CHAPTER 1

INTRODUCTION

CHAPTER 2

LITERATURE SURVEY

CHAPTER 3

RESULTS AND DISCUSSION

CHAPTER 4

EXPERIMENTAL

CHAPTER 5

SUMMARY AND FUTURE PERSPECTIVES

APPENDIX 1

^{1}H NMR SPECTRA

APPENDIX 2

REFERENCES

SYNTHESIS AND FUNCTIONALISATION OF POLYEPICHLOROHYDRIN

Thesis submitted in fulfilment of the requirements for the degree

Magister Scientiae

in the
Faculty of Natural and Agricultural Sciences
Department of Chemistry
University of the Free State
by

Thebe Phillip Mokone

Supervisor: Prof. J. C. Swarts

December 2004

IN MEMORY OF MY FATHER

ACKNOWLEDGEMENTS

I would like to extent my sincere gratitude towards the following people who all contributed directly or indirectly to the preparation of this thesis.

God Almighty for His guidance and grace that carried me through the course of this study.

Prof. J. C. Swarts at the University of the Free State, as my supervisor for his leadership during this study, his willingness to share his expertise with me and the example he set me in scientific thinking. I especially appreciate his patience.

Collectively, all my fellow post-graduate colleagues for all their discussions on Chemistry and helpful advise in experimental techniques.

Mr. P. T. N. Nonjola, Ms. E. Erasmus and Mr. K. C. Kemp for the many NMR spectra they drew for me, Mr. K. von Eschewege for the Afrikaans translations he helped me with and Mrs. T. Swarts for always being there when I needed help.

My mother Akidi and father Tshiso, for all their love, patience, understanding and support.
My sisters and friends for all their love and support.

Lastly, I wish to thank the NRF for their financial support which made this study possible.

ABSTRACT

During this study, benzo-15-crown-5 was synthesised as sodium cation scavenging ligand. This crown ether moiety was then functionalised to 4'-formylbenzo-15-crown-5 and 4'-(hydroxymethyl)benzo-15-crown-5. The first synthesis of ferrocyl isocyanate is reported. The reaction between this compound and 4'-(hydroxymethyl)benzo-15-crown-5 provided a novel new benzo-15-crown-5 / ferrocene conjugate that is linked by a urethane bond.

Epichlorohydrin was polymerised to polyepichlorohydrin derivatives having molar masses of 2 000 and 20 000 g mol^{-1} following a cationic ring-opening process and utilising a BF_3 / phenol initiator system. The chloro-containing alkyl side chains of polyepichlorohydrin were then re-functionalised to $-N_3$, $-NH_2$, -NCO and -OH functional groups.

The reactivity of the $-NH_2$, -NCO and -OH functional groups on these polymers was tested through various model reactions. These included anchoring of the carboxylic acid-containing ferrocene series, Fc-$(CH_2)_n$COOH with n = 0 – 3, onto the amine-functionalised polymer under the influence of the coupling reagent *O*-benzotriazolyl-*N*,*N*,*N'*,*N'*-tetramethyluronium hexafluorophosphate. The four newly obtained polymer-bound ferrocene derivatives may have appreciable anticancer activity.

Through the course of this study eleven hitherto unknown compounds were synthesised for the first time. These include three highly reactive polymeric derivatives of polyepichlorohydrin, five polymer-bound ferrocene derivatives, a polymer-bound phenyl derivative, ferrocyl isocyanate and a ferrocene-crown ether conjugate.

Keywords: benzo-15-crown-5, alcohol, aldehyde, polyepichlorohydrin, azide, amine, isocyanate, hydroxy, ferrocene

OPSOMMING

Gedurende hierdie ondersoek is benso-15-kroon-5 gesintetiseer as natrium-ioon-soekende ligand, en gefunksionaliseer tot 4'-formielbenso-15-kroon-5 en 4'-(hidroksiemetiel)benso-15-kroon-5. Die eerste sintese van ferrosielisosianaat is gerapporteer. Die reaksie tussen ferrosielisosianaat en 4'-(hidroksiemetiel)benso-15-kroon-5 het tot 'n nuwe benso-15-kroon-5 / ferroseen konjugaat wat deur middel van 'n uretaan binding geheg is gelei.

Deur van die BF_3 / fenol inisiëerder sisteem en 'n kationiese ring-ontsluitingproses gebruik te maak, is epichlorohidrien gepolimeriseer tot poliepichlorohidrien derivate met molêre massas van 2 000 en 20 000 g mol^{-1}. Die chloorbevattende alkiel sykettings van poliepichlorohidrien was daarna geherfunksionaliseer om $-N_3$, $-NH_2$, -NCO and -OH funksionele groepe te bevat.

Die reaktiwiteit van die $-NH_2$, -NCO en -OH funksionele groepe in die polimeer was deur verskeie modelreaksies getoets. Dit het die ankering van die karboksielsuurbevattende ferroseen reeks, $Fc\text{-}(CH_2)_nCOOH$ met $n = 0 - 3$, op die amien-gefunksionaliseerde polimeer onder die invloed van die koppelingsreagens, *O*-bensotriasoliel-N,N,N',N'-tetrametieluronium heksafluorofosfaat ingesluit. Die vier nuut-gesintetiseerde polimeergebonde ferroseen derivate mag 'n betekenisvolle mate van anti-kanker aktiwiteit toon.

Tydens die verloop van hierdie projek is elf onbekende verbindings vir die eerste keer gesintetiseer. Dit sluit in drie hoogs reaktiewe polimeriese derivate van poliepichlorohidrien, vyf polimeergebonde ferroseen derivate, 'n polimeergebonde feniel derivaat, ferrosielisosianaat en 'n ferroseen-kroon eter konjugaat.

Sleutel woorde: benso-15-kroon-5, alkohol, aldehied, poliepichlorohidrien, asied, amien, isosianiaat, hidroksie, ferroseen.

TABLE OF CONTENTS

CHAPTER 1

CHAPTER 2

CHAPTER 5

APPENDIX 1

APPENDIX 2

LIST OF FIGURES

p.

CHAPTER 1

CHAPTER 2

CHAPTER 3

LIST OF SCHEMES

p.

CHAPTER 2

CHAPTER 3

LIST OF TABLES

p.

CHAPTER 3

The following abbreviations were used throughout this thesis:

PECH	polyepichlorohydrin
GAP	poly(glycidyl azide)
polyGLYN	poly(glycidyl nitrate)
NaN_3	sodium azide
$LiAlH_4$	lithium aluminium hydride
BER	borohydride exchange resin
BH_4^-	borohydride anion
THF	tetrahydrofuran
DMF	*N*,*N*-dimethylformamide
DMSO	dimethyl sulphoxide
$MgSO_4$	magnesium sulphate
Pd	palladium
KNCO	potassium isocyanate
AgNCO	silver isocyanate
K_2CO_3	potassium carbonate
$Ni(OAc)_2.4H_2O$	nickel acetate tetrahydrate
cm^{-1}	wavenumber
IR	infrared
NMR	nuclear magnetic resonance
m.p.	melting point
ppm	parts per million

Although water is one of the most widely occurring substances on earth, only 2.53 percent is fresh water while the remainder is salt water. Some two thirds of this fresh water is locked up in glaciers and permanent snow cover,[1] and almost all or the rest exist in the form of soil humidity or in water tables that are too deep to be tapped. According to United Nations Educational, Scientific and Cultural Organization (UNESCO),[1] fresh water supplies are falling while the demand for fresh water is dramatically growing at an unsustainable rate. The decline in fresh water quality is mainly due to untreated sewerage, chemical waste, fuel leakage, dumped garbage, and the contamination of soil by chemicals used by farmers. Industrial processes frequently generate large volumes of contaminated wastewater.

The existing methods that are employed for the purification of wastewater, such as ion exchange, evaporation and reverse osmosis, are expensive or time consuming and do not remove contaminants from the total volume of industry-generated wastewater effluents. These traditional purification processes operate by concentrating the contaminants from the bulk of the polluted water (the entire volume) into a much smaller volume fraction, thereby creating concentrated solutions of salts, or “brines”, 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 practice creates unforeseen problems. If, for any reason, the sludge dams holding these brines leak into underground water storage sites, contamination of these reservoirs takes place and the water becomes unfit for supporting life. As the total volume of these brines becomes larger, the need to clean them becomes more essential.

To circumvent this undesirable and tragic state of affairs, a new method of cleaning up brines to achieve purification of the *total* volume of wastewater effluents generated by industrial processes, is needed. Towards this end a new technique for water purification was patented recently by this laboratory.[2] This technique make use of an insoluble elastomeric solid support with metal cation scavenging ligands, anchored onto its surface *via* water-soluble polymeric spacers. The patent describes especially 15-crown-5 derivatives as ligands which are selective in binding Na^+ ions. The water-soluble spacers attached to the solid support make use of dendrimer technology applied to polymers to anchor huge amounts of metal cation-scavenging ligands onto it. Use of an insoluble elastomeric solid support allows for easy recovery of the metal ion trapping device, while the water-soluble spacer/ligand system allows for optimum interaction with dissolved metal ions. This set of circumstances enhance fast and effective binding between the metal ion scavenging device and contaminating metal ions found in industrial wastewater. Figure 1.1 shows a section of such a device.

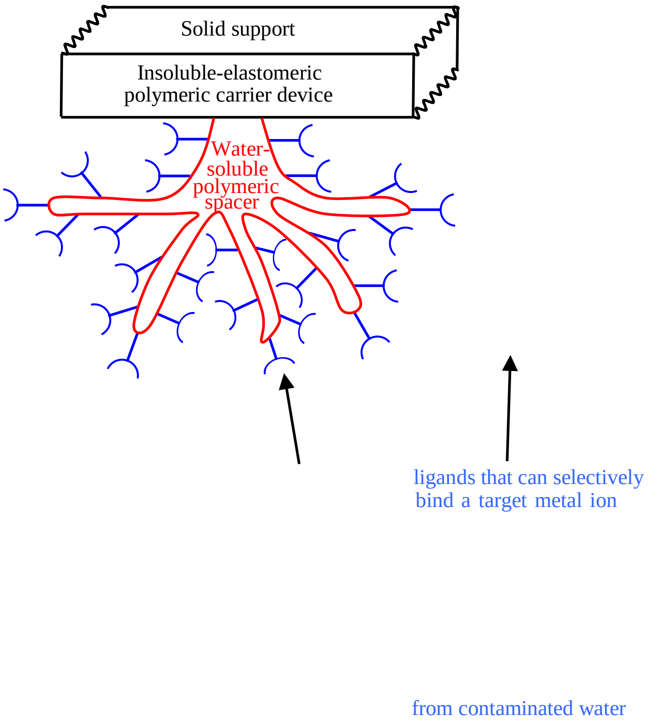


Figure 1.1: A schematic representation of a device developed to trap metal cations dissolved in industrial waste water. Black: insoluble elastomeric solid support; red: water-soluble polymeric spacer system to which a large amount of selective metal cation scavenging ligands (blue) is covalently bound.

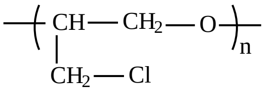
In order to visualise how the contaminant trapping device of the described patent works, one may think of the Na^+ ion-scavenging crown ether ligand as bound to the surface of a water-insoluble polymeric carrier, cast in the form of a rod or woven as a conveyor belt. Although the carrier-polymer is water-insoluble, the spacer side chains to which the crown ether ligands are attached are made to be very hydrophilic. When the conveyor belt is run through sodium cation containing wastewater, the crown ether ligand will coordinate Na^+ ions, remove it from the wastewater and thereafter release it in a suitable reservoir, under previously determined conditions. In principle, one will eventually enrich a reservoir with a sodium salt to the point where it will begin to precipitate. The precipitate may then be reclaimed and recycled in an appropriate industry.

The described patent opens up an enormous amount of research projects. The process need to be refined for removal of other metals, and not only sodium cations. This requires ligands which are specific for other identified metal ions. The device should also be adapted to complex anions like HSO_4^- selectively, as well as neutral organic molecules and non-metallic cations like NH_4^+. Modification of the technique to trap ions must also be done. For example, it is not necessary that a conveyer belt is the most effective way to bring trapping ligands in contact with polluting metal ions dissolved in large quantities of wastewater. Different ligand systems required to selectively trap contaminating heavy metals; precious metals and anions from large volumes of water call for unique tailor-made water-soluble polymeric spacer units to bind the metal or anion trapping ligand onto the elastomeric solid support in large quantities. These spacer polymers will differ from ligand to ligand in properties and structure.

This research program is focusing on developing and studying one such water-soluble polymeric spacer system capable of acting as the linking unit between the elastomeric solid support and metal ion scavenging ligand. It focuses on synthesising and derivatising polyepichlorohydrin.

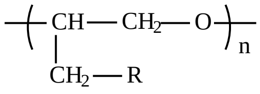
The following goals were set for this study:

1. Polymerisation of epichlorohydrin to polyepichlorohydrin

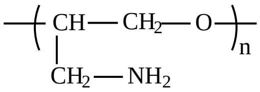
   $$-\left(\underset{CH_2-Cl}{\underset{|}{CH}}-CH_2-O\right)_n-$$

   with molar mass of 2 000 and 20 000 g mol^{-1}.
2. Re-functionalisation of the chloro-containing side chains of polyepichlorohydrin to

   $$-\left(\underset{CH_2-R}{\underset{|}{CH}}-CH_2-O\right)_n-$$

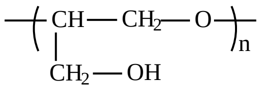
   where side chains have the terminal groups R = N_3, NH_2, OH and NCO.
3. Determination of the NH_2 side chain reactivity on



$$-\left(\underset{\displaystyle CH_2-NH_2}{\underset{|}{CH}}-CH_2-O\right)_n-$$

by binding to it a series of ferrocene-containing carboxylic acids $Fc(CH_2)_nCOOH$ with Fc = ferrocenyl and n = 0, 1, 2 and 3.

4. Determination of the OH side chain reactivity on



$$-\left(\underset{\displaystyle CH_2-OH}{\underset{|}{CH}}-CH_2-O\right)_n-$$

by reacting it with a model isocyanate.

Part and parcel of most of the above functionalisation reactions are the study of model reactions before attempts are made to synthesize the actual target molecules.

---

[1] UNESCO web page: http://www.unesco.org.

[2] J. C. Swarts, *RSA Patent 2004/0076*, **2004**

2.1 Introduction

Since this research program proposes the use of functionalised polymers to anchor crown ethers as ligands to complex or trap wastewater contaminants, a survey of functionalised polymers is deemed essential. For the purpose of this study, functionalised polymers are macromolecules to which some reactive functional groups are covalently bound. They differ from small molecules possessing the same functional groups, especially in the number of functional groups available per macromolecule. The polymer molecules have much more functional groups than small monomer molecule. The usefulness of the polymer is related to both the number of reactive functional groups and to the unique physical properties they may have because of their polymeric nature.

The attachment of functional groups to a polymer is frequently the first step towards the preparation of a functionalised polymer for a specific use. However, the proper choice of the polymer is an important factor for a successful application. In principle, the reactive functional group may be part of the polymer backbone, as end groups, or linked to a side chain as a pendant group either directly or *via* a spacer group. A required active functional group can be introduced onto a polymeric support chain

a) by incorporation during the synthesis of the polymer itself through polymerisation and copolymerisation of monomers containing the desired functional groups,
b) or by chemical modification of a preformed polymer and
c) by a combination of (a) and (b)

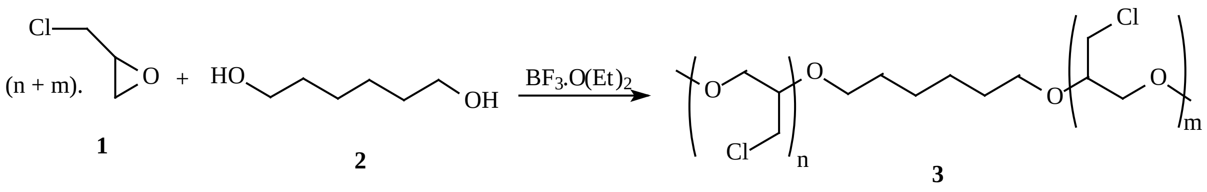
To choose between the different ways of obtaining functional polymers one has to consider the required chemical and physical properties of the polymer for a specific application and unwanted side reactions which reactive parts of the monomer may participate in during polymerisation. For this study, both methods a) and b) of introducing active functional groups onto a polymer were employed.

2.2 Polyepichlorohydrin

The main goal of this study was to synthesise and investigate different methods for re-functionalisation of polyepichlorohydrin (PECH). It is therefore appropriate to discuss this polymer. Polyepichlorohydrin is a polymeric derivative of epichlorohydrin. The polymer is normally obtained by cationic ring-opening polymerisation of epichlorohydrin in the presence of an initiator. The resulting polymer ranges from liquids and rubbery amorphous materials to a crystalline polymer, depending on the stereo-regularity of the final product.

2.2.1 Synthetic strategies for obtaining polyepichlorohydrin

Polyepichlorohydrin is prepared by the ring-opening polymerisation of a substituted oxirane monomer called epichlorohydrin using different types of initiators. Though three-membered epoxy ring compounds are known to undergo polymerisation by both anionic and cationic ring opening reactions, polymerisation of epichlorohydrin is usually brought about by the cationic route using a small amount of water and Lewis acids such as BF_3, $SnCl_4$, $SbCl_5$ or $FeCl_3$ as initiators (Scheme 2.1).[3] By performing the reaction in the presence of a small amount of dialcohol, a dihydroxy terminated polymer of targeted molecular mass may be obtained.[4] Other initiators like water/aluminium alkyl, trialkyl oxonium salts[5] like triethyl tetraflouroborate and esters and anhydrides of superacids[6] like CF_3SO_3R or FSO_3R are also used to initiate the polymerisation of epoxy compounds.

