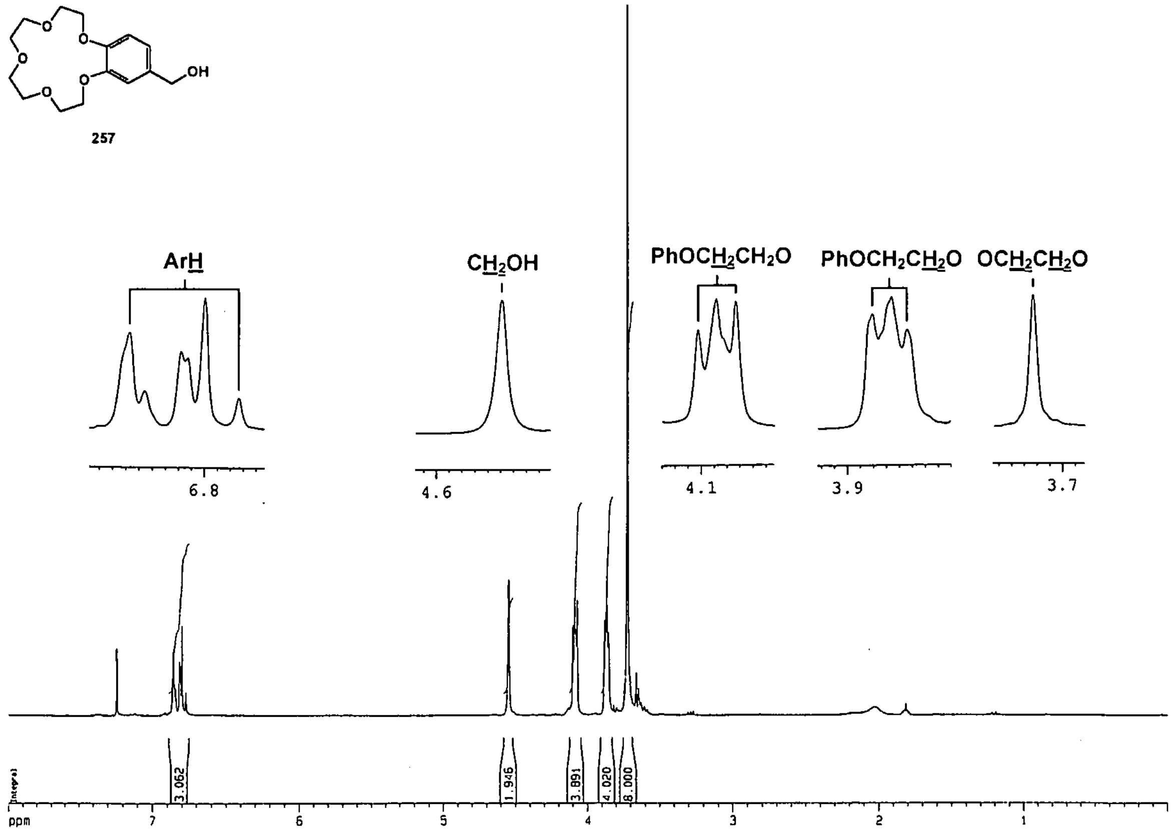

Figure 6. 4. ^{1}H NMR spectrum of 4'-(hydroxymethyl)benzo-15-crown-5 (257).

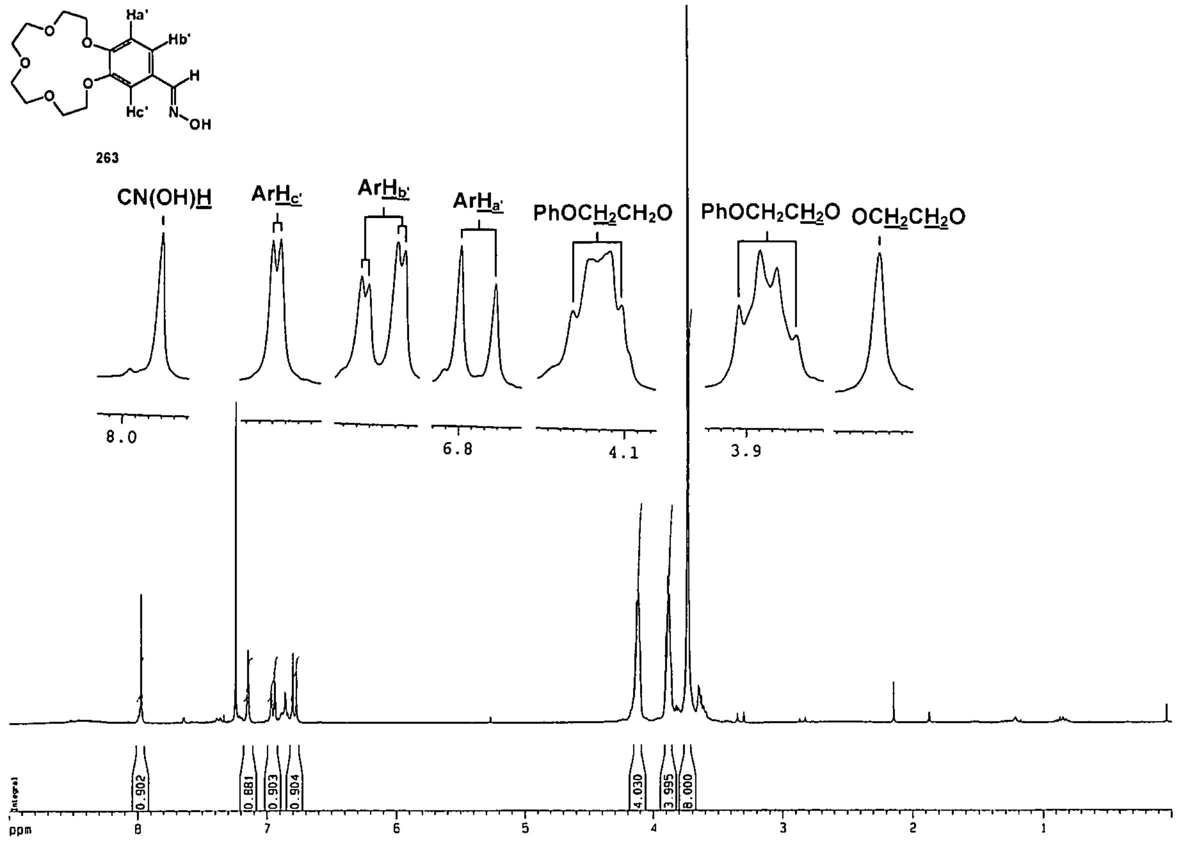

Figure 6. 5. ^{1}H NMR spectrum of 4'-(oximinomethyl)benzo-15-crown-5 (263).

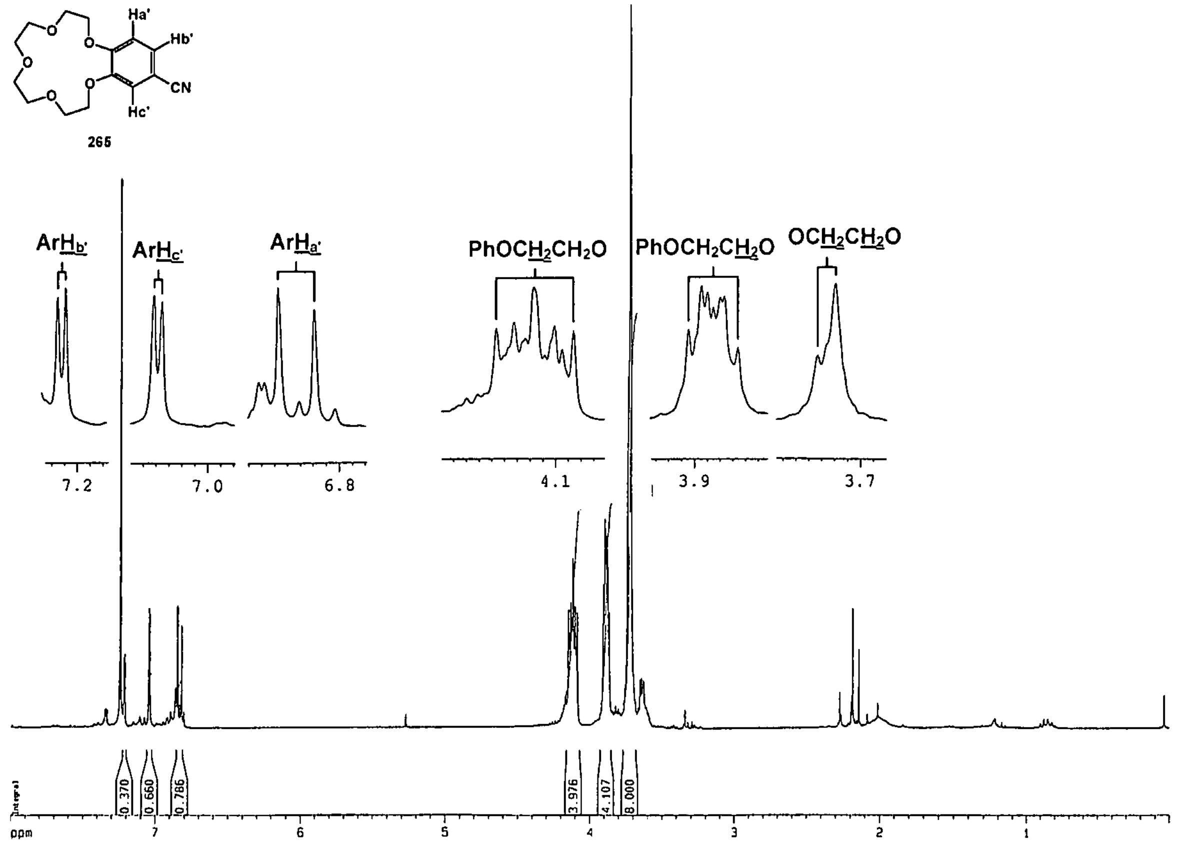

Figure 6. 6. ^{1}H NMR spectrum of 4'-cyanobenzo-15-crown-5 (265).