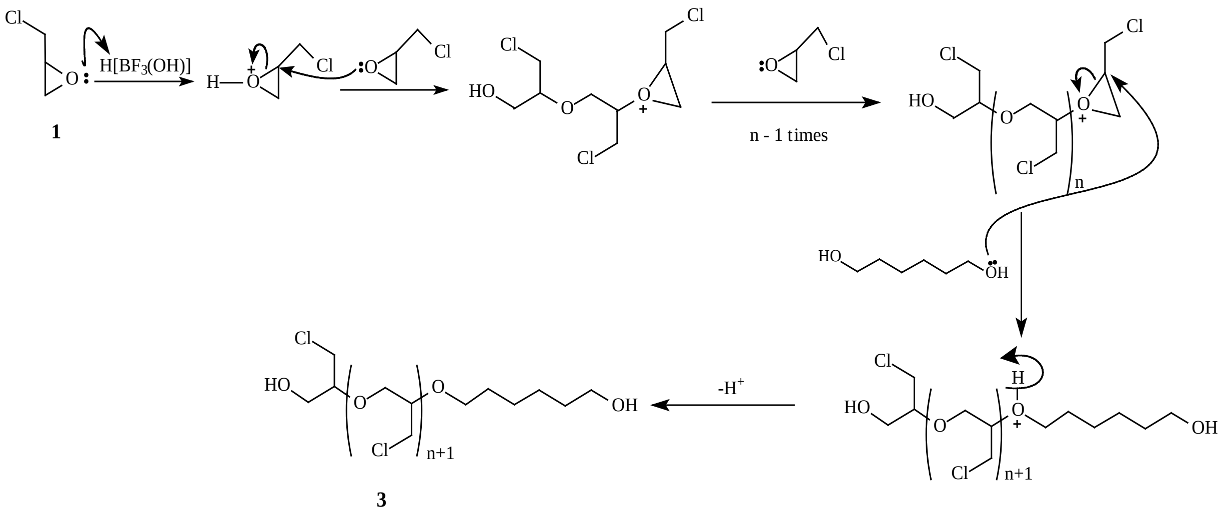


Scheme 2.1: Synthesis of hydroxy terminated polyepichlorohydrin (3) from epichlorohydrin (1) in the presence of a small amount of dialcohol (2).[*]

---

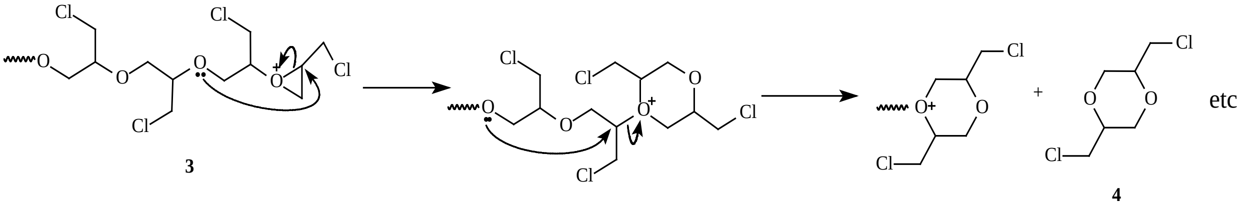
[*] Although the structure of **3** is indicating a regular head-tail coupling, this is not necessarily the case. In practice, the structure of **3** consists of a *random mixture* of head-tail, head-head and tail-tail coupling.

The product obtained during the polymerisation of epichlorohydrin depends on the type of initiator and the mechanism of propagation. Two types of mechanistic pathways for the cationic ring opening polymerisation reaction of epichlorohydrin exist. The first is labeled the active chain end mechanism and is illustrated in Scheme 2.2. In this mechanism there is always an excess of epichlorohydrin present, and the growing point of the polymer is not destroyed before all the starter monomer is used. A dialcohol **(2)** is finally added to produce a polymer which is hydroxy terminated.



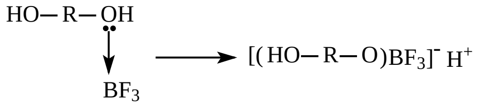
Scheme 2.2: Cationic ring opening polymerisation of epichlorohydrin (1) according to the active chain end mechanism.

A disadvantage associated with the activated chain end mechanism is the polymer chain possesses highly reactive end groups which react not only with the monomer but also with hetero-atoms of the polymer main chain, leading to the formation of cyclic oligomers (dioxanes), as shown in Scheme 2.3, p. 10. This results in a polymer with a molecular mass smaller than the one desired.

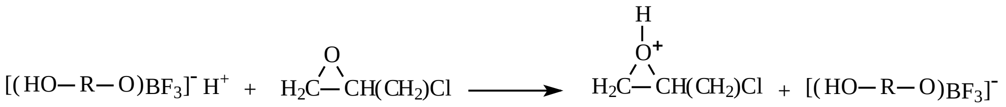


Scheme 2.3: Elimination of dioxane derivatives (4) from growing polyepichlorohydrin (3). The mechanism is accelerated by an increase in reaction temperature.

To reduce the risk of cyclic oligomer formation, a protic compound such as water, alcohol or diol is required as co-initiator or chain transfer agent[7,8,9] at the beginning of the reaction rather than as a terminating agent. It interacts with Lewis acids like BF_3 as shown in Eq. (1), and protonation of monomer produces a secondary oxonium ion (activated monomer) as shown in Eq. (2).

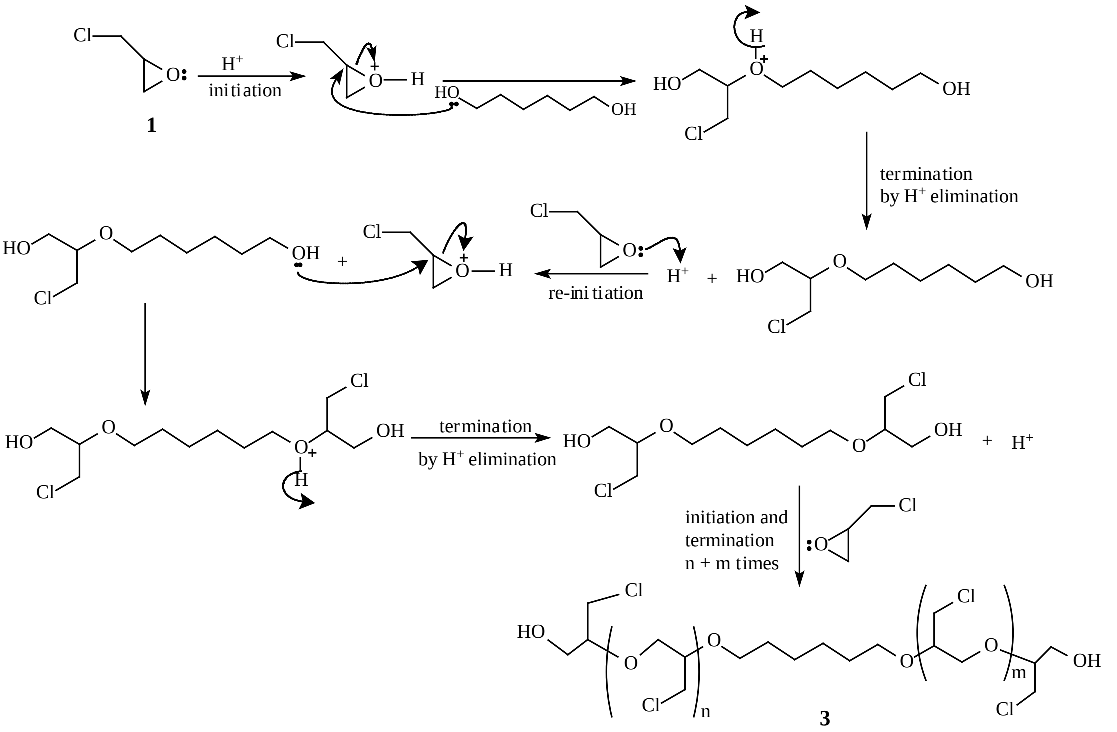


$$\underset{BF_3}{\underset{\downarrow}{HO-R-\ddot{O}H}} \longrightarrow [(HO-R-O)BF_3]^- H^+ \qquad (1)$$



$$[(HO-R-O)BF_3]^- H^+ + H_2C\overset{O}{\frown}CH(CH_2)Cl \longrightarrow H_2C\overset{\overset{H}{|}}{\overset{O^+}{\frown}}CH(CH_2)Cl + [(HO-R-O)BF_3]^- \qquad (2)$$

The activated monomer further reacts with the diol molecule to give hydroxy terminated macro-monomers which in turn undergo further reaction with activated monomer leading to high-molecular-weight polyepichlorohydrin (PECH) with hydroxy end groups. This mechanism is labeled the active monomer mechanism and is illustrated in Scheme 2.4, p. 11. In this mechanism, the growing point of the polymer is terminated after each separate epichlorohydrin attack on the dialcohol. These two mechanisms can coexist and the proportion of their contribution to the chain growth depends on the oxirane monomer structure and the polymerisation conditions. When the instantaneous ratio of epichlorohydrin to the dialcohol is kept lower than one, that is epichlorohydrin is never in excess, the conditions favor chain growth by the activated monomer mechanism. The average molecular weight (M_n) of the product formed is governed by the final reactant ratio of the epichlorohydrin to diol taken during the reaction.



Scheme 2.4: Cationic ring opening polymerisation of epichlorohydrin (1) according to the active monomer mechanism. This mechanism limits the probability of elimination of substituted dioxanes as illustrated in Scheme 2. 3, p. 10.

2.2.2 Industrial application of polyepichlorohydrin

Since the discovery of the use of polymers as reactive molecules by Merrifield,[10] in the early 1960's, the use of functionalised polymers has found widespread application in organic synthesis and related chemical fields. In recent years a considerable effort has been devoted to the synthesis and characterization of intrinsically energetic polymers for use as binders in propellant and explosive compositions. An energetic polymer may be defined as a macromolecule bearing a functional group rich in chemical energy, e.g. nitro, azido and nitrato moieties.[11] To date, only a few classes of energetic binders have been shown to possess the necessary combination of acceptable properties and facile synthesis which make them candidates for widespread use within the explosive and propellant industry.[11] The presence of an active group in the polymer side chain of polyepichlorohydrin offers an important possibility in the widespread use of this polymer within the explosive and propellant community.

Hydroxy-terminated polyepichlorohydrin (PECH) is used as a starting material for manufacturing glycidyl azide polymer (GAP, **5**)[12] and glycidyl nitrate polymer (PolyGLYN, **6**) (Figure 2.1).[13] The prepolymers GAP and PolyGLYN were recently developed for use as high energetic polymeric binders and performance-improving additives in the preparation of solid rocket propellants.[11] Solid propellants based on these polymers in combination with environment-friendly oxidizers are eco-friendly and they are capable of delivering specific impulses greater than that obtained when using conventional propellants based on hydroxy terminated polybutadiene and ammonium perchlorate.

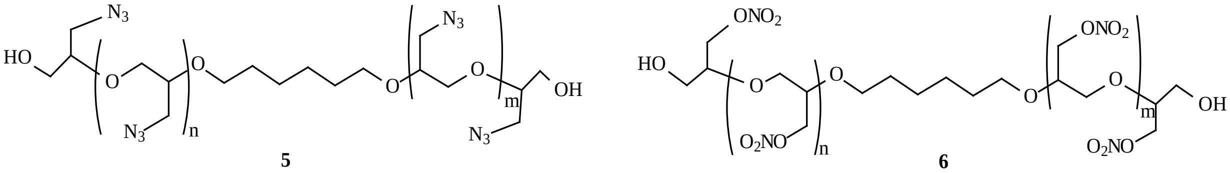


Figure 2.1: Examples of more energetic derivatives of polyepichlorohydrin (3), namely, poly glycidyl azide (GAP, 5) and poly glycidyl nitrate (PolyGLYN, 6).

Polyepichlorohyrin polymers are saturated but are readily vulcanised through the chloromethyl group by a variety of reagents, e.g. diamines, urea, and ammonium salts. The vulcanisates have good oil, flame and aging resistance.[14] Homopolymers of epichlorohydrin are strong rubbers, i.e. they are somewhat comparable to natural rubber.[15] They are also flame-retardant, resistant to heat aging and have lower permeability to air.[14] In contrast, 1:1 copolymers of epichlorohydrin and ethylene oxide are superior in low temperature flexibility and are chemically inert, e.g. they are resistant to oil degradation.[15] Because of these unique properties, polyepichlorohydrin rubber has received a broad application in wire and cable jackets, hose and belting material, packaging material, and as seals in mechanical goods.[15] Polyepichlorohydrin roofing membrane is a factory-fabricated copolymer of epichlorohydrin and ethylene oxide.[15] It is an elastomeric homogenous roof covering. It may be used for new single-ply roof construction and reroofing applications where increased resistance to hydrocarbons, aromatic solvents, grease and oil resistance is a design criterion.

2.2.3 Functionalisation of polyepichlorohydrin

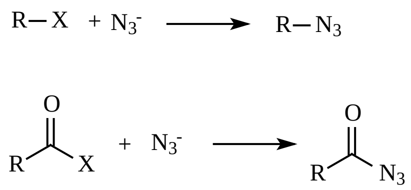
The preparation of functionalised polymers by chemical modification is an important technique which has been used extensively both industrially to modify the properties of polymers for various technological applications and in the area of polymer-supported chemistry to prepare chemically reactive polymers.[16,17,18,19,20,21] The application of chemical modification processes to polymers make it possible to create new classes of polymers which cannot be prepared by direct polymerisation of the corresponding monomers owing to their instability or unreactivity. A chemical modification process also makes it possible to modify the structure and physical properties of commercial polymers to make them suitable for specific applications.

A functional group attached to a polymer chain may have quite a different reactivity from an analogous group on a small molecule because of its macromolecular environment. Thus more drastic reaction conditions may be required to reach satisfactory high-yield conversion. The design of a new reactive polymer must be planned by considering important factors which affect its synthesis. This includes:

a) the type of solvents and reagents to which the polymer must be subjected during the course of its functionalisation or subsequent reactions
b) and the chemical behavior of the polymer which depends on its physical form, crosslinking density, the flexibility of the chain segments and the degree of substitution.

For this study, chemical modifications of polyepichlorohydrin (PECH) to some of its polymeric derivatives, which are highly reactive and require less energy to react with other functionalities, were investigated. In particular azide ($-N_3$), amine ($-NH_2$), isocyanate (-NCO) and hydroxy (-OH)-functionalised epichlorohydrin polymers were required. It was, thus considered appropriate to briefly discuss general techniques used to synthesise alkyl azides, alkyl isocyanates, alkyl amines and alkyl alcohols.

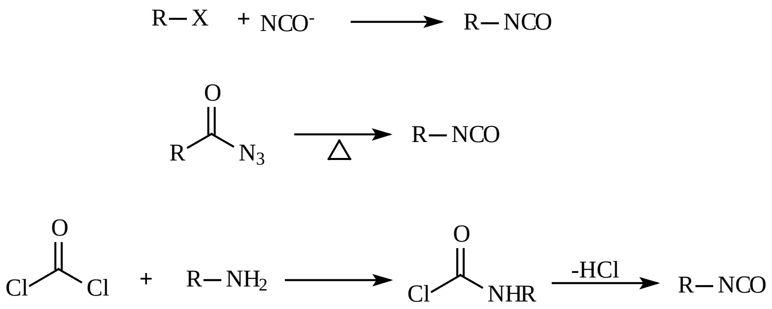
2.2.3.1 Formation of azides



Scheme 2.5: The formation of azides from alkyl and acyl halides. The source of N_3^- is normally sodium azide (NaN_3).

Preparation of alkyl and acyl azides can be carried out by the treatment of alkyl and acyl halides with the azide anion[22] in the presence of a phase transfer catalyst[23] or under the influence of ultrasound.[24] Treatment of tertiary alkyl halides with NaN_3 in the presence of $ZnCl_2$ in CS_2[25] can be used to obtain tertiary alkyl azides. Tertiary alkyl azides can also be prepared from tertiary alkyl alcohols with NaN_3 in the presence of CF_3COOH[23] or with HN_3 in the presence of $TiCl_4$[26] or BF_3.[27]

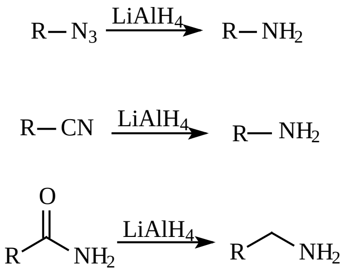
2.2.3.2 Formation of isocyanates



Scheme 2.6: The formation of isocyanates from alkyl halides, acyl halides and amides.

One of the goals of this study was to synthesise isocyanate-containing compounds. Isocyanates can be produced by either the reaction of an alkyl halide with the isocyanate ion,[28] or by the Curtius rearrangement from acyl azides,[29] or *via* the chloroformamides, ClCONHR, which are produced by the reaction between phosgene and primary or aromatic amines.[30] The use of chloroformamides is the most common and versatile method for the synthesis of isocyanates.[30] Primary alkyl halides have been converted to isocyanates by the use of sodium nitrocyanamide ($NaNCNNO_2$) and *m*-chloroperbenzoic acid.[29] The Curtius rearrangement involves migration of an –R group from the C=O carbon to the neighboring nitrogen with the simultaneous loss of a leaving group, this reaction usually gives good yields of the isocyanates, if there is no water present in the system. The Curtius rearrangement is a very general reaction and it can be applied to any azides, i.e. aliphatic, aromatic, alicyclic, heterocyclic, and unsaturated.[31]

2.2.3.3 Formation of amines



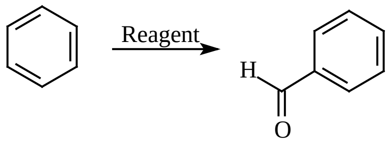
Scheme 2.7: The reduction of azides, nitriles and amides to amines.

The reduction of azides to amines by lithium aluminium hydride ($LiAlH_4$),[32] or by catalytic hydrogenation, represents an important tool in organic chemistry.[33] Amides can also be reduced to amines with $LiAlH_4$ or by catalytic hydrogenation, though high temperatures and pressure are often required for the latter.[34] Even with $LiAlH_4$ the reaction is more difficult than the reduction of most other functional groups, and other groups can often be reduced without disturbing an amide function. Other reducing agents include borohydride exchange resin (BER),[35] $NaBH_4$,[36] borane,[37] and sodium in 1-propanol. Although aliphatic azides were reduced to give poor yields of the corresponding amines by sodium borohydride itself, the yields of amines were improved substantially in the presence of phase transfer agent, by dropping methanol in tetrahydrofuran, or in the presence of nickel chloride.[36]

These reactions are pertinent with respect to the amine derivatives that were synthesised in this study according to goal 3 (Chapter 1).

2.3 General functionalisation techniques

2.3.1 Formylation



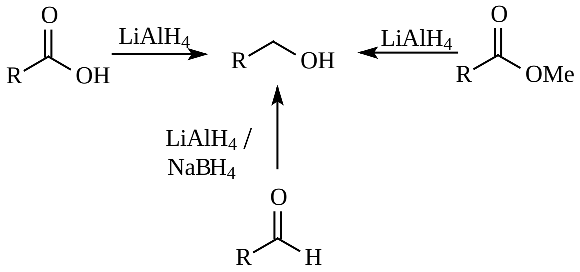
Scheme 2.8: The formation of an aromatic aldehyde.

Several one-step formylation methods have been reported over the years, using formylation agents such as formyl fluoride, formic anhydride, acetic-formic anhydride,[38] 2-(*N*-methyl-*N*-formylamino)pyridine, dimethylchloro-methyl-ammonium chloride, *N*-formylbenzotriazole,[39] and *N,N*-dimethylformamide,[40] among many others.[41] The Vilsmeier-Haack reaction is the most versatile method for the formylation of aromatic rings.[42] This reaction occurs between an aromatic compound and disubstituted formamides in the presence of phosphorous oxychloride.[43] *N*-Phenyl-*N*-methylformamide[42] is the reagent of choice.

Formylation with $Zn(CN)_2$ and HCl can also be carried out in the so-called Gattermann[44] reaction. This reaction can be applied to alkylbenzenes, phenols and their ethers, and many heterocyclic compounds.[42] Chloroform and hydroxide ions are also often used to formylate aromatic rings.[42] This type of reaction is known as the Reimer-Tiemann[45] reaction and is useful only for phenols and certain heterocyclic compounds such as pyrroles and indoles. The Duff[46] reaction is closely related to the Reimer-Tiemann reaction, but in this reaction chloroform is replaced by hexamethylenetetramine. This reaction can be applied to phenols and amines.[42] The formylation of the *ortho*-position of phenols can also be accomplished by using *para*-formaldhyde, $SnCl_4$ and a tertiary amine,[47] or 2-ethoxy-1,3-dithiolane.[48]

With respect to this research program, formylation of benzo-15-crown-5 **(29)** was a pursued reaction.

2.3.2 Formation of alcohols



Scheme 2.9: The reduction of carbonyl containing compounds to alcohols by both $LiAlH_4$ and $NaBH_4$.

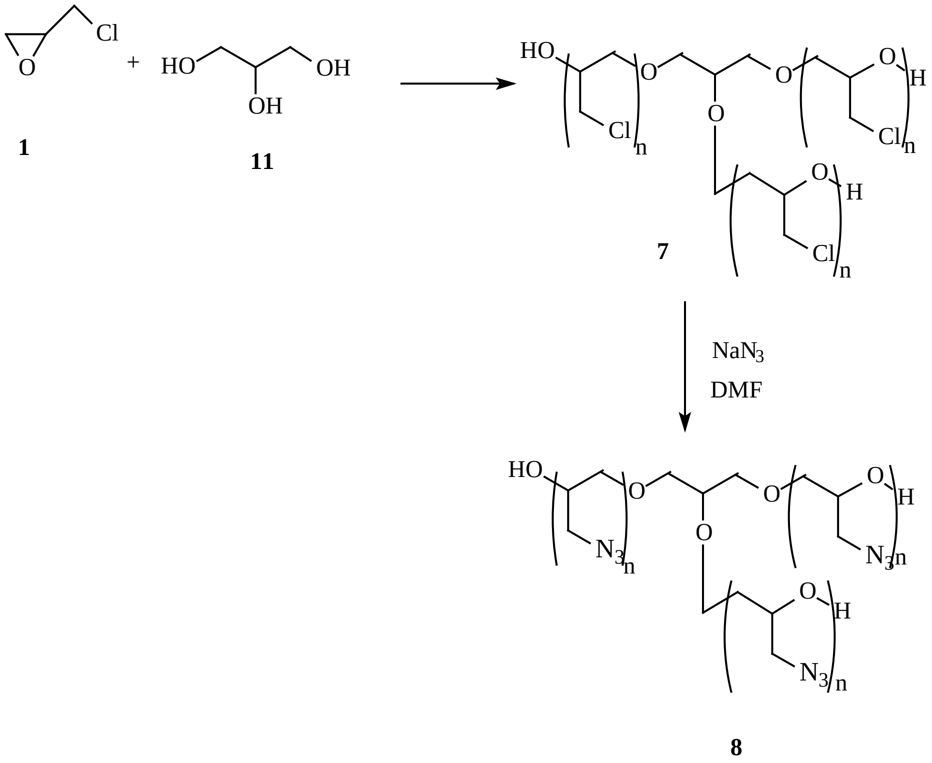
One of the most general methods for the preparation of alcohols is by reduction of carbonyl compounds. Aldehydes are easily reduced to yield primary alcohols with $LiAlH_4$, with the advantage that it does not reduce carbon-carbon double, or triple bonds.[49] $LiAlH_4$ easily reduces aliphatic, aromatic, alicyclic and heterocyclic aldehydes, containing double or triple bonds and/or non-reducible groups such as NR_3, OH, OR, and F.[49] $NaBH_4$ has a similar scope of reactions as $LiAlH_4$, but it is more selective and may be used for aldehyde reduction without reducing such as NO_2, Cl, COOR and CN-groups that maybe present in the molecule.[49]

The two oldest methods for the reduction of the carbonyl group of aldehydes and ketones to liberate alkanes are the Clemmensen reduction and the Wolff-Kishner reduction.[50] The former reaction occurs when aldehydes or ketones are reduced in the presence of zinc amalgam and aqueous HCl,[51] while the latter reaction occurs when aldehydes or ketones are heated with hydrazine hydrate and a base (usually NaOH or KOH).[52] The Wolff-Kishner reaction has recently been replaced by the Huang-Minlon modification, which is carried out in diethylene glycol.[53]

2.4 Polymeric derivatives of polyepichlorohydrin and their properties

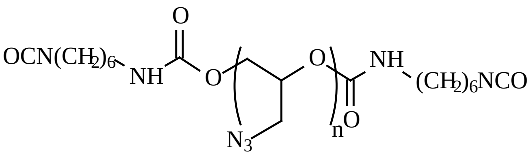
2.4.1 Poly(glycidyl azide) (GAP)

Poly(glycidyl azide) (GAP) was first synthesised in 1972 by Vandenburg[54] by the reaction of sodium azide in dimethylformamide with polyepichlorohydrin (PECH). Optimization of hydroxy terminated PECH production has led to the successful development of a process which yields GAP polymers having an average molecular mass of 2 100 and functionalities (the number of reactive hydroxyl groups per molecule) of 1.6 to 3.1 depending on the catalyst, the initiator and the ratio of epichlorohydrin (ECH) / initiator. The hydroxy functionality of linear GAP is nearly 2, and to achieve the desired level of crosslinking to produce a tough and elastomeric rubber **(8)**, it must be raised by addition of triols **(11)** or used with triisocyanate crosslinkers, as shown in Scheme 2.10.



Scheme 2.10: Synthesis of GAP triol.

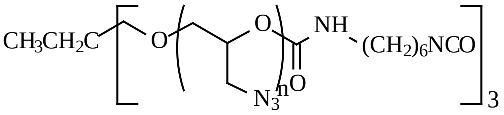
Functionalisation of GAP with various other groups is also possible. Frankel *et al.*[55] have patented a process whereby linear GAP is terminated with isocyanate groups to give α,ω-diisocyanate-functionalised GAP, such as **9** in Figure 2.2. The polymer was prepared by the reaction of GAP with hexamethylene diisocyanate.



9

Figure 2.2: α,ω-Diisocyanate-functionalised GAP

Alternatively, only one end of the chain can be functionalised with the isocyanate. Figure 2.3 shows trifunctional GAP isocyanate **(10)**, which has one end of the chain functionalised with isocyanate.



10

Figure 2.3: α-Isocyanate GAP

The physico-chemical properties of GAP depend on the degree of polymerisation, structure and method of preparation. GAP has a low glass transition temperature (-45 ^{0}C) and a low weight percentage of polymer weight-bearing chain, which results in an energetically favorable binder system.[56] However at low temperatures GAP is hard and brittle as a consequence of the rigid, conjugated $–N_3$ groups that limit the flexibility of the polymer backbone. The energetic properties of GAP are not a consequence of its oxidation products, but are rather due to scission of the azide group, which gives off nitrogen gas. The heat of scission is -957 kJ kg^{-1} at 5 MPa.[57] GAP also contains a relatively high concentration of carbon atoms, and therefore has high "combustion potential",[58] burning smoothly at elevated temperatures and pressure (> 0.3 MPa) without explosion.[59]

Differential thermal analysis and thermo-gravimetric studies (DTA/TGA) of the decomposition of GAP under helium atmosphere (0.1 MPa) revealed an exothermic decomposition at 202 - 277⁰C accompanied by a 40% weight loss, followed by a secondary weight loss without heat liberation.

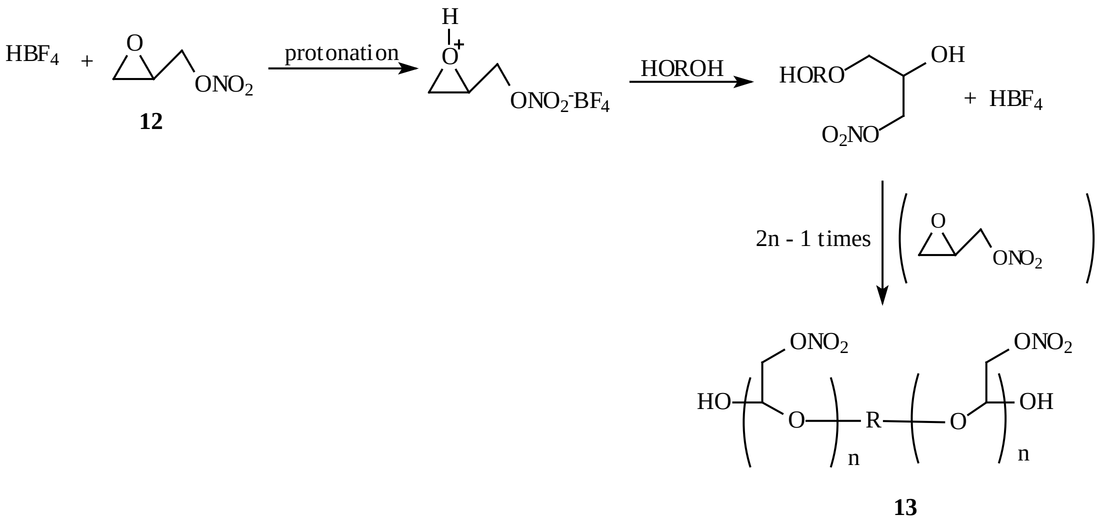
Kubota[58] has suggested that initial decomposition of GAP follows the reaction:

$$R—CH_2—N{=}N_2 \longrightarrow R—C{\equiv}N + N_2 + H_2$$

corresponding to the release of 685 kJ mole^{-1}, and the subsequent decomposition of the resulting nitrile leads to carbonaceous by-products. Differential scanning calorimetry (DSC) studies on GAP have also been carried out by Leu *et al.*,[60] who observed initial decomposition at 240 ⁰C, followed by degradation at 260 – 500 ⁰C.

2.4.2 Poly(glycidyl nitrate) (PolyGLYN)

Glycidyl nitrate (GLYN) can be prepared by the nitration of glycidol, and may be polymerised to give hydroxy terminated prepolymer. Urethane crosslinking with isocyanates leads to poly(glycidyl nitrate) cured rubbers. Polymerisation of the prepolymer employs a tetraflouroboric acid etherate initiator combined with a di-functional alcohol (glycol), to give a nominally di-functional polymer (Scheme 2.11).[61]

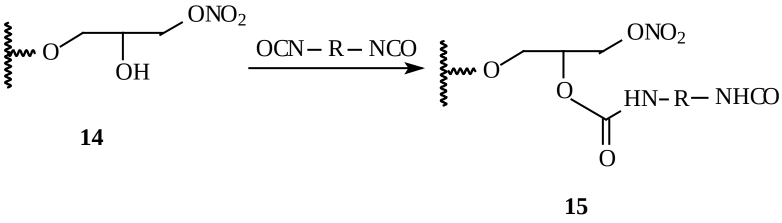


Scheme 2.11: Active monomer polymerization to form polyGLYN

PolyGLYN prepolymer is a clear, yellow liquid high in energy and density with a low glass transition (T_g). Its sensitivity is too low to require classification as

Class 1 explosive (UK classification). PolyGLYN has a calculated explosion energy of 2 661 kJ kg^{-1} [$\Delta H_{expl.}$ (calc.)], which is higher than that of GAP (2 500 kJ kg^{-1}).[62]

Uncured polyGLYN prepolymer **(14)** exhibits good chemical stability. However, when cured with isocyanates, as shown in Scheme 2.12, the resulting urethane rubber **(15)** shows poor stability. Long term or accelerated aging results in degradation of the rubber. Further, degradation is not prevented by the addition of stabilizers, or by exclusion of oxygen. This decomposition of polyGLYN is attributed to a low degradation activation energy associated with chain scission at the urethane linkage and has little to do with the normal nitrate ester degradation process.

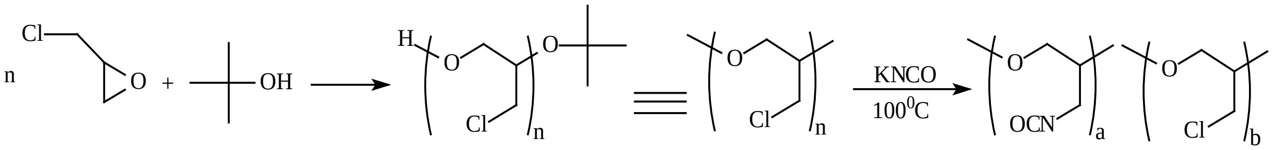


Scheme 2.12: Curing of polyGLYN

Instability appears to be an inherent problem with polyGLYN prepolymer and has little to do with the isocyanate used. The problem can be overcome by the modification of the chain ends to give diol-terminated polyGLYN prepolymer.

2.4.3 Polyisocyanate polymer

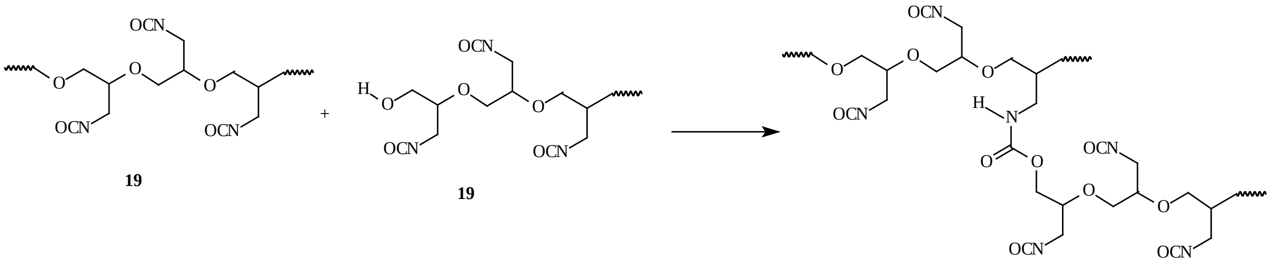
Low isocyanate-containing polyepichlorohydrin derivative **(18)**, is obtained by the reaction of polyepichlorohydrin **(17)** with KNCO in the presence of a phase transfer catalyst (tetrabutylammonium bromide) and a base, K_2CO_3, as shown in Scheme 2.13, p. 22.[63] This colourless liquid polymer contains highly reactive isocyanate functional groups.



1 **16** **17a** **17** **18**

Scheme 2.13: The synthesis of isocyanate-functionalised polyepichlorohydrin derivative, i.e. polymer 18, whereby a ≈ 0.1n.

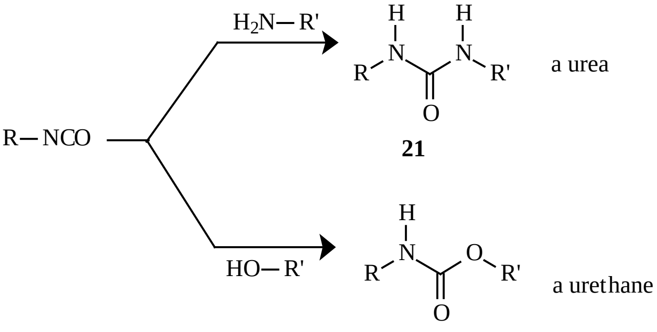
When the isocyanate group is attached to polyepichlorohydrin containing many hydroxy terminals, it reacts with these terminal alcohol groups. If the hydroxy functionality in **18** is more than one, an insoluble cross-linked polymeric product such as **20,** Scheme 2.14, is formed. As a result, polyisocyanate polymer is normally synthesised from polyepichlorohydrin derivative containing at most one hydroxy terminal group. The polyepichlorohydrin used in this study for synthesis of poly isocyanate polymer was originally from a mono-alcohol-initiator, which leads to a mono-hydroxy-terminated polyepichlorohydrin derivative.