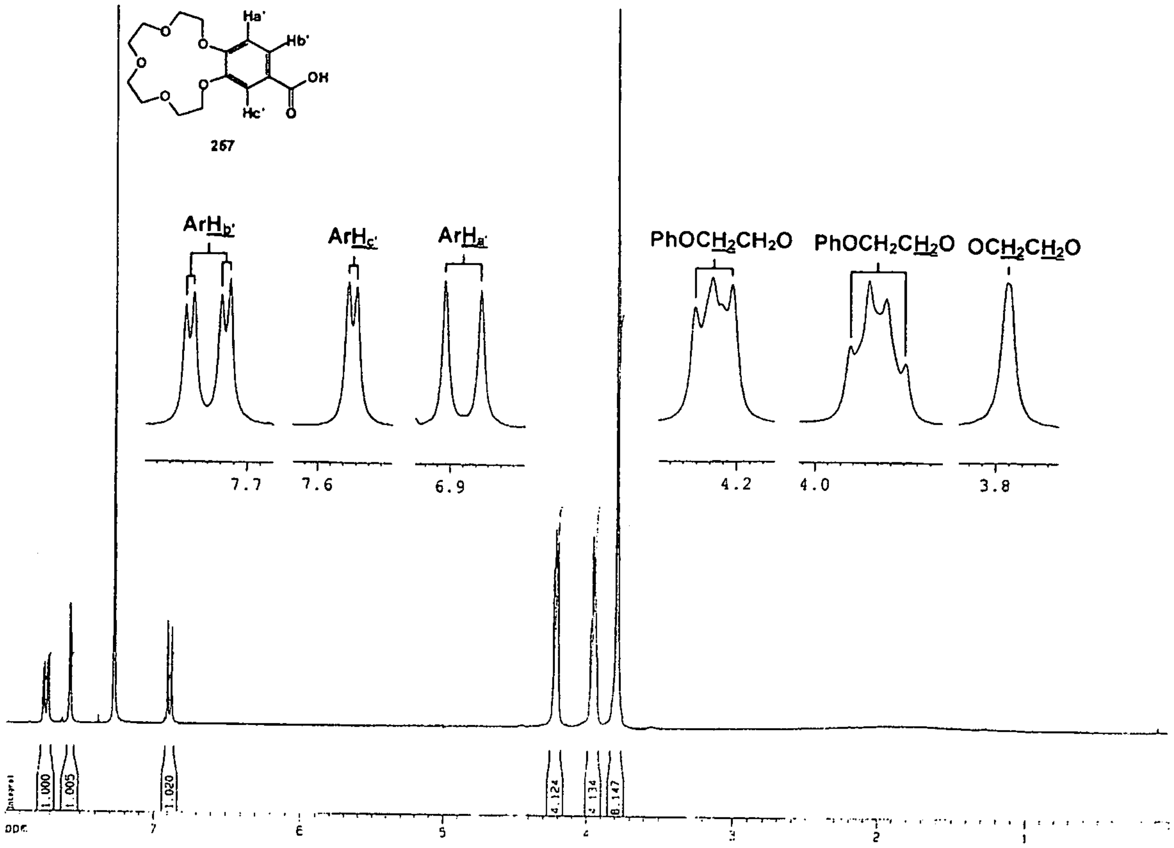

Figure 6. 7. ^{1}H NMR spectrum of 4'-carboxybenzo-15-crown-5 (258).

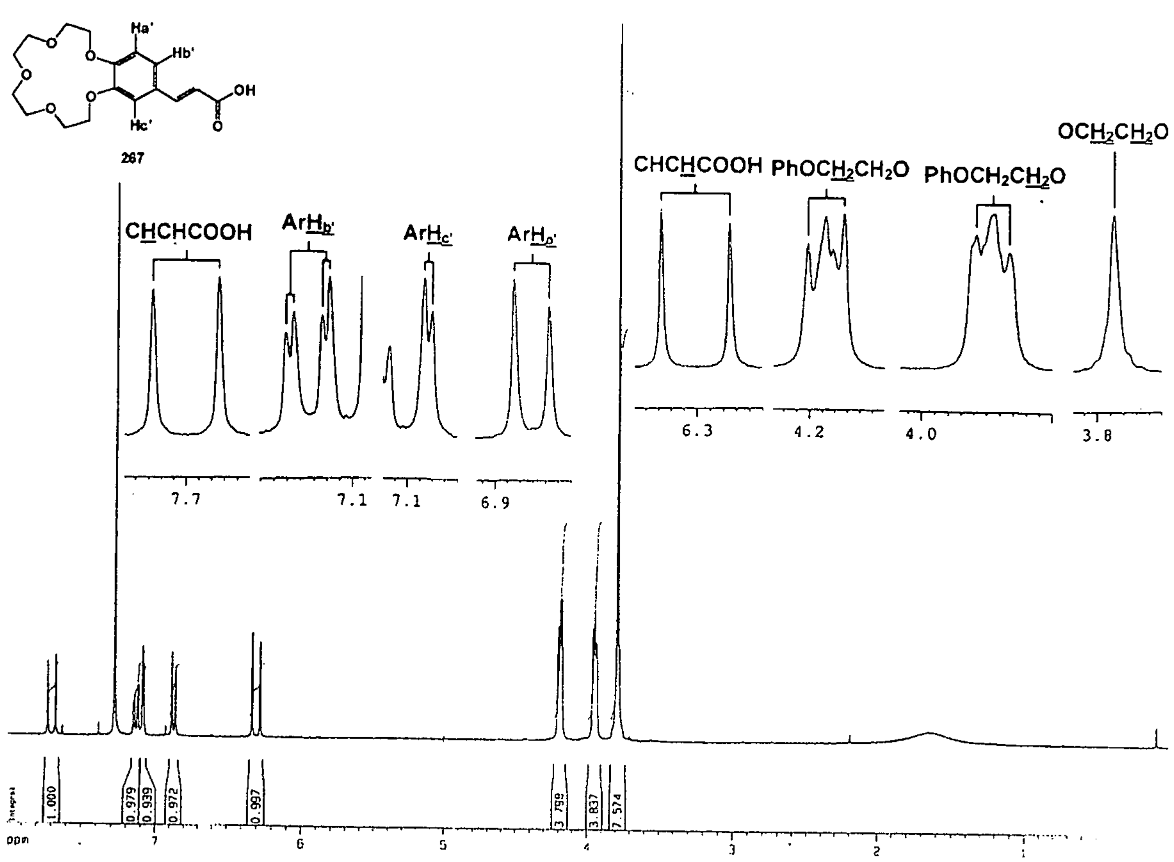

Figure 6. 8. ^{1}H NMR spectrum of 4'-(acrylic acid)benzo-15-crown-5 (267).

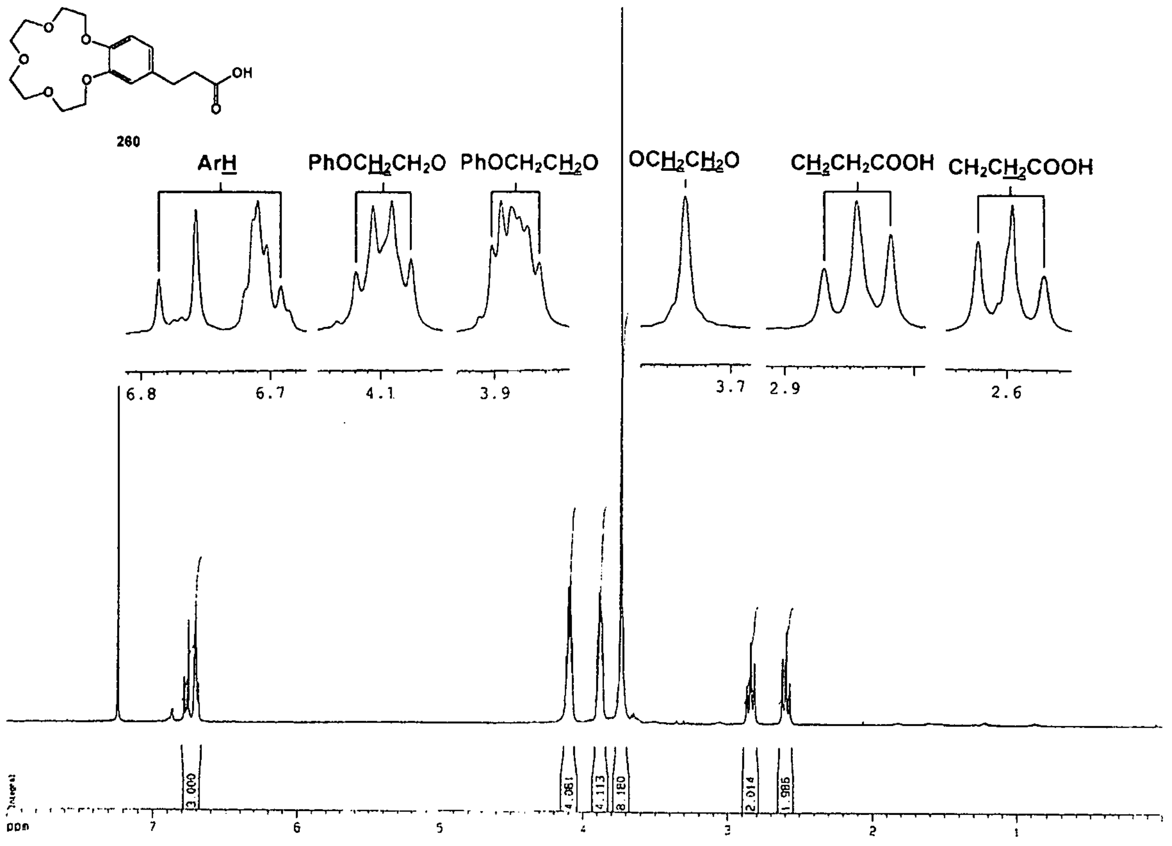

Figure 6. 9. ^{1}H NMR spectrum of 4'-(propanoic acid)benzo-15-crown-5 (260).