19 **19** **20**

Scheme 2.14: The crosslinking of polyisocyanate polymer with itself to produce the insoluble cross-bound polymer 20.

Polyisocyanate polymers can react with alcohol or amine functionalised compounds to produce either a urethane **(22)** or a urea **(21)**, as shown in Scheme 2.15, p. 23.



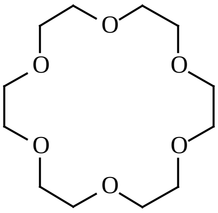
21

22

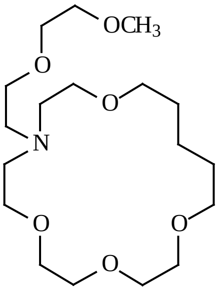
Scheme 2.15: The reaction between an isocyanate derivative with either an amine- or alcohol-functionalized compound to produce a urea or a urethane.

2.5 Crown ethers and related compounds

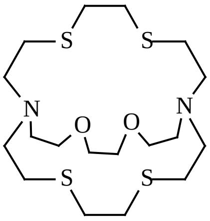
Since Pedersen’s discovery of crown ethers and their abilities to bind strongly with metal ions in 1967,[64, 65] the study of crown ethers has grown at an incredible rate. The synthesis of many different types of crown ethers, e.g. crown ether diesters, azacrown ethers, thiacrown ethers, and chiral crown ethers have been documented in the literature and their bonding properties such as binding selectivity and strength towards a wide range of metal ions, non-metal ions, and neutral molecules have been investigated.[66,67] Due to their remarkable binding properties, the study of crown ethers has largely contributed to the development of host-guest chemistry and the emergence of supramolecular chemistry. Some examples of crown ethers are shown in Figure 2.4, p. 24.



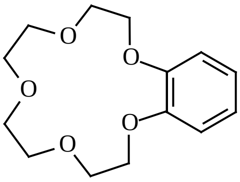
26



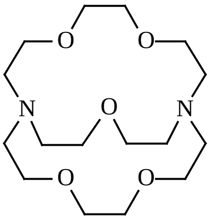
27



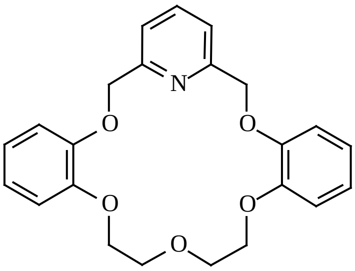
28



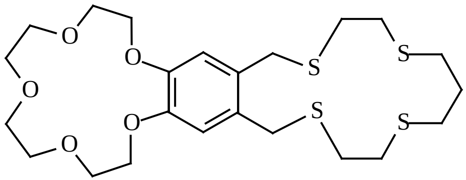
29



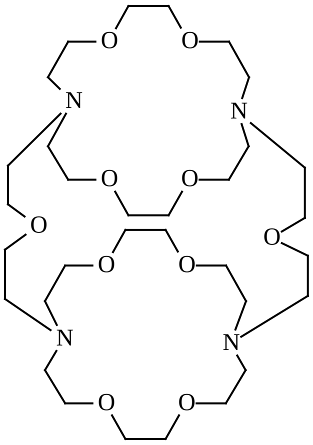
30



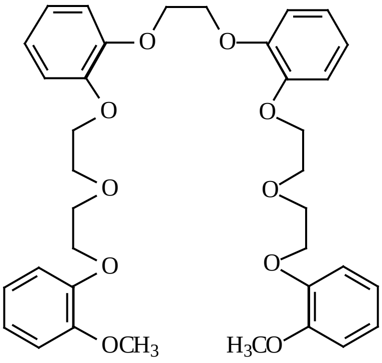
31



32



33



34

Figure 2.4: Example of crown ether derivatives.

The stability of the crown ether-metal ion complex is dependent on the number of ether donor atoms. Of particular importance is the size and shape of the cavity relative to the cation size.[68] Though crown ethers tend to form their most stable complexes with ions having diameters comparable to their opened cavity, they can also form complexes with ions of larger size.[69] If the ion is able to fit within the cavity, the crown ether-metal ion complex forms in a 1:1 ratio. If the ion is larger than the crown cavity, there is a tendency for the crown ether moieties to "sandwich" the metal ions between adjacent crown units.[70]

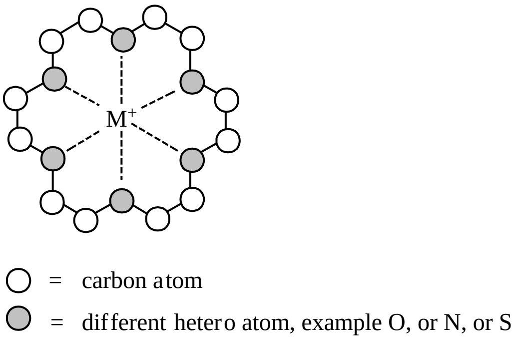


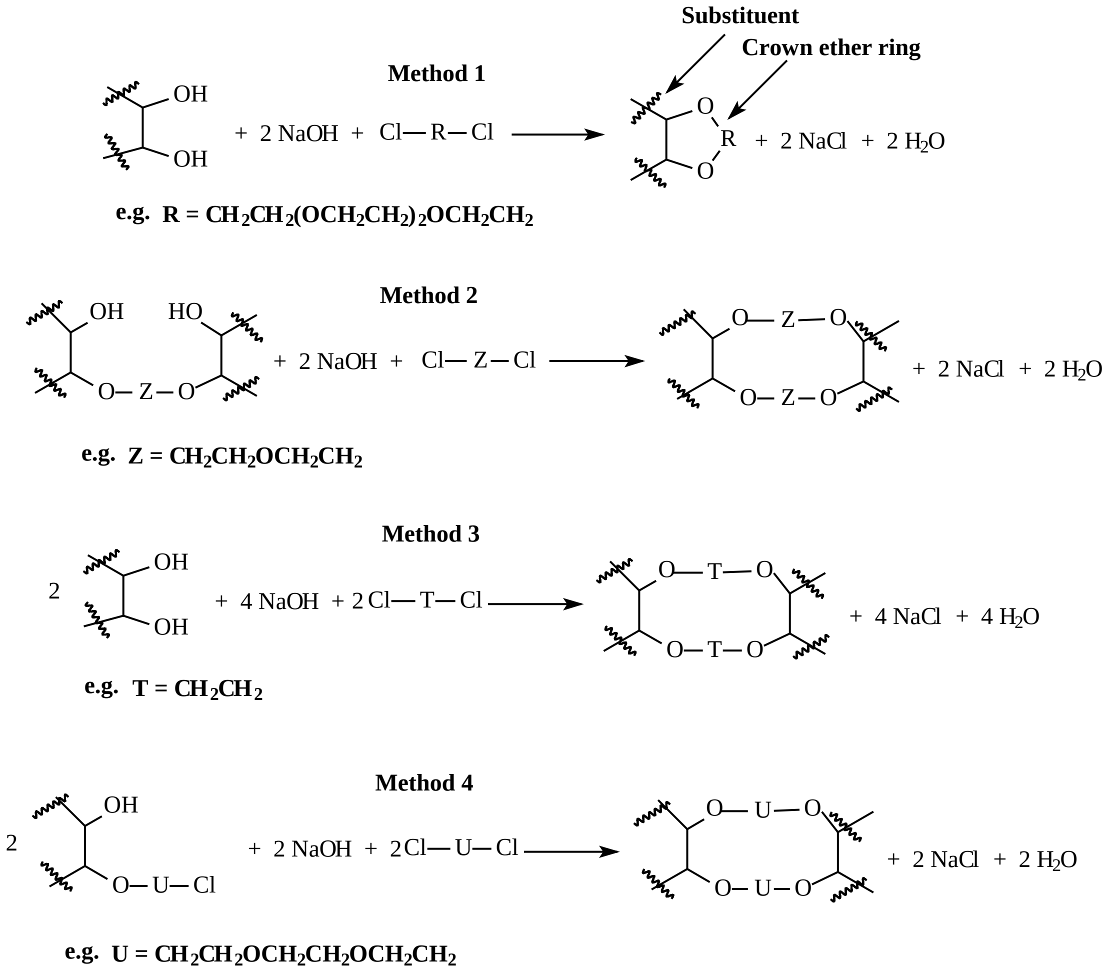
Figure 2.5: Crown ether-metal complexation

While the first crown ethers that were characterised contained only oxygen donor atoms, sulfur and nitrogen-containing crown ethers were subsequently prepared. Figure 2.5 shows a characteristic atom arrangement and metal complexation by crown ethers. Due to the differences in polarisability, nitrogen-containing crown ethers (azacrowns) and sulfur-containing crown ethers (thiacrowns) display different cationic metal preferences from oxygen-containing crown ethers. These differences in behavior as a function of donor atoms can be explained by hard-soft acid-base theory.[71,72] Soft ligands, such as those that contain sulfur, provide polarisable sites that have increased affinities for soft metal ions, including precious metal. In contrast, hard ligands that have sites of low polarisability have increased affinities for hard metal ions such as the alkali and alkaline earth metals.[73,74]

As stated in Chapter 1, this research program was inspired by the crown ethers' ability to complex metal ions. In order to immobilise crown ethers onto functionalised polymers, one has to functionalise crown ethers to obtain a handle by which the crown ether can be anchored onto a polymeric solid support. This approach is briefly discussed in Section 2.3.1, p. 16.

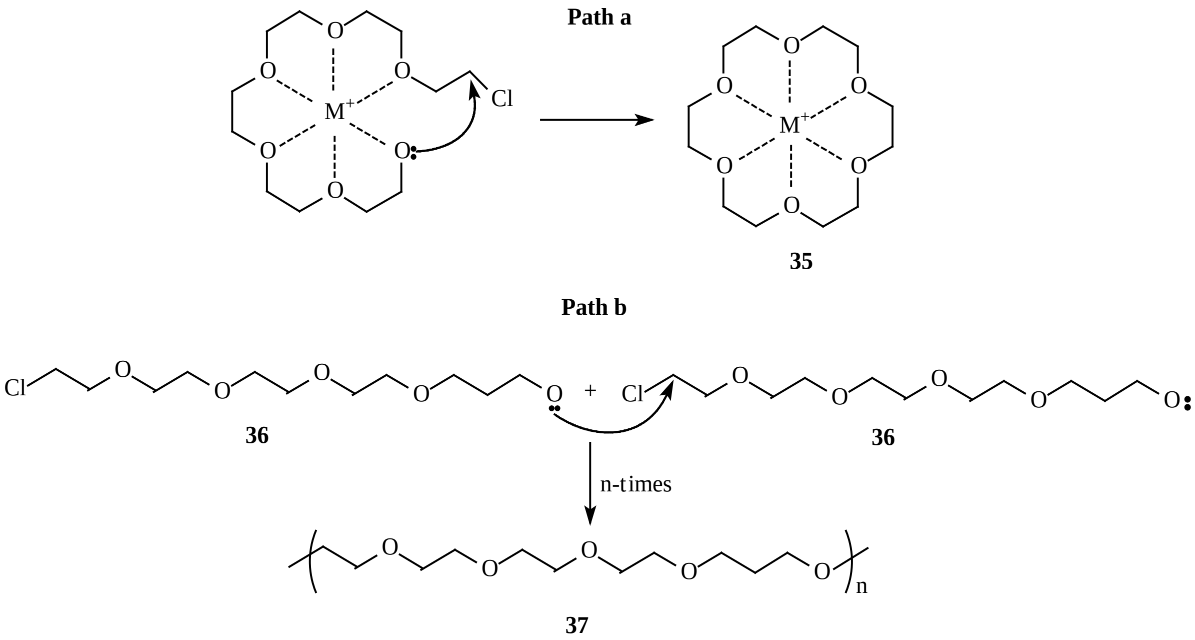
2.5.1 Synthesis of crown ethers

Crown ethers are trivially named as x-crown-y where x denotes the total number of atoms in the cyclic backbone and y denotes the number of oxygen atoms. Many methods exist for the synthesis of crown ethers, but only four were considered for this discussion. Four different synthetic pathways are shown in Scheme 2.16, where R, Z, T, and U represent organic groups, which may or may not be identical. Method 2 is the most versatile for the synthesis of macrocycles containing two or more benzo groups, and it also gives the highest yield. 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.[75]



Scheme 2.16: Four methods for the synthesis of crown ethers.

To prevent formation of linear by-products, which is one major problem during synthesis of cyclic crown ethers, high dilution techniques are employed to enhance cyclisation of crown ethers over the oligomerisation. Another way to overcome this problem is through the use of the “template effect”, whereby the synthesis of the crown ether is done in the presence of a metal cation.[67] The metal cation helps to stabilise the transition state leading to the formation of a cyclic macrocycle. The template effect helps to organise the nucleophilic and the electrophilic ends of the molecule, so that intramolecular products or cyclic products are formed rather than intermolecular products, or non-cyclic products.



Scheme 2.17: 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.

The template effect takes place because of 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 chain containing the oxygen atoms organises itself around the cation as seen in Scheme 2.17. The formation of a circle or semicircle around the cation enhances the likelihood of the two ends of the reacting molecule being close enough for the cyclisation reaction to take place.

2.5.2 Functionalisation of macrocycles

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 crown ethers that contain an aromatic ring as the starting material to obtain functionalised molecules. These macrocycles can be halogenated, nitrated or condensed with formaldehyde, and the substitution usually occurs at the 4'-position.

The functionalisation of the benzene ring has an effect on the macrocycle's ability to complex cations.[76] The presence of an electron withdrawing group, such as the nitro group, NO_2, would cause an increase in the decomplexation rate and a decrease in the complexation rate. However, this observation seems to be less pronounced if weak electron-withdrawing groups are introduced onto the aromatic ring.

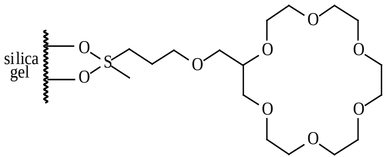
2.6 Polymer-bound macrocycles

Macrocyclic compounds containing oxygen, sulfur and nitrogen as donor atoms have gained attention for their ability to form stable complexes with ions within their central cavity. The *selective* complexing properties exhibited by crown ethers towards metal ions have led to their incorporation into polymeric matrices. Polymer supported reagents offer many advantages, including ease of handling and recoverability when used in the removal of toxic metal ions from the environment.[77,78] Due to the increased concern with the remediation of waste water, polymer-supported reagents, including immobilised crown ethers, have been studied for the selective removal of targeted metal ions.[79,80,81]

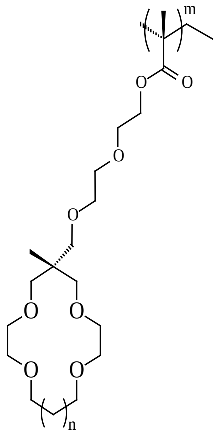
There are three principal methods by which the crown ethers can be incorporated into polymer matrices. The first mode is direct polymerisation of the crown ether through a step-growth mechanism; the second mode is the polymerisation through a chain growth; and the third mode is post-functionalisation wherein crown ether are covalently bound to a pre-formed polymer backbone. The last method requires the crown ether to have a reactive functional group that can be bound to the polymer, and the choice of polymer can influence the degree of cationic accessibility to the grafted crown ether.[82]

In recent years, highly selective extraction-chromatographic materials have been developed in which macrocycles are covalently attached,[83] or sorbed[84] onto solid supports. Such materials allow for repeated use of macrocycles since the materials can be regenerated after each use. Polymer-bound crown ethers and cryptands, as well as other salts have been applied to phase-transfer reactions.[85,86,87,88,89,90] When the polymer-bound crown ether phase-transfer catalyst has been used under heterogeneous conditions, the crown ether catalyst can be separated at the end of the reaction by simple filtration and reused for another run. Moreover, the products are easily isolated by evaporation of the solvent; therefore, the use of crown ether immobilised on a polymer support as catalyst is attractive in terms of recycling the catalyst. According to Bradshaw *et al.*,[83] silica gel-bound crown ethers such as polymer **38** (Figure 2.6, p. 30), could be used indefinitely to perform separations, recoveries and determinations without the loss of the crown ether moiety. This implies the bond that anchors the crown ether to the silica gel is very stable. They[83] also found that the polymer-bound crown ether exhibited the same affinity for metallic cations as the unbound parent macrocycle.

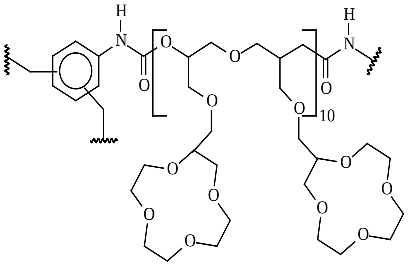
A series of crown ether-functionalised polymers based on a poly(methylacrylate-*co*-ethylene glycol dimethacrylate)[91] or poly(styrene-*co*-divinylbenzene)[92] have also been described. More examples of polymer bound crown ethers are shown in Figure 2.6. Introduction of ionic ligand sites in the macromolecular matrix increased the hydrophilicity of the polymeric ligands and enhanced the kinetics of cation binding.[92,93] The reaction of glycidylated polymers with functionalised ligands[93] and crown ethers[94] afford polymers with favourably fast metal-binding kinetics.



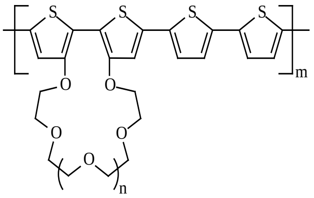
38



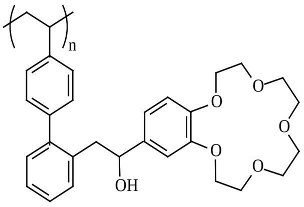
39 n = 0
40 n = 1



41



42 n = 0
43 n = 1
44 n = 2
45 n = 3



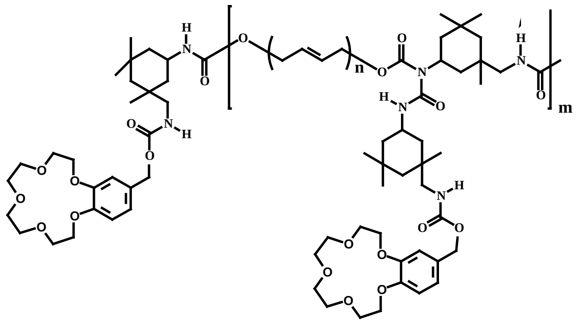
46

Figure 2.6: Examples of polymer-bound crown ether compounds

Good hydrophilicity and high mobility / flexibility of polymers to which crown ethers are bound make an important contribution to metal binding. To enhance the accessibility of the crown ether to metal ions, the use of flexible polymers with low temperatures of glass transition are required.[95] The high mobility / flexibility of the polyether chain contribute to the high efficiency of complexation.

Recent advances in construction of starburst molecules or dendrimers to create macromolecular superstructures also proved to be important in accomplishing maximum efficiency in metal binding of polymeric crown ether conjugates. Dendrimer chemistry[96] provides an excellent degree of control over the covalent synthesis of dendritic superstructures using a wide range of organic and inorganic methodologies. A variety of receptors such as dendritic porphyrins,[97] dendroclefts[98] and dendrophanes[99] have been used to bind diverse guest molecules.

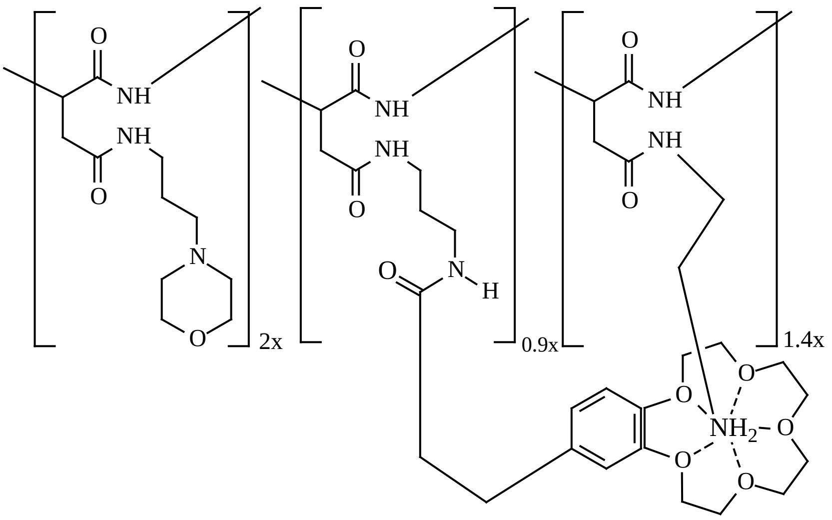
In a recent study,[63] 4’-(hydroxymethyl)benzo-15-crown-5 was anchored onto an insoluble elastomeric solid support *via* a diisocyanate linking group to give device **110**, as shown in Figure 2.7. Koortzen[63] found that when this crown ether moiety was supported onto an elastomeric solid support system, made from curing of hydroxy terminated polybutadiene (HTBP) with isophorone diisocyanate, the elastomeric crown ether device **(110)** could remove 0.264 g Na^+ / m^2 surface area of the sodium cation scavenging device.



110

Figure 2.7: The crown ether derivative grafted onto the polymeric solid support utilising a diisocyanate linking group, here shown to be isophorone-diisocyanate.

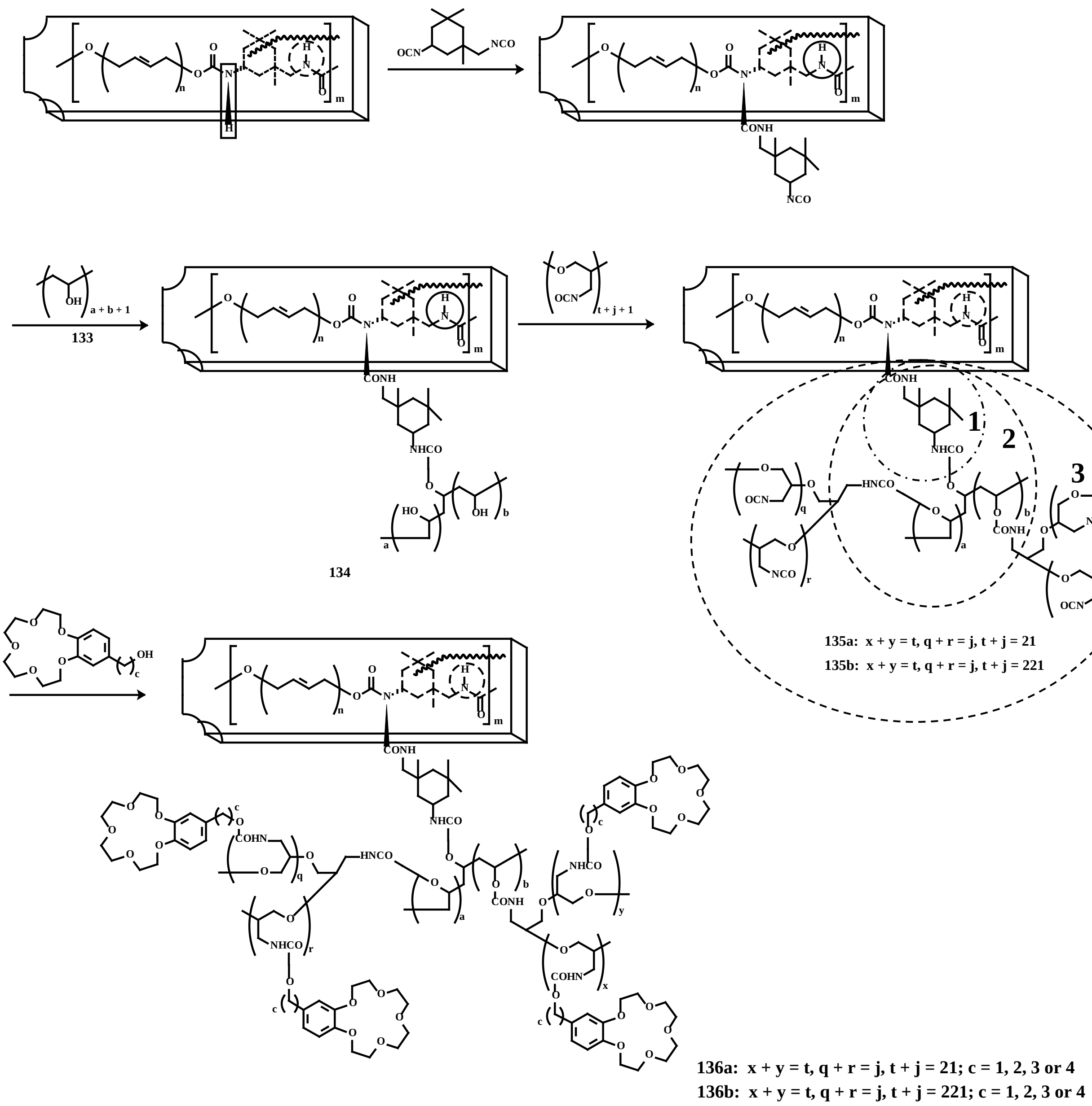
On the other hand, when 4’-(hydroxymethyl)benzo-15-crown-5 was anchored onto polyaspartic acid and some of its derivatives, Na^+ ion complexing abilities of the crown ether-device was only 0.098 g Na^+ / m^2 surface area of the sodium cation-scavenging device. These poor results were thought to be due to possible interaction of the free amines in the polymer with the empty crown ether cavity,[63] as shown in Figure 2.8, p.32.



47

Figure 2.8: The interaction between an amine and an empty crown ether cavity.

However, Swarts[2] found that the efficiency of the sodium scavenging devices, such as **110**, could be enhanced by increasing the surface area of the crown ether exposed to dissolved metal ions. When polyvinyl alcohol (72 000 g/mol) and polyisocyanate were also introduced between the elastomeric solid support and the crown ether, device **136** was developed, as shown in Scheme 2.18, p. 33. The efficiency of device **136**, to remove Na^+ ions is 1.28 g Na^+ / m^2 surface area of the sodium cation-scavenging device. The sodium cation-complexing effeciency of device **136**, in comparison with **110**, showed an improvement of more than 2 800 % in removing sodium cations from contaminated wastewater.

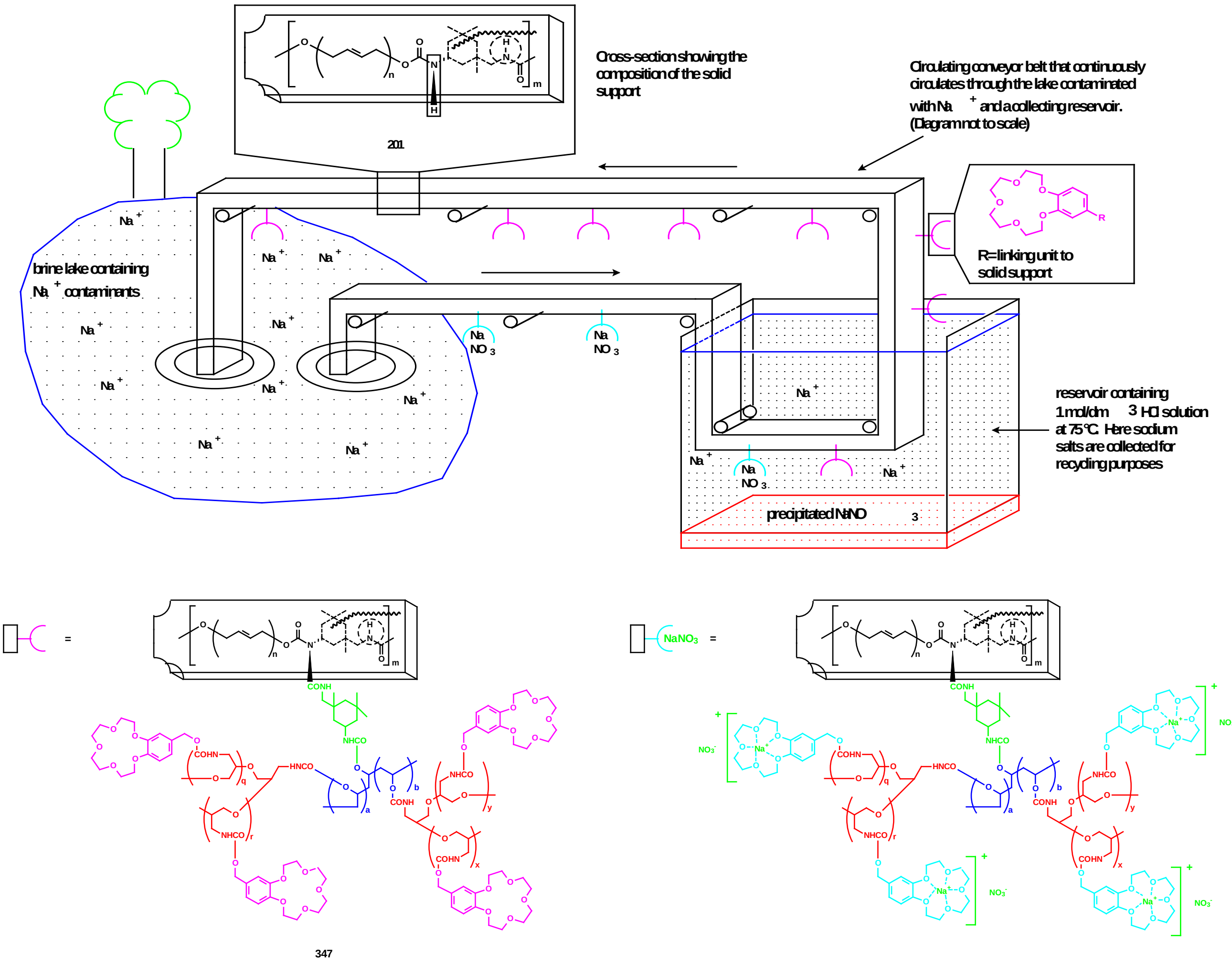


Scheme 2.18: Synthesis of a Na$^+$ scavenging devices heavily coated with crown ether moieties. The numbers 1, 2 and 3 identifies the first, second and third generation of the starburst (= polymeric dendrimer) structure (reference 2). The symbol 〰 is used to demonstrate that the solid support is a crosslinked polymer. Cross-linking arises from the hydroxy-content of 2.2 for hydroxy terminated polybutadiene.

Crucial to these substantial improvements in the binding efficiency of device **136** (Scheme 2.18) over device **110** was the use of the polymeric spacers as shown in the second and third generation of the starburst structure of polymer **135** (Scheme

2.18). The present study is focusing in more detail on these polymeric spacers as per the goals described in Chapter 1.

Figure 2.9 shows how a device such as **136** works. The solid-support works like a conveyer-belt. The macrocyclic ligand, attached to the solid support, complexes the metal ions as the conveyor-belt goes through contaminated wastewater effluents and releases these metal ions in a predetermined resevoir.



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 2.9: A schematic representation of the process of transferring Na^+ from a sodium aqueous phase to a suitable reservoir. This figure was reproduced with permission from University of the Free State from the PhD thesis of J. G. Koortzen (reference 63).

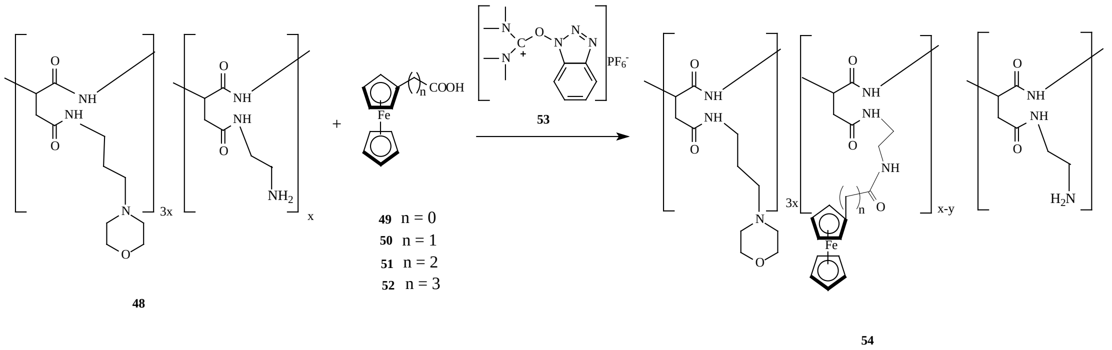
2.7 Polymer-bound ferrocene derivatives

Metal- and metalloid-containing compounds exhibit a wide range of biological and biocidal activities, some of which have been employed in medicines and drugs. Polymers containing metal or metalloid functions become a natural extension of this effort; just as organic compound drugs have been chemically bound to polymers or physically embedded into polymer matrices in order to provide a variety of useful advantages. With respect to this study, ferrocene derivatives are important.

The chemistry of ferrocene and its derivatives has been well documented.[100,101,102,103,104,105] Most ferrocene-containing compounds may be prepared from only a few starting materials. All reactants are easily prepared from ferrocene itself and are sufficiently versatile to be converted to many derivatives. The enhanced aromatic reactivity of the ferrocenyl group make possible a wide range of electrophilic substitution reactions, which can often be affected under mild conditions.[100,102]

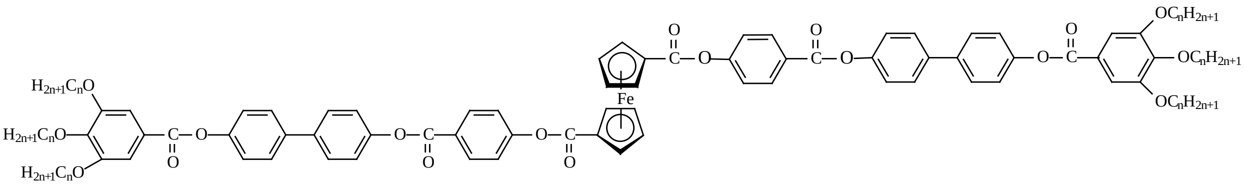
Water-soluble and biocompatible polymers containing bioreversibly attached ferrocene units, i.e. ferrocene units that can be bound and unbound from a polymeric carrier by biological processes, as side chain terminals have in recent years attracted interest in drug research. In preliminary biological screening experiments, polymers of this type showed high antiproliferative activity against selected human carcinoma cell lines, paired with low *in vivo* toxicity.[106] They may thus lend themselves as efficacious prodrugs in cancer chemotherapy.

According to Swarts *et al.*,[107] when ferrocene is covalently bound through *N*-acylation[108] to water-soluble substrates of polyaspartamide drug carriers containing amine functions as side-group terminals, amide groups are generated. The amide bond is a biofissionable bond that upon enzymatic cleavage, allows for the release of the free monomeric ferrocene compound from the polymeric carrier. The cell growth inhibition shown by these polymer-bound ferrocenyl derivatives compared very well with those of the square-planar structural skeleton of the cisplatin type anticancer drug system as the bioactive agent.

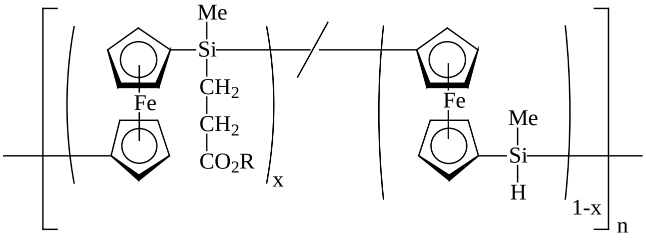


Scheme 2.19: The anchoring of carboxy-functionalised ferrocene derivatives onto water soluble polymer 48, y ≈ 0.1x , according to reference 107.