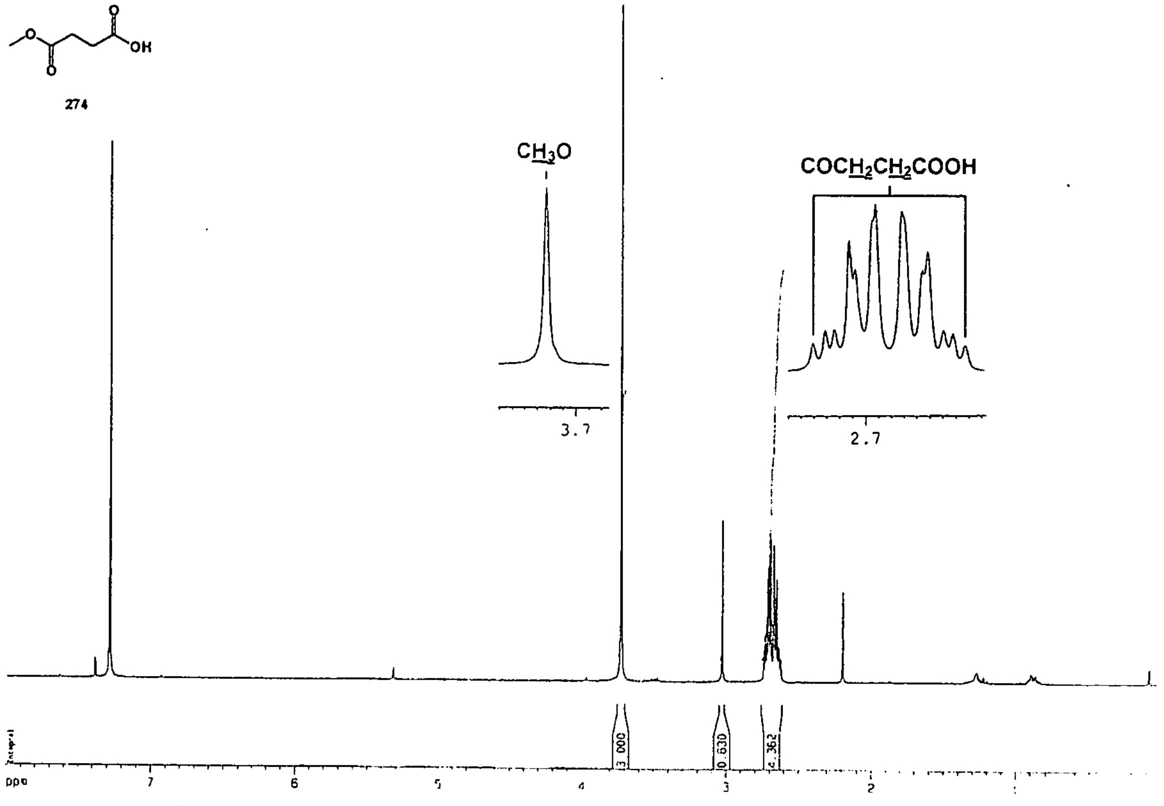

Figure 6. 10. ^{1}H NMR spectrum of methyl succinate (274).

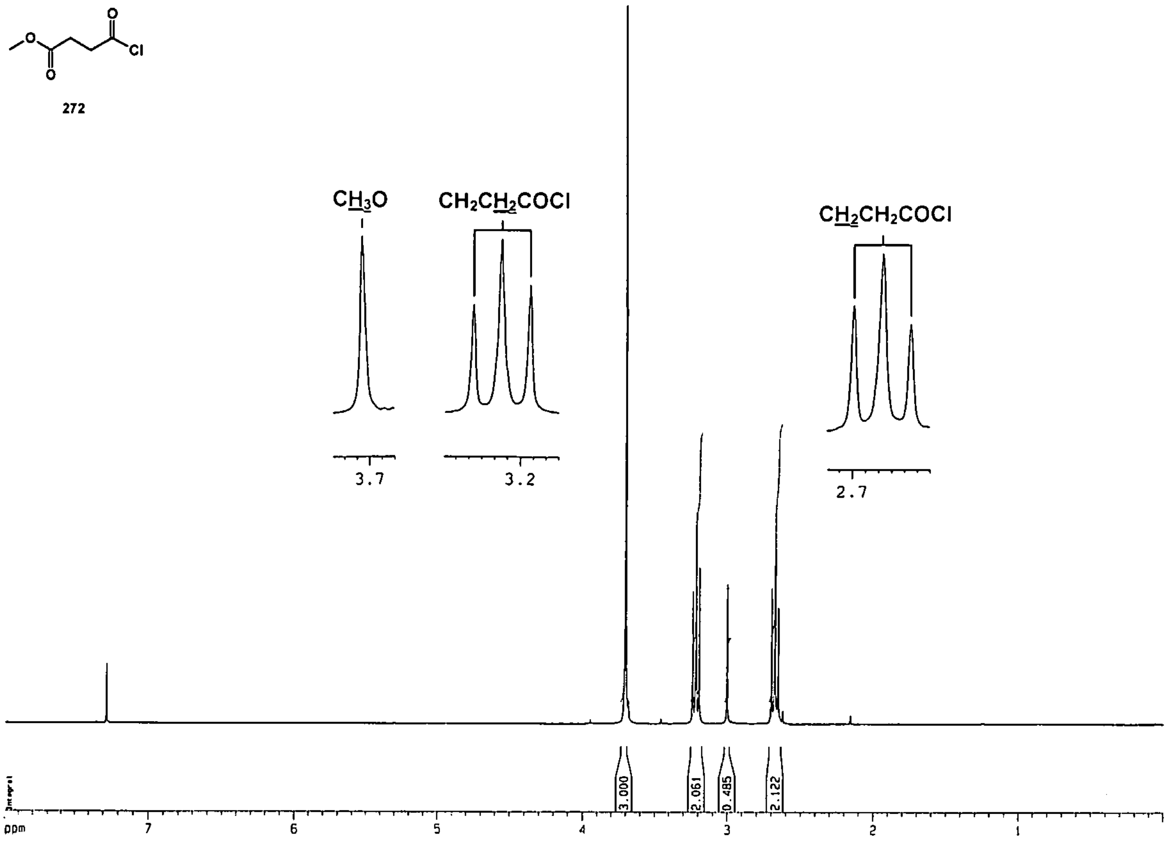

Figure 6. 11. ^{1}H NMR spectrum of methyl succinate chloride (272).

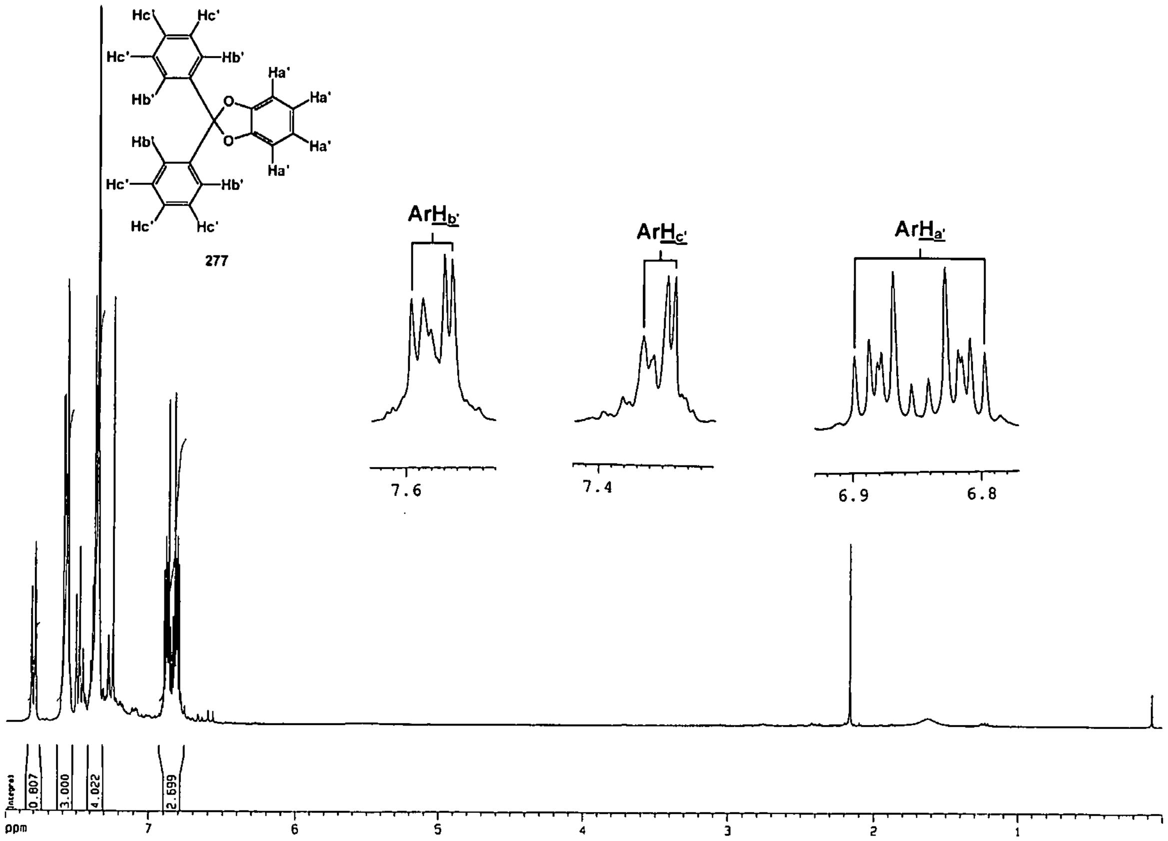

Figure 6. 12. ^{1}H NMR spectrum of the oxetane 277.