Ferrocene units are also of considerable interest as components of liquid-crystalline materials due to their high thermal stability, tunable redox characteristics and their structural variability which might lead to intriguing effects on mesophase morphology.[109] Metallomesogenic polymers, such as those shown in Figure 2.10, are particularly attractive as they have the potential to combine the advantageous properties of polymers (e.g. excellent mechanical properties, low thermal expansion, and excellent processibility) with those of transition-metal complexes (e.g. colour, polarizability, magnetic characteristics).[110,111]



56



57

Figure 2.10: Examples of metallomesogenic polymers containing ferrocene

These studies provide a healthy motivation for more extended studies on polymeric derivatives of ferrocene. In terms of this study, carboxylic acid functionalised derivatives of ferrocene were anchored onto amine-functionalised derivatives of polyepichlorohydrin to establish how easily new mesogens may interact with new polyepichlorohydrin derivatives.

---

[3] S. Inoue, T. Aida, Cyclic Ethers. Int*:* K. J. Ivin and T. Saegusa, editors, *Ring Opening Polymerization* , **vol. 1**, Elsevier Applied Science Publishers Ltd.; **1984**. pp. 185 [Chapter 4]

[4] S. Penzeck, P.Kubisa K. Matyjaszewski, Oxirane. Int: *Cationic ring opening polymerization Part II: synthetic applications. Advance polymer Science,* **vol. 68/69**. Berlin: Springer Verlag; **1985**, pp. 52 [Chapter 4]

[5] J. M. Hammond, J. F. Hooper, W. G. P. Reobertson, *J. Polym. Sci., Part A I,* **9 (1971)**, 265.

[6] B. Tadeusz, K. Przemyslaw, P. Stanislaw, *J. Polym. Sci., Part A: Polym Chem,* **29 (1991)**, 619

[7] E. J. Goethals, editor. *Telechelic polymers: synthesis and application,* CRC press, **1989**, p. 121

[8] A. U. Francis, S. Venkatachalam, Int: S. Venkatachalam, V. C. Joseph, R. Ramaswamy and V. N. Krishnamuurthy, editors. *Macromolecules: Current Trends,* New Delhi: Allied Publishers; **1995**, pp. 1

[9] A. U. Francis, S. Venkatachalam, In: S. Krishnan and S. K. Athitan, editors. *Propellants explosives rockets and guns(Proceedings of the Second International High Energy Materials Conference and Exhibit December 8-10,1998, IIT Madras, Chennai, India),* Chennai: Allied Publishers; **1998**, p. 253

[10] R. B. Merrifiled, *J. Am. Chem. Sci., 85,* **85 (1963)**, 2149

[11] A.U. Francis et al, *European Polymer Journal,* **39 (2003)**, 831

[12] M. B. Frankel and J. E. Flanagan, *US Patent 4 268 450,* **1981**

[13] G. E. Manser, *US Patent 4 393 199,* **1983**

[14] J. P. Kennedy and E. G. M. Törnquist, *Polymer Chemistry of Synthetic Elastomers,* Wiley: New York, **vol. 23 1973**, pp. 382

[15] K. J. Saunders, *Organic Polymer Chemistry,* Chapman and Hall Int. Ed., **1973**, pp. 162

[16] E. M. Fettes, Ed., *Chemical Reaction of Polymers,* Wiley Interscience: New York, **1964**

[17] J. M. J. Frechet, and M. J. Farrall, *Chemistry and Properties of Crosslinked Polymers* (ed. S. S. Labana), Academic press: New York, **1977**, p. 59

[18] J. A. Moore, ed., *Reaction of Polymers,* D. Reidel: Boston, MA., **1973**

[19] R. W. Lenz, *Organic Chemistry of Synthetic High Polymers,* Wiley Interscience: New York, **1967**, [Chapter 17]

[20] L. D.Loan and F. H. Winslow, *Reactions of Macromolecules,* in *Macromolecules: An Introduction to Polymer Science* (eds. F. A. Bovey and F. H. Winslow), Academic Press: New York, **1979**, [Chapter 7]

[21] R. J. Ceresa, *The chemical modification of polymers,* in *Science and Technology of Rubber* (ed. F. R. Eirich), Academic Press: New York, **1978**, [Chapter 11]

[22] E. F. V. Scriven, K. Turnbull, *Chem. Rev.,* **88 (1988)**, 351

[23] Y. Nakajima, J. Oda, Y. Inouye, *Tetrahedron Lett.,* **34 (1978)**, 3107

[24] J. March, *Advanced Organic Chemistry,* 4th ed., Wiley: New York, **1992**, pp. 428

[25] J. A. Miller, *Tetrahedron Lett.,* **(1975)**, 2959

[26] A. Hassner, R. Fibiger, D. Andisik, *J. Org. Chem.,* **49 (1984)**, 4237

[27] G. Adam, J. Andrieux, M. Plat, *Tetrahedron,* **41(1985)**, 399

[28] J. March, *Advance Organic Chemistry,* 4th ed., Wiley: New York, **1992**, p. 429

[29] J. March, *Advance Organic Chemistry,* 4th ed., Wiley: New York, **1992**, pp. 1091

[30] S. Ozaki, *Chem. Rev.,* **72 (1972)**, 457; H. J. Twitchett, *Chem. Soc. Rev.,* **3 (1974)**, 209

[31] *Organic Syntheses,* **III**, 846-847, **IV**, pp. 819

[32] J. March, *Advance Organic Chemistry,* 4th ed., Wiley: New York, **1992**, pp. 1219

[33] E. J. Corey, K. C. Nicolaou, R. D. Balanson, Y. Machida, *Synthesis,* **(1975)**, 590

[34] J. March, *Advance Organic Chemistry,* 4th ed., Wiley: New York, **1992**, pp. 1212

[35] G. W. Kabalka, P. P. Wadgoankar, N. Chatla, *Synth. Commun.,* **20 (1990)**, 293

[36] T. Satoh, S. Suzuki, Y. Suzuki, Y. Miyaji, Z. Imai, *Tetrahedron Lett.,* **(1969)**, 4555; A. Rahman, A. Basha, N. Waheed, S. Ahmed, *Tetrahedron Lett.,* **(1976)**, 219; M. E. Kuehne, P. J. Shannon, *J. Org. Chem.,* **42 (1977)**, 2082; S. R. Wann, P. T. Thorsen, M. M. Kreevoy, *J. Org. Chem.,* **46 (1981)**, 2579; S. B. Mandal, V. S. Giri, S. C. Prakashi, *Synthesis,* **(1987)**, 1128

[37] H. C. Brown, P. Heim, *J. Org. Chem.,* **38 (1973)**, 912; S. Krishnamurthy, *Tetrahedron Lett.,* **23 (1982)**, 3315

[38] P. Strazzolini, A. G. Giumanini, S. Cauci, *Tetrahedron,* **46 (1990)**, 1081

[39] A. R. Katritzky, H. X. Chang, B. Yang, *Synthesis,***(1995)**, 503

[40] J. Barluenga, P. J. Campos, E. Gonzalez-Nuňenz, G. Asensio, *Synthesis,* **(1985)**, 426

[41] G. A. Olah, L. Ohannesian, M. Arvanaghi, *Chem. Rev.,* **87 (1987)**, 671

[42] J. March, *Advance Organic Chemistry,* 4th ed., Wiley: New York, **1992**, pp. 542

[43] *Organic Syntheses,* **II**, pp. 98, **IV**, pp. 331; pp. 539; pp. 915

[44] *Organic Syntheses,* **III**, pp. 549

[45] *Organic Syntheses,* **III**, pp. 463

[46] *Organic Syntheses,* **IV**, pp. 866

[47] G. Casiraghi, G. Casnati, G. Puglia, G. Sartofi, G. Terenghi, *J. Chem. Soc.*, **Perkin Trans. (1980),** 1862

[48] S. Jo, S. Taimoto, T. Sugimoto, M. Okano, *Bull. Chem. Soc. Jpn,* **54 (1981)**, 2120

[49] J. March, *Advance Organic Chemistry,* 4th Ed., Wiley: New York, **1992**, pp. 910

[50] J. March, *Advance Organic Chemistry,* 4th Ed., Wiley: New York, **1992**, pp. 1209

[51] *Organic Syntheses,* **II,** 499-501, **III,** pp. 444, pp. 786; **IV**, pp. 203

[52] *Organic Syntheses,* **IV**, pp. 510-512

[53] Huang-Minlon, *J. Am. Chem. Soc.,* **68 (1946)**, 2487; Huang-Minlon, *ibid***, 71 (1949),** 3301

[54] E. J. Vandenburg, *Polymers Containing Azidomethylside Chains,* US Patent 3 645 917, **1972**

[55] M. B. Frankel, E. R. Wilson and D. O. Woolery, *European Patent 0 296 310,* **1988**

[56] I. B. Mishra, D. E. Rickenbaugh, C. L. Ashmore, A. K. Mehrotra-Dev, *GAP-TAGN-PEG Propellant-Part 1 – Study of Ingredients Vol. II; JANNAF Propulsion meeting,* New Orleans: LA, John Hopkins University Chemical Propulsion Information Agency, **1984**, pp. 153

[57] N. Kubota, Combustion Mechanism of Azide Polymer, *Prop. Explos. Pyro.,* **13 (1988)**, 172

[58] N. Kubota, T. Sonobe, A. Yamamoto, H. Shimuzu, *J. Prop. Power,* **6 (1990)**, 686

[59] H. Tokui, T. Saitoh, K. Hori, K. Notono, A. Iwama, *Synthesis and Physico-Chemical Properties of GAP and the Application of GAP/AN Based Propellants to a small Motor, 21st Int. Conf. ICT,* Karlsruhe: Gemany, Fraunhofer Insitut für Chemische Technologie, **1990**, Section: 7-1

[60] A. Leu, S. Shen, B. Wu, *Thermal Characteristics of GAP/BDNPA/BDNPF and the Energetic Composites, 21st Int. Ann. Conf. ICT,* Karlsruhe: Germany, Fraunhofer Insitut für Chemische Technologie, **1990,** Section: 6-1

[61] R. L. Millar, A. G. Stern, R. S. Day, *US Patent 5 017 356,* **1992**

[62] H. J. Desai, A. V. Cunliffe, R. W. Millar, N. C. Paul, M. J. Stewart, A. J. Amass, *Polymer,* **37 (1996)**, 3471

[63] J. C. Swarts, J. G. Koortzen, Unpublished Results

[64] C. J. Pedersen, *J. Am. Chem. Soc.,* **89 (1967)**, 7017

[65] C. J. Pedersen, *J. Am. Chem. Soc.,* **89 (1967)**, 2495

[66] J. S. Bradshaw, R. M. Izatt, A. V. Bordunov, C. Y. Zhu, J. K. Hathaway, *Crown Ethers;* J. S. Bradshaw, R. M. Izatt, A. V. Bordunov, C. Y. Zhu, J. K. Hathaway, Ed.; Pergamon, **vol. 1**, **1997**, pp. 35

[67] G. W. Gokel, *Crown ethers and Cryptands;* The Royal Society of Chemistry: Cambridge, **1991**

[68] N. N. Greenwood, A. Earnshaw, in: *Chemistry of the Elements,* Pergamon Press Inc: Tarrytown, **1984**, pp.105

[69] B. Fabre, J. Simonet, *Coordin. Chem. Rev.,* **178-180 (1998)**, 1211

[70] R. W. Saalfrank, N. Low, S. Kareth, V. Seitz, F. Hampel, D. Stalke, M. Teichert, *Angew. Chem.,* Int. Ed. **37 (1998)**, 172

[71] R. G. Pearson, *J. Am. Chem. Soc.,* **85 (1963)**, 3533

[72] R. G. Pearson, *Science,* **151 (1966)**, 172

[73] S. D. Alexandratos, *Sep. Purif. Meth.,* **21 (1992)**, 1

[74] Z. Zong, S. Dong, Y. Hu, Y. Xu, W. Liu, *Eur. Polym. J.,* **34 (1998)**, 761

[75] E. Weber, *Phase Transfer Catalyst, Merck,* **1995**, pp. 34

[76] R. M. Izatt, J. S. Bradshaw, S. A. Nielsen J. D. Lamb, J. J. Christensen, D. Sen, *Chem. Rev.,* **85 (1985)**, 271

[77] U. Tunca, Y. Yagci, *Prog. Polym. Sci.,* **19 (1994)**, 233

[78] J. M. J. Frechet, *Tetrahdron,* **37 (1981)**, 663

[79] T. F. Baumann, J. G. Reymolds, G. A. Fox, *React. Funct. Polym.,* **44 (2000)**, 111

[80] T. F. Baumann, J. G. Reymolds, G. A. Fox, *Chem. Commun.,* **(1998)**, 1637

[81] S. D. Alexandratos, D. W. crick, *Ind. Eng. Chem. Res.,* **35 (1996)**, 635

[82] J. C. Salamone (Ed.), *Polymeric Materials Encyclopedia,* CRC Press, Boca Raton, **vol. 2**, **1996**

[83] J. S. Bradshaw, R. L. Bruening, K. E. Krakowiak, B. J. Tarbet, B. J. Bruening, R. M. Izatt, J. J. Christensen, *J. Chem. Soc. Chem. Commun.,* **(1988)**, 812

[84] E. Ph. Horwitz, M. L. Dietz, R. Chiarizia, *J. Radioanal. Nucl. Chem., Articles,* **161**, **(1992)**, 575

[85] M. Cinouini, S. Colonna, H. Molinari, F. Montanari, *J. Chem. Soc. Chem. Commun.,* **(1976)**, 394

[86] F. Montanari, P. Tundo, *J. Org. Chem.,* **46 (1981)**, 2125

[87] P. L. Anelli, B. Czech, F. Montanari, S. Quici, *J. Chem. Soc.,* **106 (1984)**, 861

[88] M. Tomoi, N. Yanai, S. Shiki, H. Kakiuchi, *J. Polym. Sci.,* **Polym. Chem. Ed. 22 (1984)**, 911

[89] M. J. Pugia, A. Czech, B. P. Czech, R. A. Bartsch, *J. Org. Chem.,* **51 (1986)**, 2945

[90] M. Tomoi, in J. C. Salamone (ed.), *Polymeric Materials Encyclopedia,* CRC Press, Boca Raton: FL, **vol. 2**, **1996,** p. 1580

---

[91] L. Collie, J. E. Denness, D. Parker, F. O'Carroll, C. Tachon, J. Chem. Soc., **Perkin Trans. 2 (1993)**, 1747

[92] G. Zimhlet, M. J. F. Leroy, J .P. Brunette, Y. Frere, Ph. Gramain, *Sep. Sci. Technol*, **28 (1993)**, 2419

[93] P. M. van Berkel, W. L. Driessen, A. A. Kodhaas, J. Reedjik, D. C. Sherrington, *J. Chem. Soc., Chem. Coomun.*, **(1995)**, 147

[94] Y. Gotoh, Y. Kohno, W. Fukuda, M. Tomoi, *J. Polym. Sci.: Part A: Polym. Chem.*, **32 (1994)**, 1543

[95] A. Favre-Régullion, N. Dumont, B. Dunjic, M. Lemaire, *Tetrahedron,* **53 (1997)**, 1343

[96] G. R. Newkome, C. N. Moorefield, F. Vögtle, *Dendrimers and dendrons, Concepts, Applications,* VCH: Weiheim, **2001**

[97] D. L. Jiang, T. Aida, *Chem. Commun.*, **(1996)**, 1523; J. P. Collman, L. Fu, A. Zingg, F. Diederich, *Chem. Commun.*, **(1997)**, 193; A. Zingg, B. Felber, V. Gramlich, L. Fu, J. P. Collman, F. Diederich, *Chim. Acta*, **85 (2202)**, 333

[98] D. K. smith, F. Diederich, *Chem. Commun.*, **(1998)**, 2501; D. Smith, A. Zingg, F. Diederich, *Helv. Chim. Acta,* **82 (1995)**, 1225; A. Bähr, B. Felber, K. Schnieder, F. Diederich, *Helv. Chim. Acta,* **83 (2000)**, 1346

[99] S. Mattei, P. Seiler, F. Diederich, V. Gramlich, *Helv. Chim. Acta,* **78 (1995)**, 1904; S. Mattei, P. Wallimann, B. Kenda, W. Amrein, F. Diederich, *Helv. Chim. Acta,* **80 (1997)**, 2391; T. Habicher, F. Diederich, V. Gramlich, *Helv. Chim. Acta,* **82 (1999)**, 1066

[100] M. Rosenblum, *Chemistry of the Iron Group Metallocenes,* Part I, Wiley-Interscience: New York, **1965**, pp. 201

[101] E. W. Neuse and H. Rosenberg in *Reviews In Macromolecular Chemistry,* eds. K. F. O'Driscoll and M. Shen, Marcel Dekker: New York, **vol. 5**, **1970**

[102] D. E. Bublitz and K. L. Rinehart Jr., *Organic Reactions,* **17 (1969)**, 1

[103] G. Wilkinson, *Comprehensive Organometallic Chemistry,* Pergamon Press: Oxford, **1988, vol. 4,** [Chapter 31] and **vol. 8**, [Chapter 59]

[104] D. W. Mango, P. D. Shaw, and M. D. Rausch, *Chem. Ind. (London),* **(1957)**, 1388

[105] R. W. Fish and M. Rosenblum, *J. Org. Chem.*, **30 (1965),** 1253

[106] M. T. Johnson, E. Kreft, D. D. N'Da, E. W. Neuse, C. E. J. van Rensburg, *J. Inorg. Org. Polym.*, **13 (2003)**, 255

[107] J. C. Swarts, E. W. Neuse, G. J. Lamprecht, *J. Inorg. Org. Polym.*, **4 (1994),** 143

[108] V. Dortoglou, B. Gross, V. Lambropolou, C. Zioudrou, *Synthesis*, **(1984)**, 572

[109] R. Deschenaux and J. W. Goodby, *Ferrocenes,* editors. A. Togni and T. Hayashi, VCH, Weiheim, **1995,** [Chapter 9]

[110] L. Oriol and J. L. Serrano, *Adv. Mater.*, **7 (1995),** 348

[111] M. Altmann and U. H. F. Bunz, *Angew. Chem. Int. Ed. Engl.*, **34 (1995)**, 569; R. Deschenaux, I. Kosztics, J. L. Marenda, H. Stoecklei-Evans, *Chemia,* **47 (1993)**, 206; M. Altmann, V. Enkelmann, G. Leiser and U. H. F. Bunz, *Adv. Mater.*, **7 (1995)**, 726; A. A. Dembek, R. R. Burch, A. E. Feiring, *J. Am. Chem. Soc.*, **115 (1993)**, 2087

3.1 Introduction

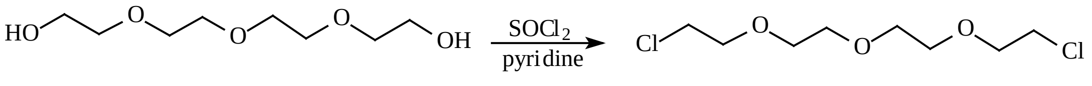
In this chapter, the research results of this study are ordered firstly to present a discussion on the synthesis and functionalisation of crown ethers, followed by the polymerisation of epichlorohydrin to polyepichlorohydrin. These discussions are followed by describing how the cited polyepichlorohydrin with chloro-containing side chains can be re-functionalised to azide-, amine-, isocyanate- and hydroxy-containing side chains. This is followed by presenting the results of the anchoring experiment of ferrocene-containing carboxylic acid onto an amine functionalised polymer *via* an amide bond to give ferrocene-containing polymers. The discussion is concluded by discussing model isocyanate reactions whereby isocyanate functionalised compounds are reacted with hydroxy-functionalised monomers and polymers.

3.2 Synthesis and functionalisation of crown ethers

3.2.1 Preparation of benzo-15-crown-5

The dialcohol precursor, tetraethylene glycol **(58)**, used in the synthesis of benzo-15-crown-5 **(29)** was first converted to the dichloride **59** (Scheme 3.1) using the general chlorination procedure described by Pedersen**Error! Bookmark not defined.** and thionyl chloride as the chlorinating reagent.

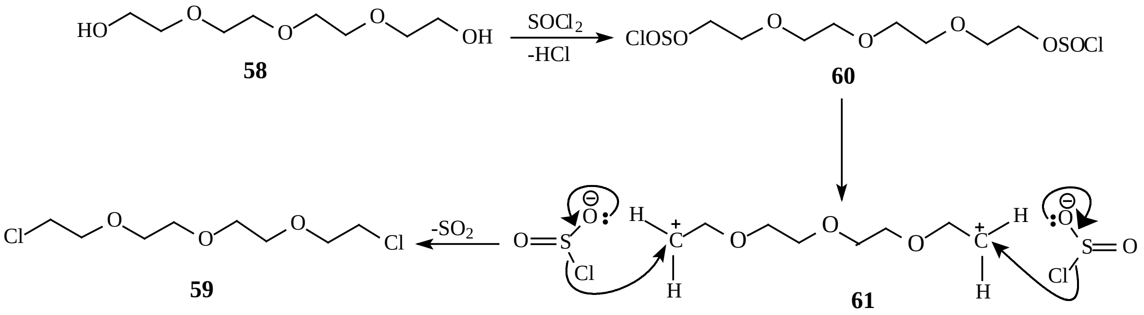
During this reaction, precursor **58** was changed from one containing a poor-leaving group, i.e. the alcohol group, to one containing a better-leaving group, i.e. the chloride group.



58 **59**

Scheme 3.1: The chlorination of tetraethylene glycol (58) to produce 1,11-dichloro-3,6,9-trioxaundecane (59).

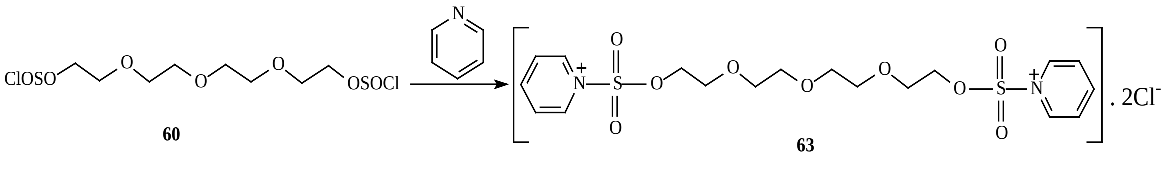
The first step in the reaction between alcohols and thionyl chloride is the formation of an alkyl chlorosulphite, such as **60** shown in Scheme 3.2. Conversion of the alkyl chlorosulphite **(60)** to an alkyl chloride **(59)** involves an internal S_N1 mechanism (*substitution nucleophilic internal*),[112] 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[113] involving SO_2Cl^- and a carbocation as in **61**. Then, in the second step, the Cl part of the SO_2Cl^- group 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 **59** and concomitant SO_2 release.



Scheme 3.2: The S_N1 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 removal of gaseous by-products drives the reaction to completion and the yields of these chlorination reactions are usually high (> 90 %).

When pyridine was added as a catalyst and HCl scavenger to the reaction, the intermediate alkyl chlorosulfite **(60)** reacted with the pyridine to produce **63**, as can be seen in Scheme 3.3.

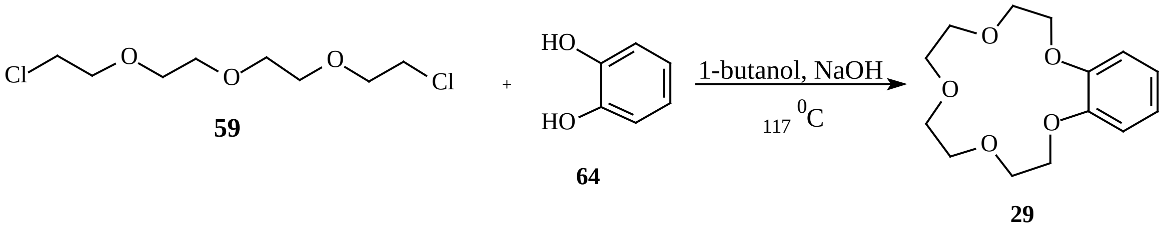


Scheme 3.3: The reaction between pyridine and the alkyl chlorosulphite (60).

1,11-Dichloro-3,6,9-trioxaundecane **(59)**, (Scheme 3.2), was obtained as an oily liquid that was in pure form after washing of the toluene solution with water and solvent removal.

It is important to mention that the reactions were done in both benzene[1] and toluene. Though benzene is a lower boiling solvent that offered easier refluxing and solvent removal than toluene, no significant changes (in terms of yields) were observed when toluene was used as a solvent. Both solvents gave yields within the same range. It follows that the carcinogenic solvent benzene can be safely replaced with the safer solvent toluene in this reaction.

Although it is possible to condense dialcohols, such as tetraethylene glycol **(58)** with catechol **(64)**, 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 **(59)** with catechol **(64)** in the presence of NaOH to produce benzo-15-crown-5 **(29)**, as indicated in Scheme 3.4, is much higher yielding reactions.



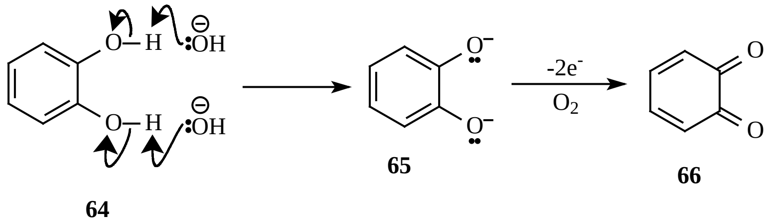
Scheme 3.4: The synthesis of benzo-15-crown-5 (29) by the condensation reaction between 1,11-dichloro-3,6,9-trioxaundecane (59) and catechol (64).

Synthesis of benzo-15-crown-5 **(29)** in the presence of air was found to lower yields of **29** substantially, and therefore the reaction was performed under a nitrogen atmosphere. Often when the reaction was done 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 **(66)**, as shown in Scheme 3.5, p. 42, in the reaction mixture due to base-catalysed oxidation of catechol by oxygen. No formation of a green

---

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

colour was observed when catechol was mixed with NaOH under oxygen-free conditions, i.e. under a nitrogen atmosphere.



Scheme 3.5: The formation of *o*-quinone (66) due to oxidation of the dianion of catechol (64) by oxygen.

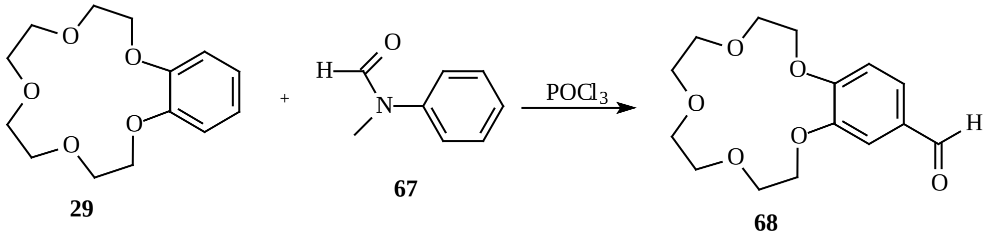
The synthesis of benzo-15-crown-5 **(29)** requires a base. Here, the hydroxyl anion is used to deprotonate catechol to produce a nucleophile that is able to attack 1,11-dichloro-3,6,9-trioxaundecane **(59)**. Based on the principle of the “template effect” (see Chapter 2, p. 27), NaOH was used as the base. The Na^+ ion promotes cyclisation to benzo-15-crown-5 over linear condensation products.

The synthetic procedure for benzo-15-crown-5 **(29)** produced a dark black, highly viscous liquid. Extraction of benzo-15-crown-5 **(29)** from this dark black liquid was achieved with hot hexane or by soxhlet extractor utilising hexane for larger scale (> 10 g) reactions. Recrystallisation was from warm hexane. Benzo-15-crown-5 **(29)** is only moderately soluble in warm hexane, and when cooled benzo-15-crown-5 **(29)** crystallised as white needles. The obtained yields were relatively high (50 – 60 %).

3.2.2 Functionalisation of benzo-15-crown-5

In order to covalently attach benzo-15-crown-5 **(29)** to polymeric carriers, it is necessary to functionalise this crown ether moiety. To achive this, an alcohol-containing side chain was introduced onto the crown ether molecule by first synthesising 4’-formyl-benzo-15-crown-5 **(68)** and then by reducing the aldehyde to an alcohol with sodium borohydride.

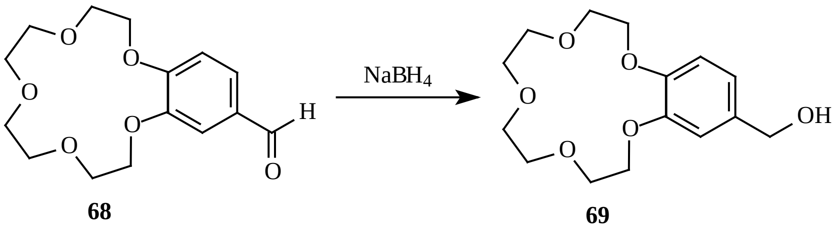
4’-Formylbenzo-15-crown-5 **(68)** was synthesised under Vilsmeier-Haack conditions[42] according to Scheme 3.6, p. 43.



Scheme 3.6: The synthesis of 4’-formylbenzo-15-crown-5 (68).

Crude 4’-formylbenzo-15-crown-5 **(68)** was isolated by soxhlet extraction utilising hexane. Recrystallisation of the crude product with warm hexane afforded pure 4’-formylbenzo-15-crown-5 **(68)**. This purification method of 4’-formylbenzo-15-crown-5 **(68)** showed a drastic increase in the overall yield of **68** when compared to the method of aldehyde purification where sodium hydrogen sulphite is used to purify the product. The yields obtained were between 50 – 60 % and gave 4’-formylbenzo-15-crown-5 **(68)** as a white crystalline solid.

To obtain the alcohol-functionalised benzo-15-crown-5 derivative **(69)**, 4’-formylbenzo-15-crown-5 **(68)** was reduced with sodium borohydride, as shown in Scheme 3.7, to produce 4’-(hydroxymethyl)benzo-15-crown-5 **(69)** as a white solid.



Scheme 3.7: The synthesis of 4’-(hydroxymethyl)benzo-15-crown-5 (69) by the treatment of 4’-formylbenzo-15-crown-5 (68) with NaBH$_4$.

Upon comparing the ^{1}H NMR spectra of the aldehyde **68** with that of the alcohol **69** several changes were obvious. First of all, the –C$\underline{H}$O signal at 9.88 ppm in the spectrum of **68** disappeared and the C$\underline{H}_2$-OH signal of the alcohol appeared at 4.57 ppm (Figure 3.1, p. 44). Subtle changes in the aromatic signals were also observed. In the case of **68**, where an electron withdrawing carbonyl group is bound to the phenyl ring, resonance of the aromatic protons adjacent to the carbonyl group resulted in the signals at 7.4 – 7.6 ppm. Upon reducing the aldehyde to an alcohol side chain, the aromatic protons all resonated at the same frequency to give signals at 6.85

ppm. This clearly demonstrates that the electron-withdrawing carbonyl group moves the signals to lower field but that the electron-donating methylene group moved the signals of the aromatic protons to a relatively higher field position. However, the aldehyde and alcohol side chains did not appreciably change the signal position of the O-C$\underline{H}_2$-C$\underline{H}_2$-O group.

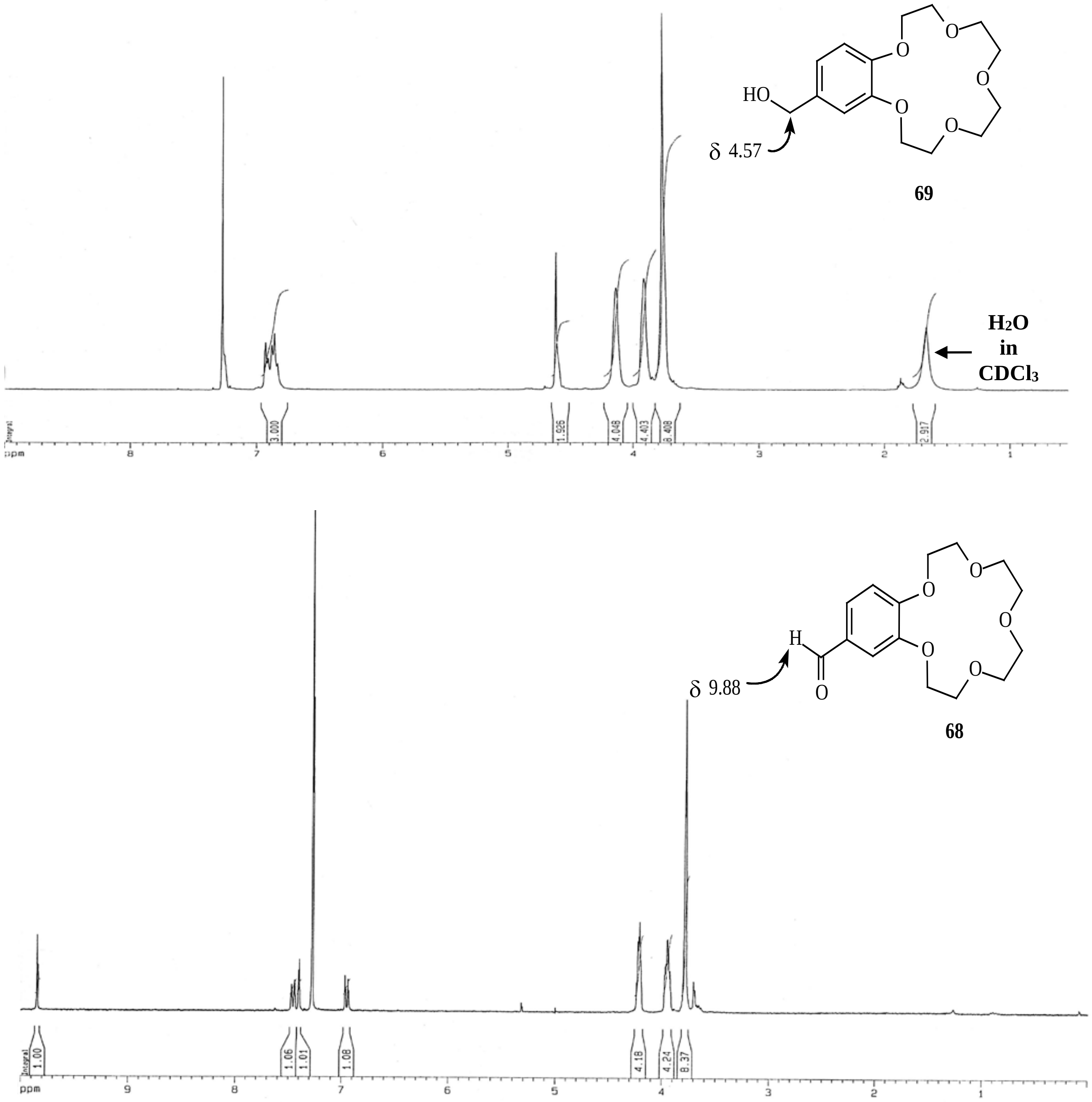
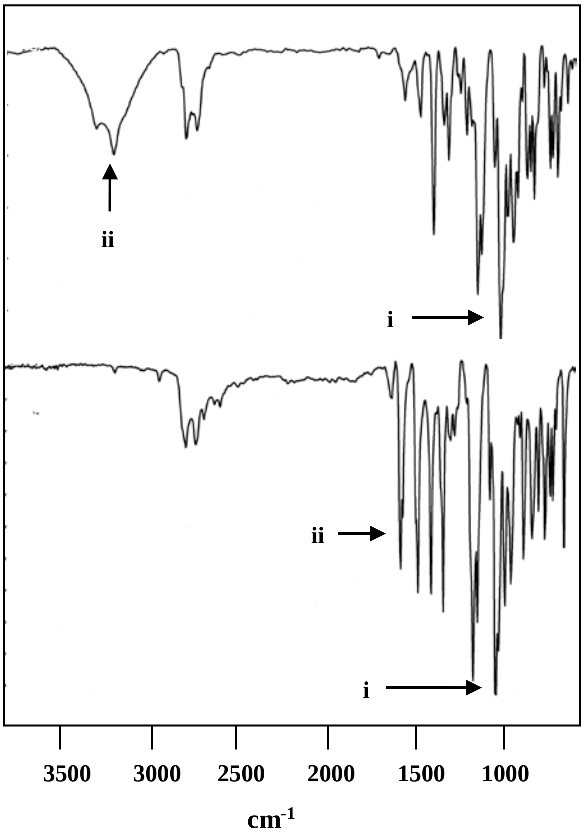


Figure 3.1: ^{1}H NMR spectra of 4’-formylbenzo-15-crown-5 (68) and 4’-(hydroxymethyl)benzo-15-crown-5 (69) in CDCl$_3$.