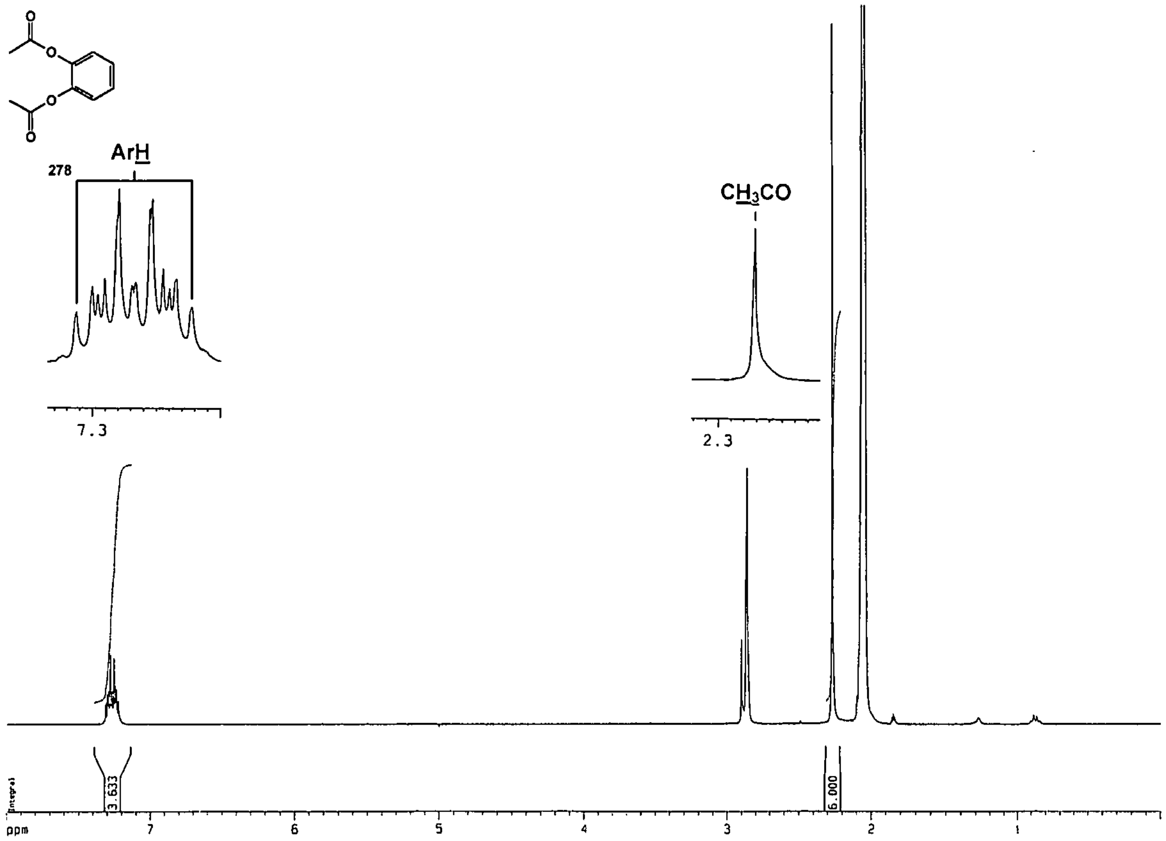

Figure 6. 13. ^{1}H NMR spectrum of the diester 278.

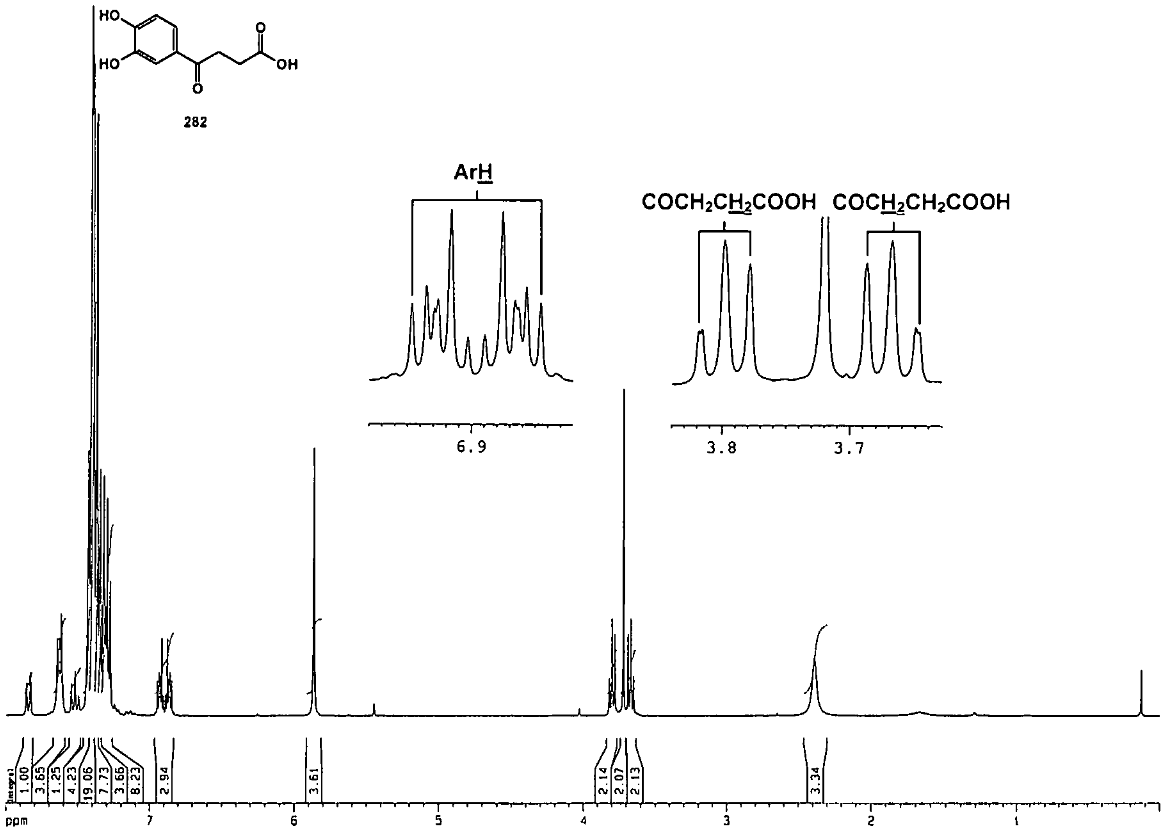

Figure 6. 14. ^{1}H NMR spectrum of compound 282.

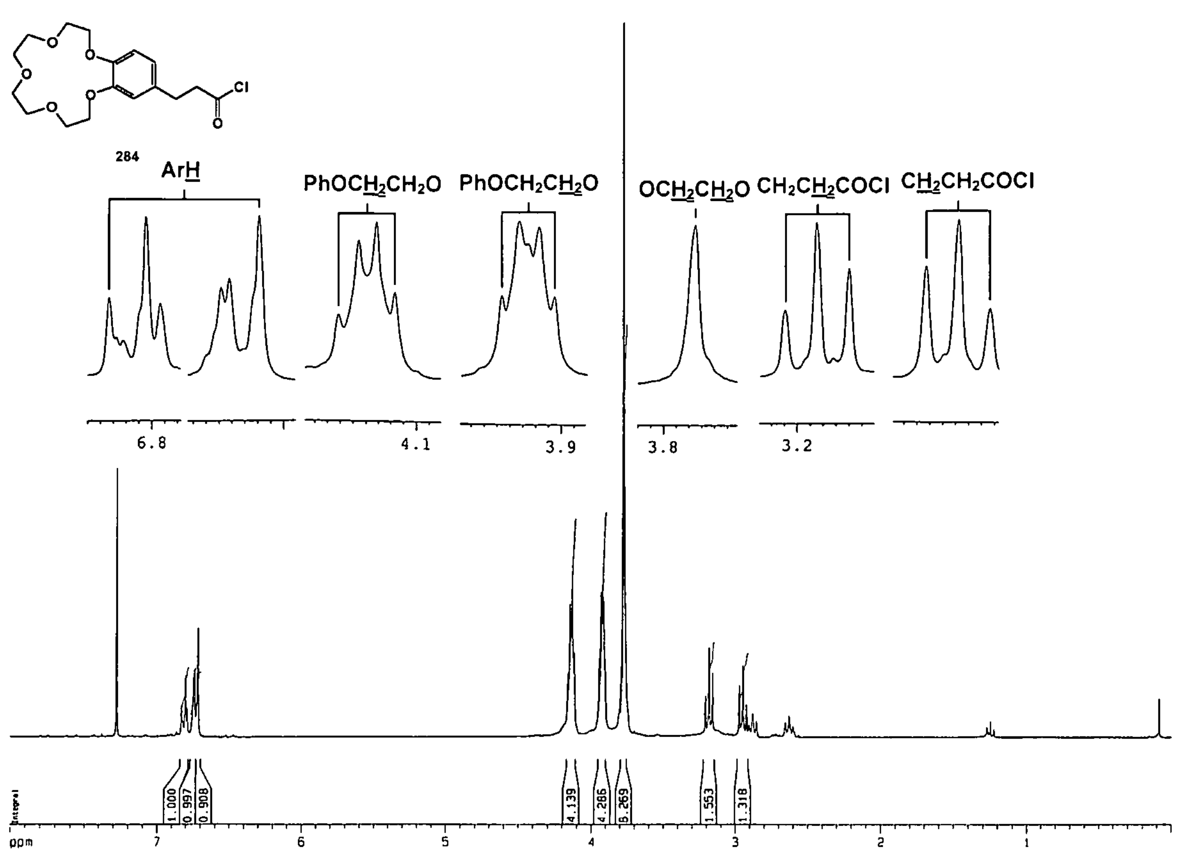

Figure 6. 15. ^{1}H NMR spectrum of 4'-(propanoyl chloride)benzo-15-crown-5 (284).

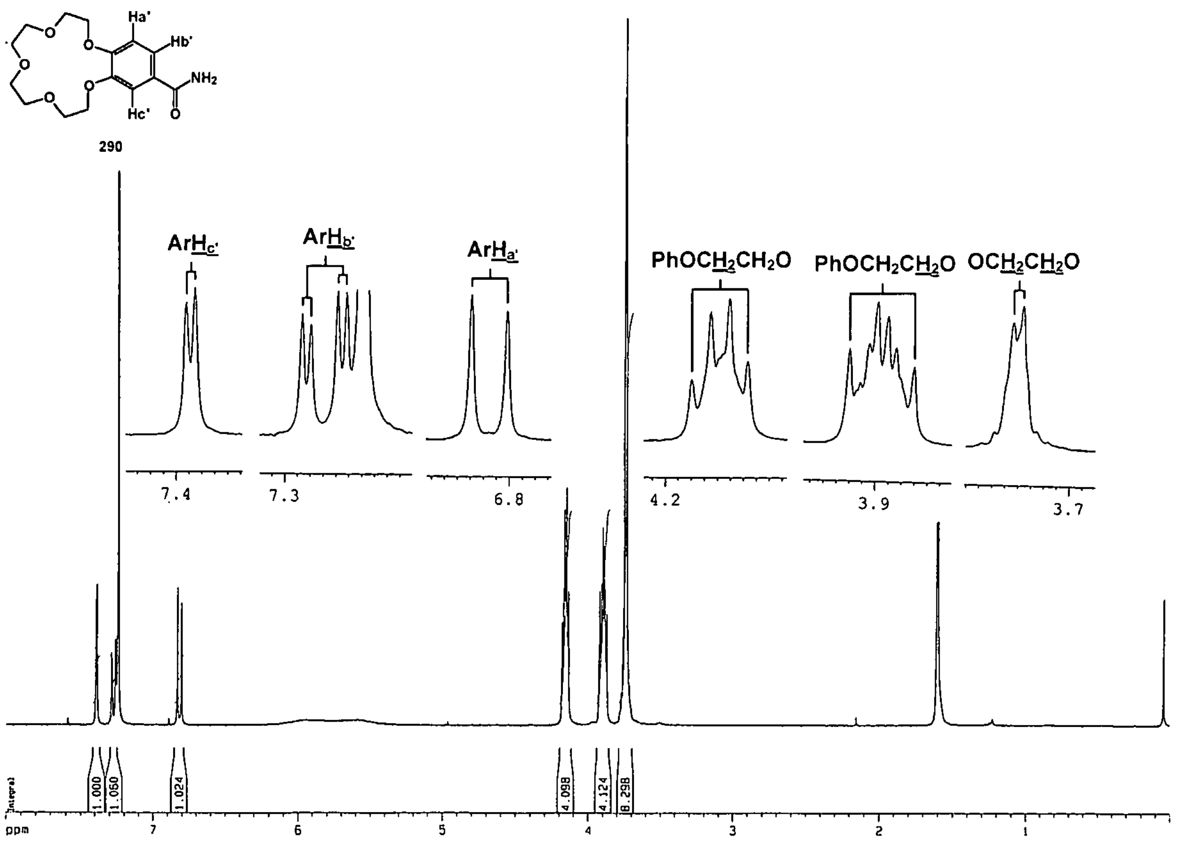

Figure 6. 16. ^{1}H NMR spectrum of 4'-amidobenzo-15-crown-5 (290).

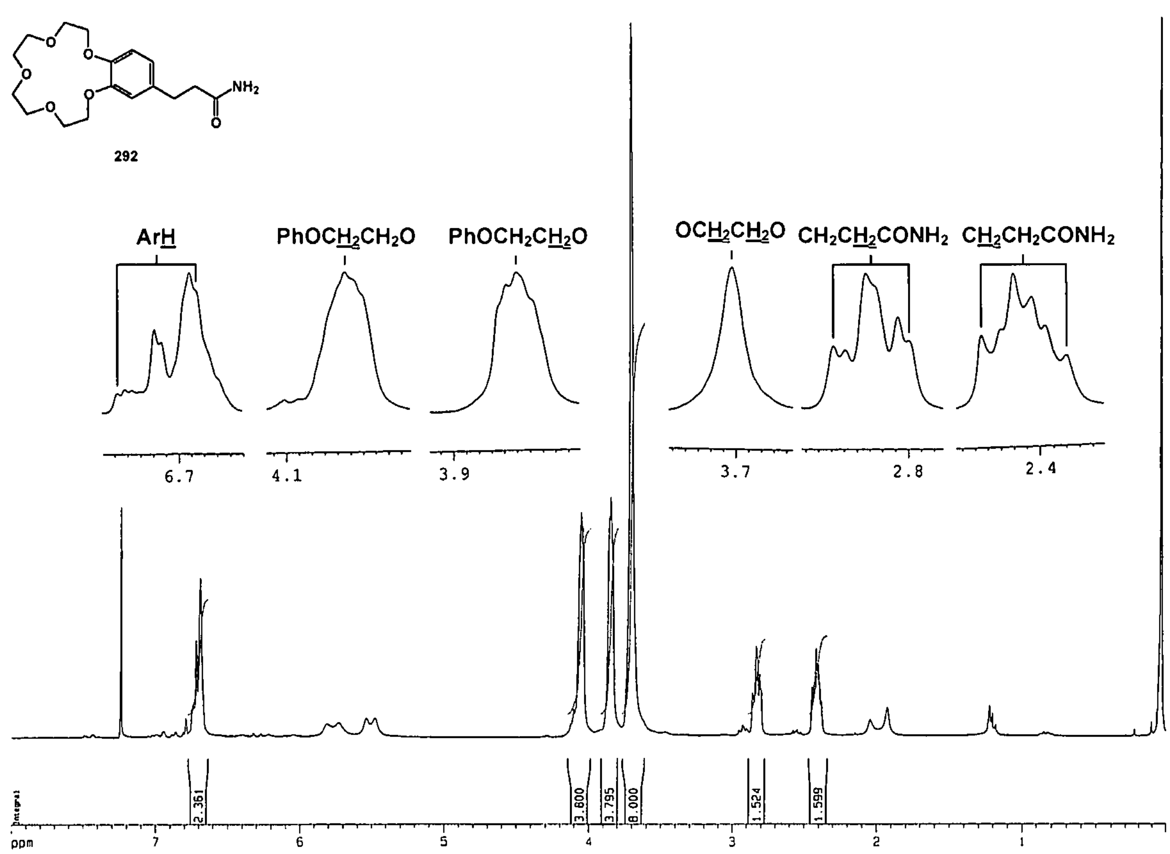

Figure 6. 17. ^{1}H NMR spectrum of 4'-(propylamide)benzo-15-crown-5 (292).

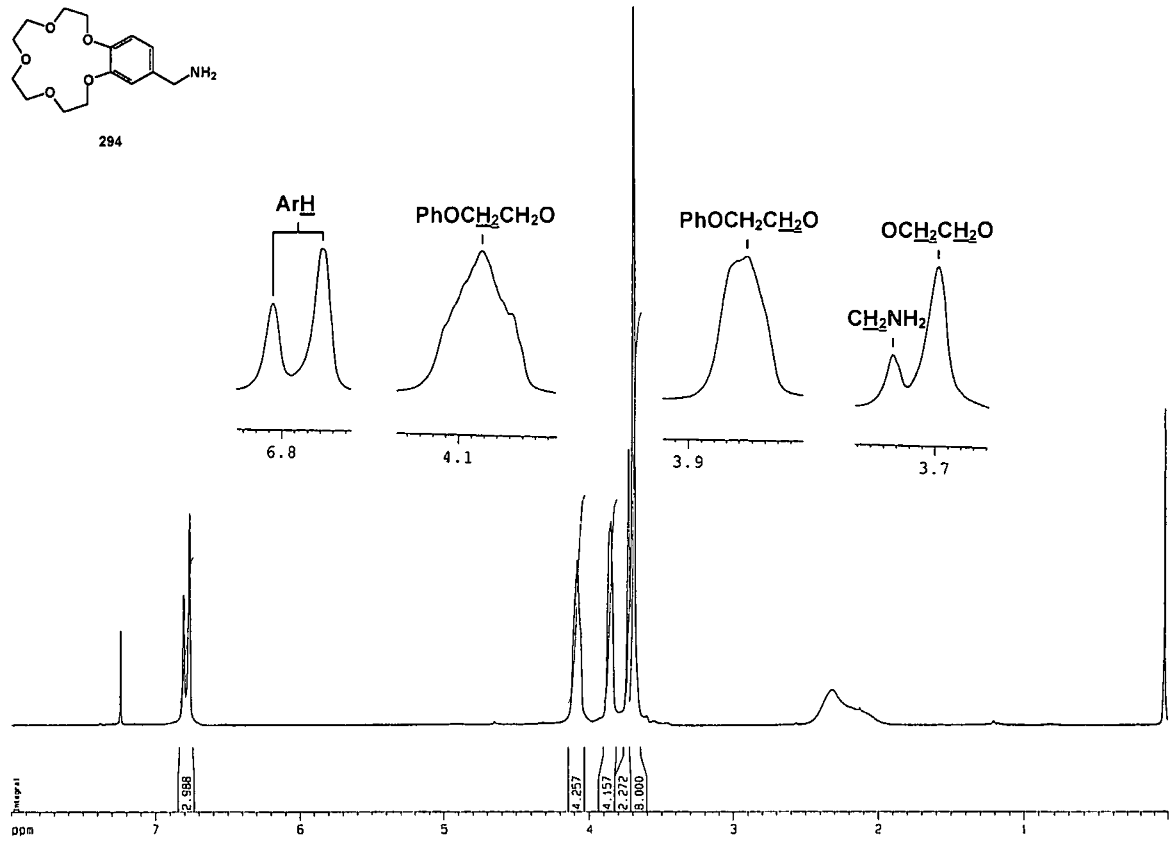

Figure 6. 18. ^{1}H NMR spectrum of 4'-(aminomethyl)benzo-15-crown-5 (294).

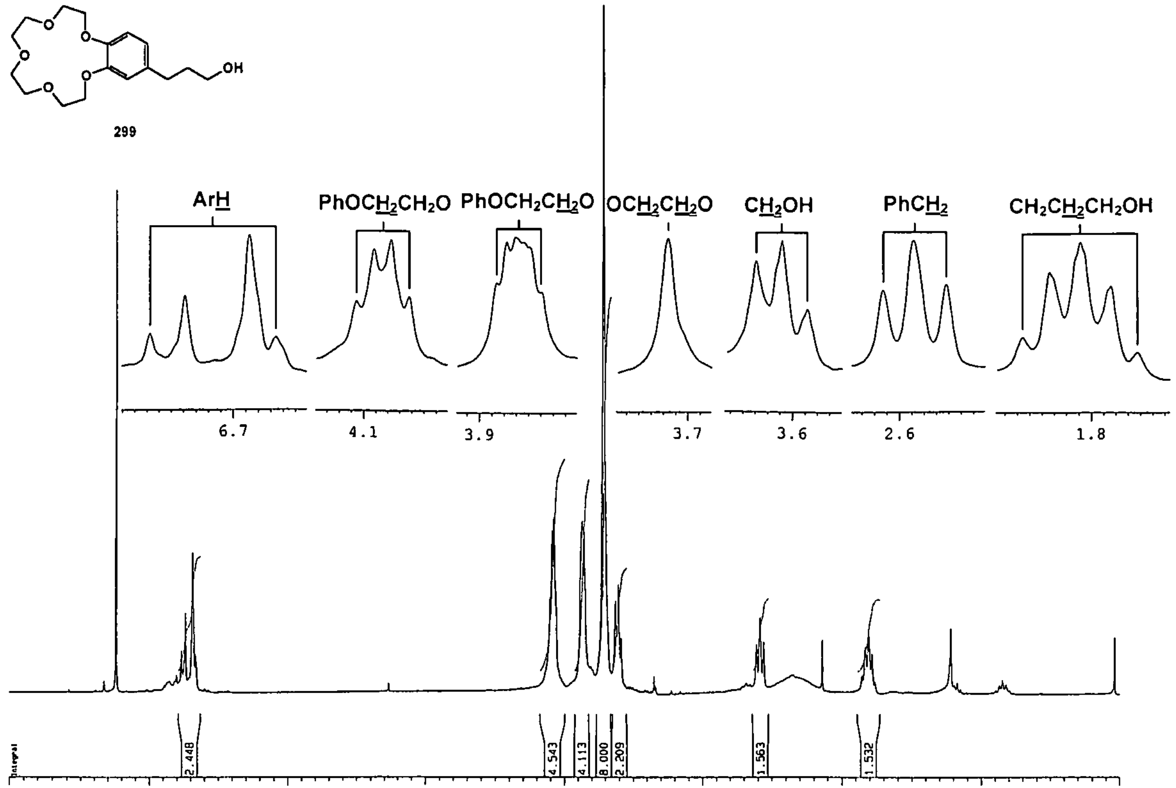

Figure 6. 19. ^{1}H NMR spectrum of 4'-(hydroxypropyl)benzo-15-crown-5 (299).

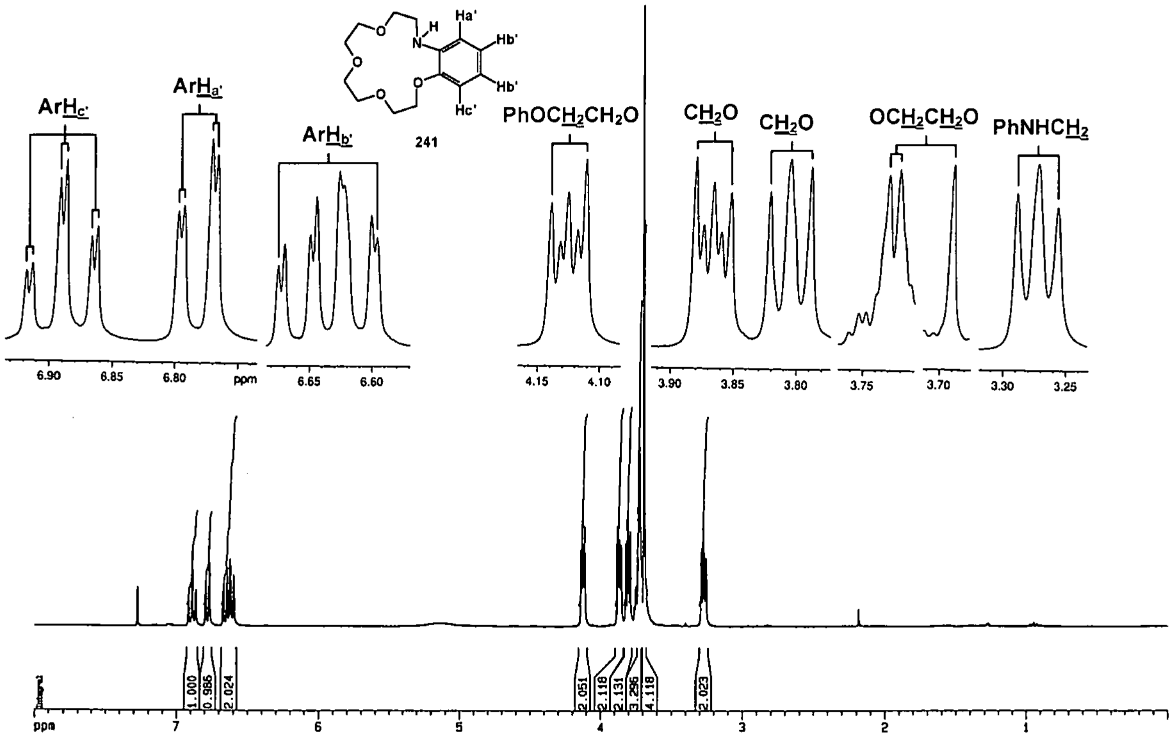

Figure 6. 20. ^{1}H NMR spectrum of benzoaza-15-crown-5 (241).

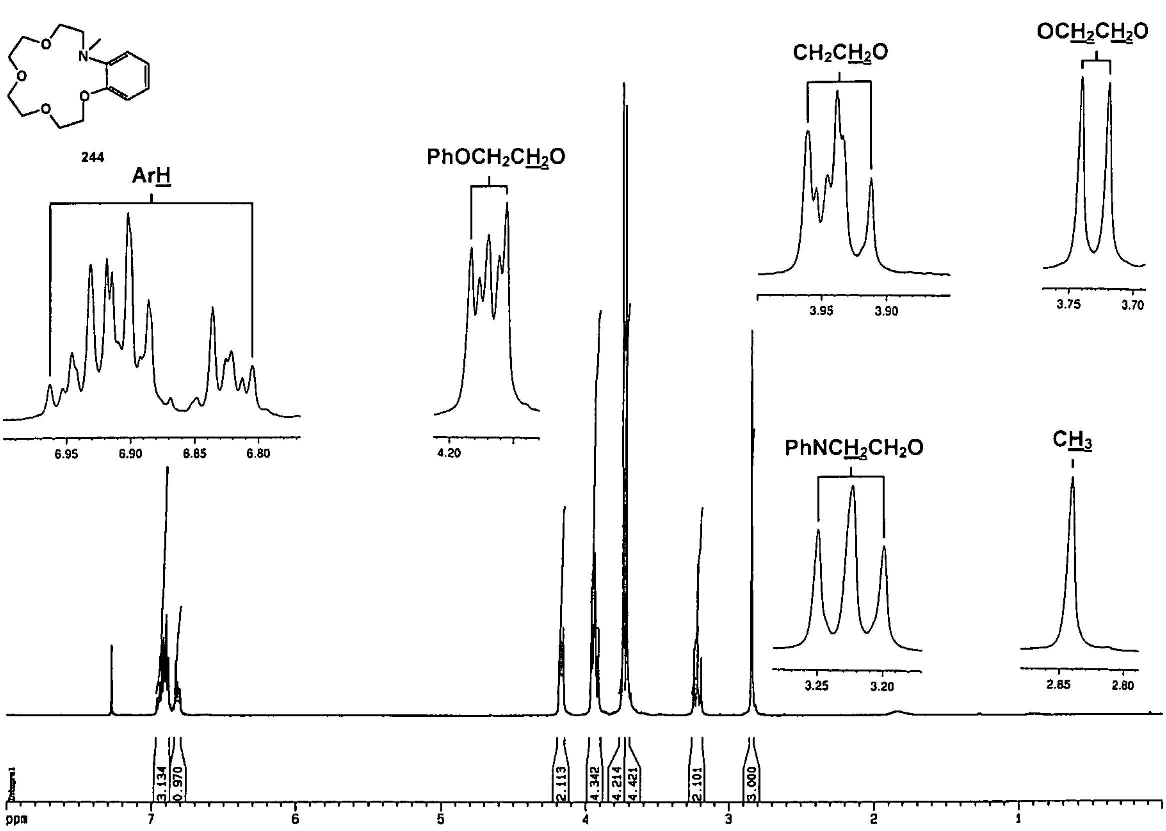

Figure 6. 21. ^{1}H NMR spectrum of *N*-methylbenzoaza-15-crown-5 (244).

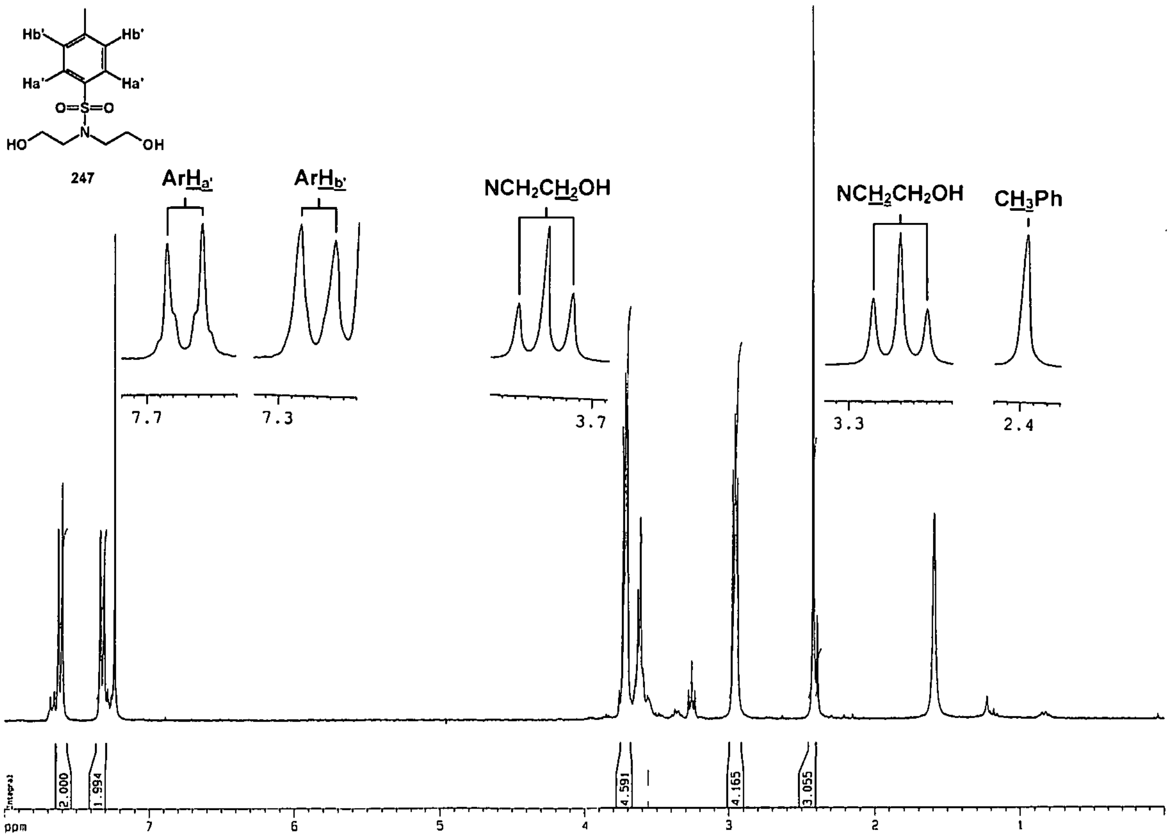

Figure 6. 22. ^{1}H NMR spectrum of *N*-*p*-tolylsulphonyldiethanolamine (247).

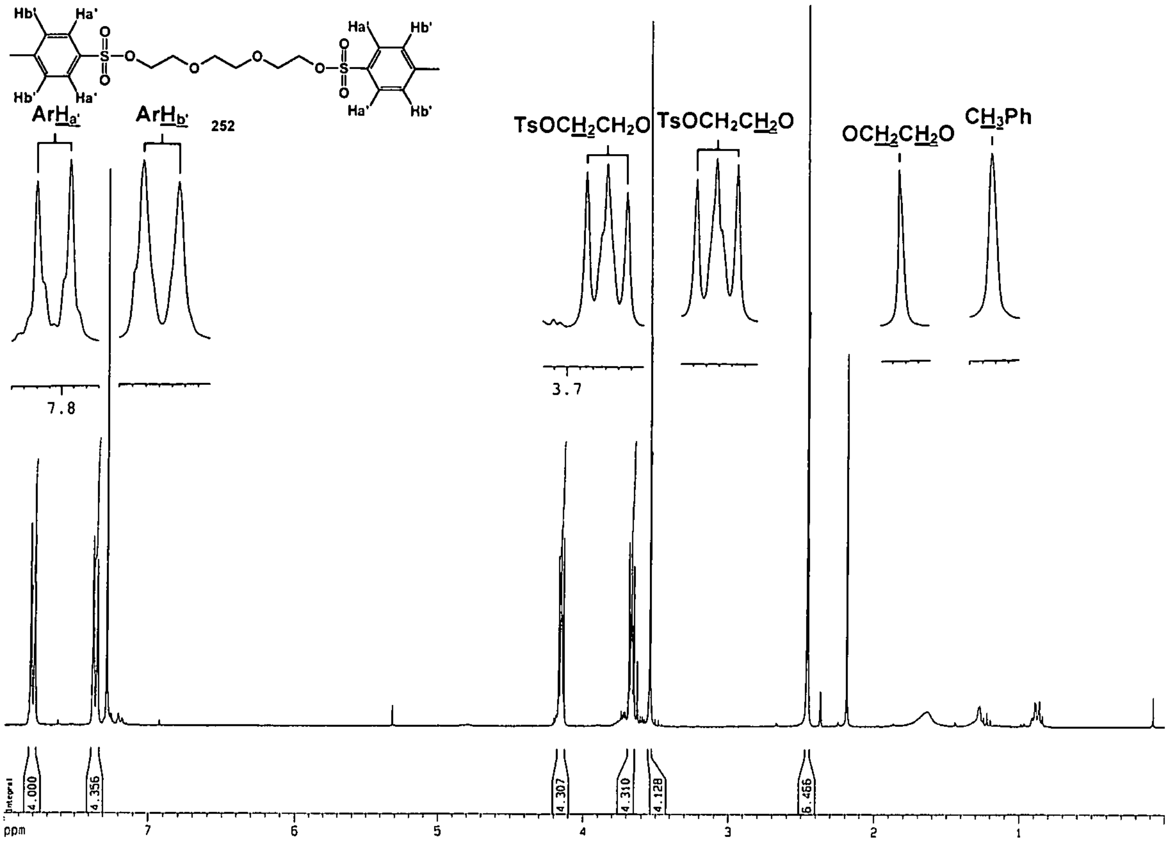

Figure 6. 23. ^{1}H NMR spectrum of triethylene glycol bis-toluene-*p*-sulphonate (252).

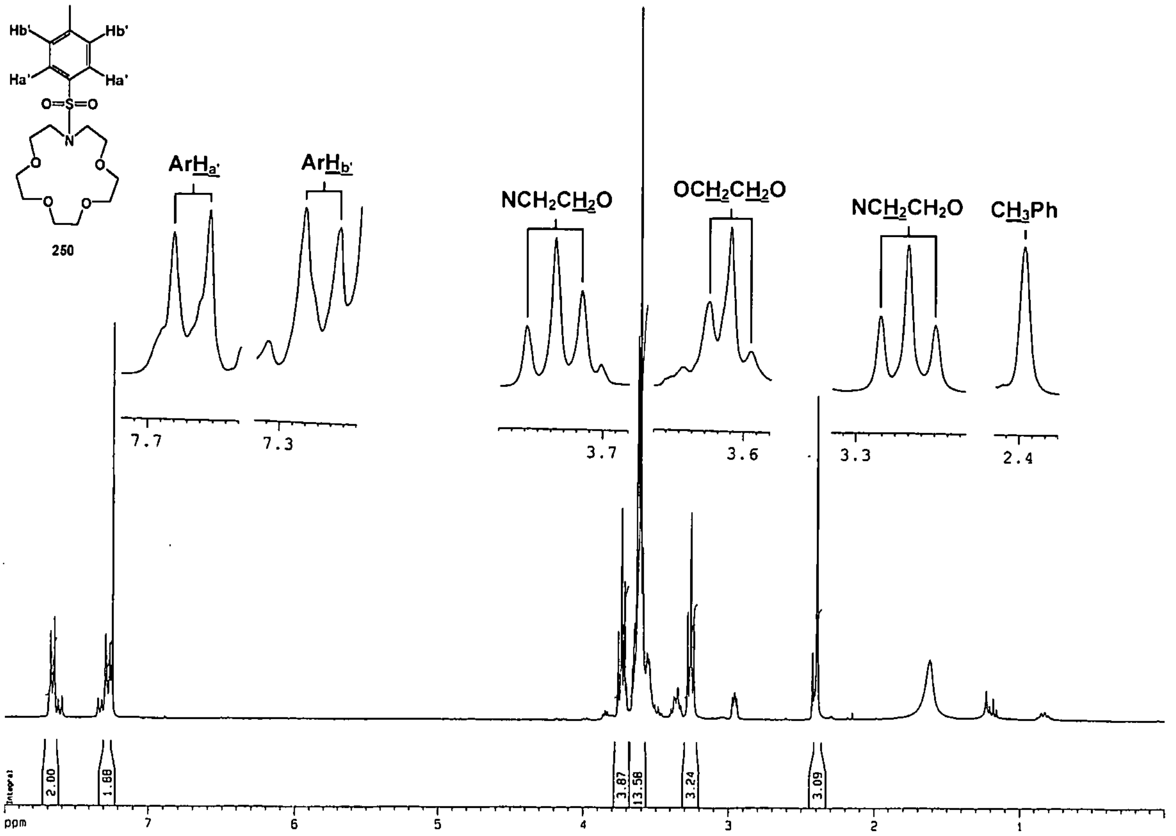

Figure 6. 24. ^{1}H NMR spectrum of *N*-tolylsulphonyl-aza-15-crown-5 (250).

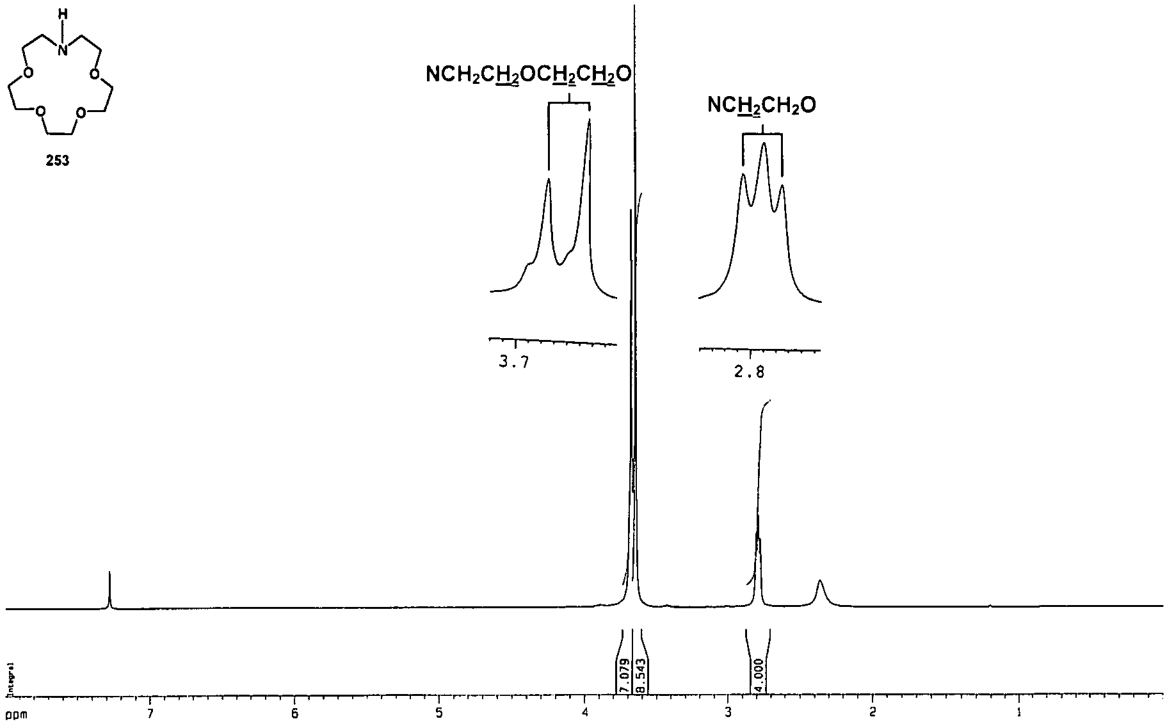

Figure 6. 25. ^{1}H NMR spectrum of aza-15-crown-5 (253).

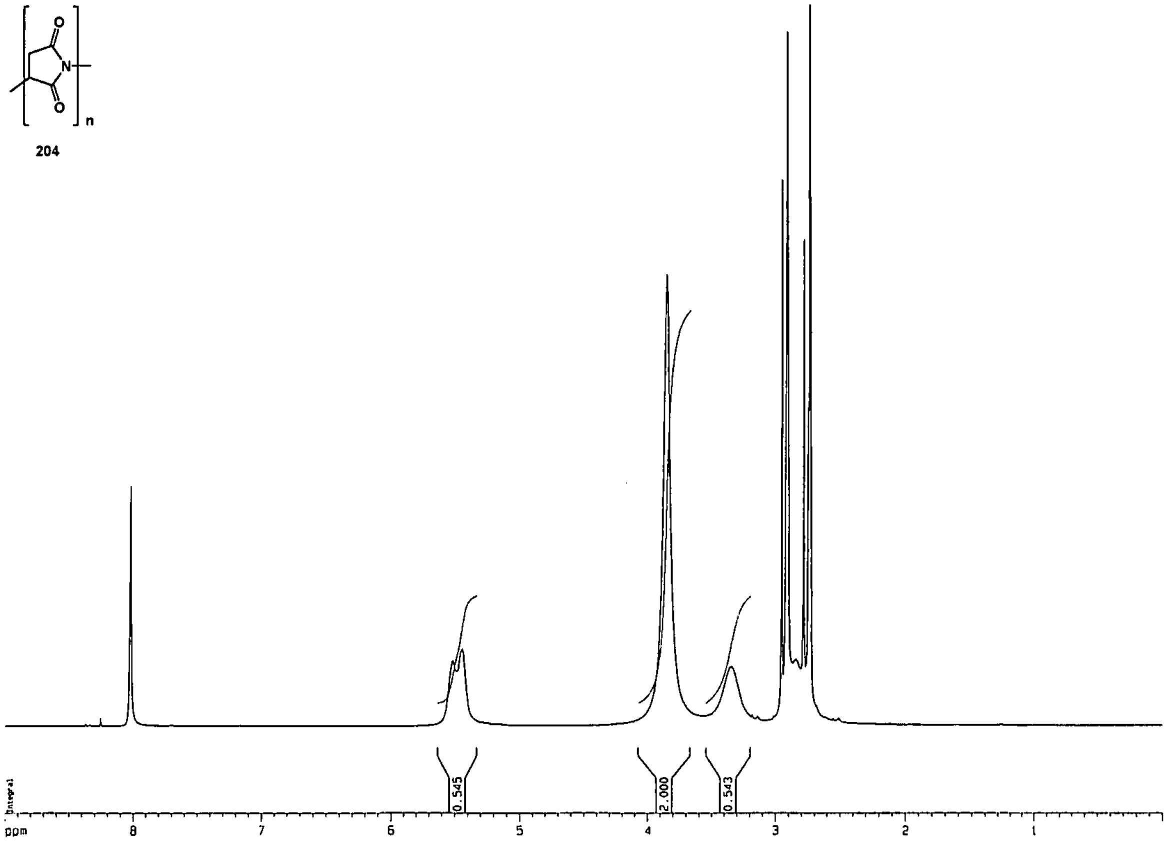

Figure 6. 26. ^{1}H NMR spectrum of polysuccinimide (204).

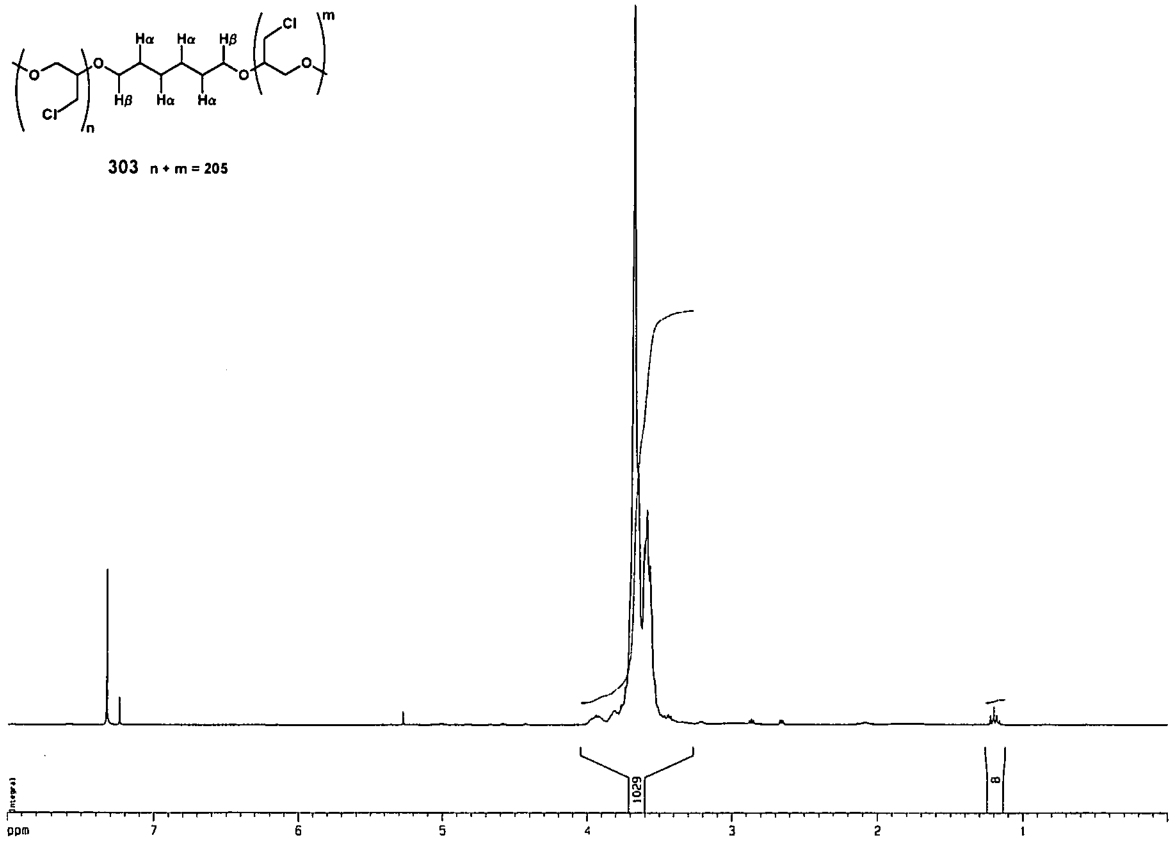

Figure 6. 27. ^{1}H NMR spectrum of polyepichlorohydrin (303).

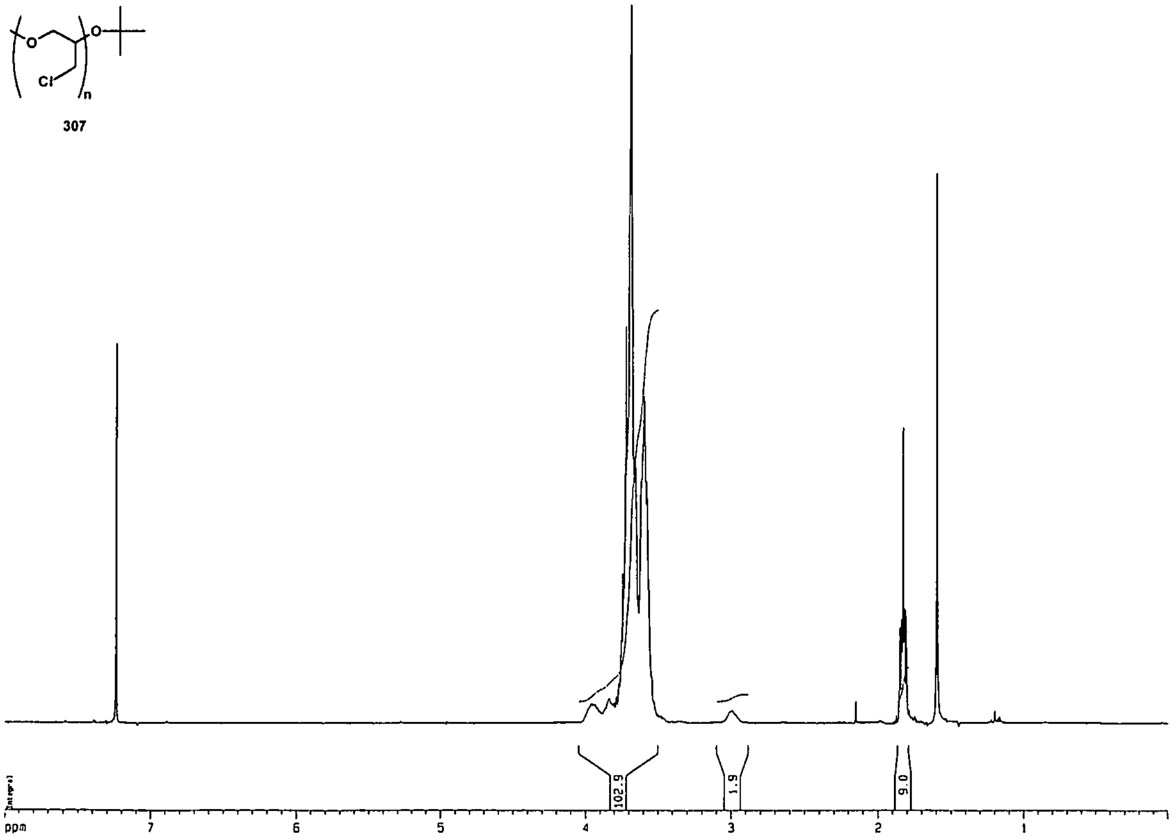

Figure 6. 28. ^{1}H NMR spectrum of polyepichlorohydrin (307).

CHAPTER 7

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