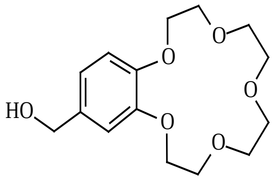
The introduction of an alcohol-containing side chain in **69** lowered the melting point (m.p.) of benzo-15-crown-5 **(29)** from 75 to 45 ^{0}C. This happened because the alcohol side chain enhanced the amorphous character of the crown ether. In contrast, the aldehyde group in **68** raised the melting point to 81 ^{0}C. This happened as a result of the polar carbonyl group that enhanced formation of van der Waals forces in the crystal structure of **68** and thereby increasing the crystalline behaviour and melting point of this benzo-15-crown-5 derivative.

Figure 3.2 shows the difference in IR spectrum as the carbonyl group in 4’-formylbenzo-15-crown-5 **(68)** is reduced with sodium borohydride to an alcohol group in 4’-(hydroxymethyl)benzo-15-crown-5 **(69)**. Most notable is the strong carbonyl signal at 1 600 cm^{-1} for the aldehyde that disappears when an alcohol is introduced, and the strong, broad -OH signal that appears at 3 353 cm^{-1} in the spectrum of the alcohol.



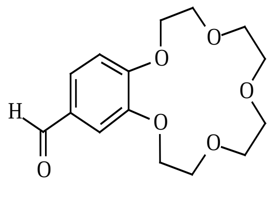
Peak assignment

i. 1 100 (C-O)
ii. 3 353 (-OH)



69

i. 1 090 (C-O)
ii. 1 600 (C=O)



68

Figure 3.2: IR spectrum (relative % transmission *versus* wavenumber) of 68 and 69 showing the emergence of a hydroxy peak at 3 353 cm^{-1} as 68 is reduced to an alcohol.

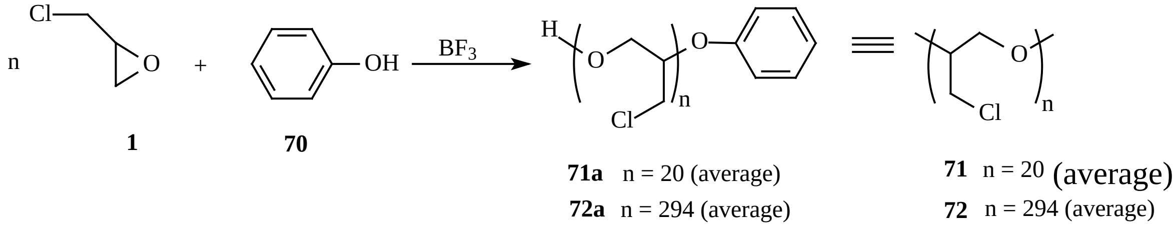
4’-(Hydroxymethyl)benzo-15-crown-5 **(69)** may be anchored, for example, onto a polymeric carrier that has an isocyanate functional group on it *via* a urethane bond, or to an acid-functionalised polymer *via* an ester bond. For the purpose of this study 4’-(hydroxymethyl)benzo-15-crown-5 **(69)** with only one methylene spacer between the crown ether moiety and the hydroxy functional group was synthesised. However, other research in this laboratory varied the number of methylene spacers from one to four.**Error! Bookmark not defined.**

3.3 Polymer synthesis and re-functionalisation

3.3.1 Polymerisation of epichlorohydrin

Having synthesised and functionalised benzo-15-crown-5 as described above, attention was focused on the synthesis of polymers that could be used as polymeric spacers between a solid support and the crown ether as discussed in Chapter 1. For the purpose of this study, it was decided to concentrate on the synthesis and modification of polyepichlorhydrin.

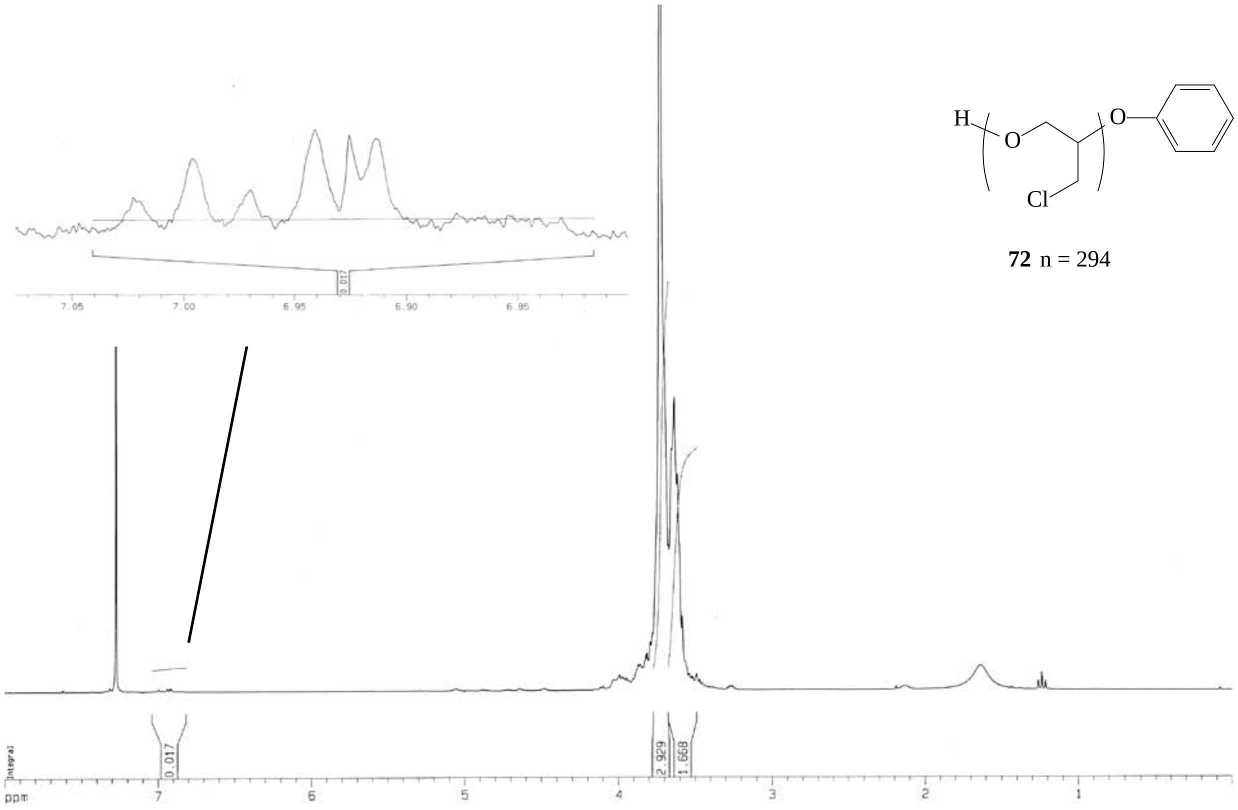
Polymerisation of epichlorohydrin **(1)** by a cationic ring-opening mechanism, according to Scheme 3.8, p. 47, in the presence of BF_3 as an initiator and phenol **(70)** as a co-initiator, led to polyepichlorhydrin (**71a)** and **(72a)**. For this study, a mono-hydroxy-terminated polyepichlorohydrin was prepared to proficiently achieve goal 2 of this study (Chapter 1, p. 4), hence, phenol was used as a co-inititiator.



Scheme 3.8: The synthesis of polyepichlorohydrin (71a) and (72a). Throughout this thesis whenever reference to polyepichlorohydrin (71) and (72) is made, it is understood to be polymers 71a and 72a respectively. For simplicity, the full structure of both polyepichlorohydrin (71a) and (72a) will hereafter be simplified by 71 and 72 respectively. As described in the footnote on p. 8 of Chapter 2, structure 71 and 72 and their derivatives described hereafter are indicated to have undergone head-tail monomer binding sequence. However, there are also some head-head and tail-tail binding sequences in the backbone of these polymers. For the purpose of this study, structures 71, 72 and their derivatives described later on, are meant to explicitly imply a random mixture of all possible binding modes.

After 24 hours of reaction, polyepichlorohydrin derivatives **(71)** and **(72)** were obtained as colourless and highly viscous liquids soluble in dichloromethane. Polymers **71** and **72** contain alkyl side chains with a chlorine atom attached to each of them.

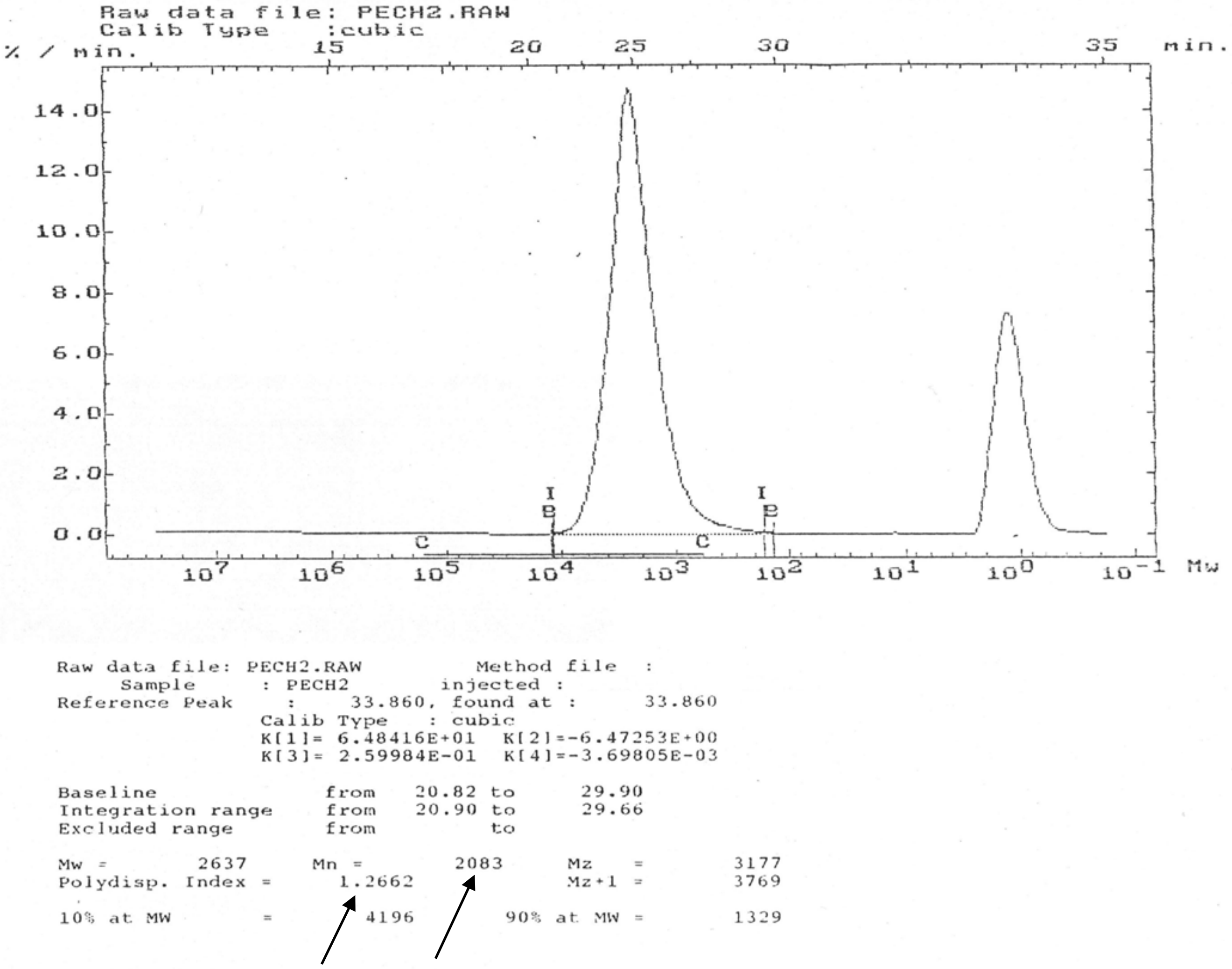
In the ^{1}H NMR spectra of **71** and **72**, the five protons of the epichlorohydrin repeating unit $[-CH(CH_2Cl)CH_2O-]_n$ are represented by two signals, positioned almost on top of each other and integrating for 5 in the region 3.6 - 4.05 ppm, as shown for **72** in Figure 3.3, p.48. The signal in the region 6.87 – 6.99 represents the aromatic protons of the terminal phenyl ring in the polymer.



72 n = 294

Figure 3.3: ^{1}H NMR spectrum of polyepichlorohydrin (PECH, 72) in $CDCl_3$.

The molecular mass of **71** was determined, with the help of Somchem, using Size Exclusion Chromatography (SEC) molecular mass determination technique. As shown in Figure 3.4, p. 49, the average molar mass of **71** was found to be 2 083 g mol^{-1}. The average molecular mass found for **71** using this technique was relatively close to the target molar mass of 2 000 g mol^{-1}. A polydispersity index (ratio M_w / M_n) of 1.2662 was found, which is very good.



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

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

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

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

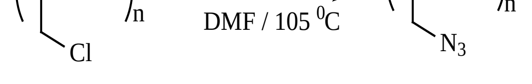
Figure 3.4: The molecular mass distribution and polydispersity of 71 in a synthesis where the target molar mass was 2 000 g mol^{-1}.

The molecular mass of polyepichlorohydrin **(71)** and **(72)** can also be determined using ^{1}H NMR spectroscopy. Utilising the ^{1}H NMR spectrum of **72**, the following method was used to calculate the number average molecular mass of polyepichlohydrin **(72a)**: in the region 6.79 – 7.04 ppm, as seen in Figure 3.3, p. 48, the signals representing the aromatic protons of the terminal phenyl ring are found. The integral value of 0.017 must therefore be corresponding to these five phenyl protons. ^{1}H NMR signals observed at 3.4 – 4.0 ppm correspond to the protons adjacent to the ether linkage and adjacent to the chloride atom, i.e. protons of the epichlorohydrin repeating unit. The integral value of 5 must therefore correspond to the five protons of the epichlorohydrin repeating units in polymer **72**. If one multiply the integral at 6.79 – 7.04 ppm to make it 5, i.e. to make it the same number as the five phenyl protons, the integral at 3.45 – 3.81 ppm then becomes 1470. Keeping in mind that each of the epichlorohydrin repeating units has 5 protons, there are therefore 1470 / 5 = 294 epichlorohydrin repeating units in polyepichlorohydrin **(72)**, i.e. n = 294. The total number average molar mass of polymer **72**, containing 294 epichlorohydrin units and 1 phenyl unit in the backbone, correspond to (294 x 92.5245 g mol^{-1}) + 94.11 = 27 296 g mol^{-1}, which is a molar mass slightly higher than the actual target molar mass of 20 000 g mol^{-1}. The M$_r$ of **71** from its^{1}H NMR spectrum was much more accurate. Using ^{1}H NMR spectroscopy the Mr of **71** was found to be 1 940, which compares very well with the value of 2 083 obtained by size exclusion chromatography (Figure 3.4).

3.3.2 Azide-functionalised polymer synthesis

The first approach in re-functionalisation of polyepichlorohydrin, as stated in goal 2 of Chapter 1, p. 4, was to re-functionalise the chloro-containing alkyl side chains of polyepichlorohydrin to get a polymer with azide-containing side chains, i.e. poly(glycidyl azide) (GAP).

Azide-containing polymers **(74)** and **(75)** were successfully prepared by S$_N$2 displacement[114] of the chloride ion with an azide ion by heating for 16 hours in *N*,*N*-dimethyl formamide (DMF) at 105 ^{0}C, as shown in Scheme 3.9. The reaction was conducted in the presence of potassium carbonate (K_2CO_3) as a base to neutralise HN_3, which is a by product of the reaction, and tetrabutylammonium bromide as phase-transfer catalyst. Substitution of chloride, Cl^-, ions with azide, N_3^-, ions poses a variety of health[115] and explosion hazards. For this study sodium azide was used as a source of azide anions because it has been reported to be a more stable azide salt.[116]



71 n = 20, Mr = 2 083

72 n = 294, Mr = 27 296

73 n = 7600, Mr = 700 000

74 n = 20, Mr = 1 981

75 n = 227, Mr = 22 473

76 n and Mr were not determined

Scheme 3.9: The synthesis of poly(glycidyl azide) (GAP 74, 75 and 76) from polyepichlorohydrin (71, 72 and 73) respectively. Polymer 73 is commercially available.

Following washing with water and solvent removal, polymer **74** and **75** were obtained in excellent yields (> 95 %) as yellow viscous liquids. The ^{1}H NMR spectrum of **72** (Figure 3.3, p. 48) showed the two signals representing the five protons of the repeating epichlorohydrin unit, i.e. $[\text{-C}\underline{\text{H}}(\text{C}\underline{\text{H}}_2\text{Cl})\text{C}\underline{\text{H}}_2\text{O-}]_n$, in the region 3.48 – 3.78 ppm. Due to introduction of an azide group in **75**, which has a weaker electronegativity than the chloride group found in polymer **72**, better resolution of the different H-atom peaks in the ^{1}H NMR spectrum of **74** and **75** was observed,
Figure 3.5.

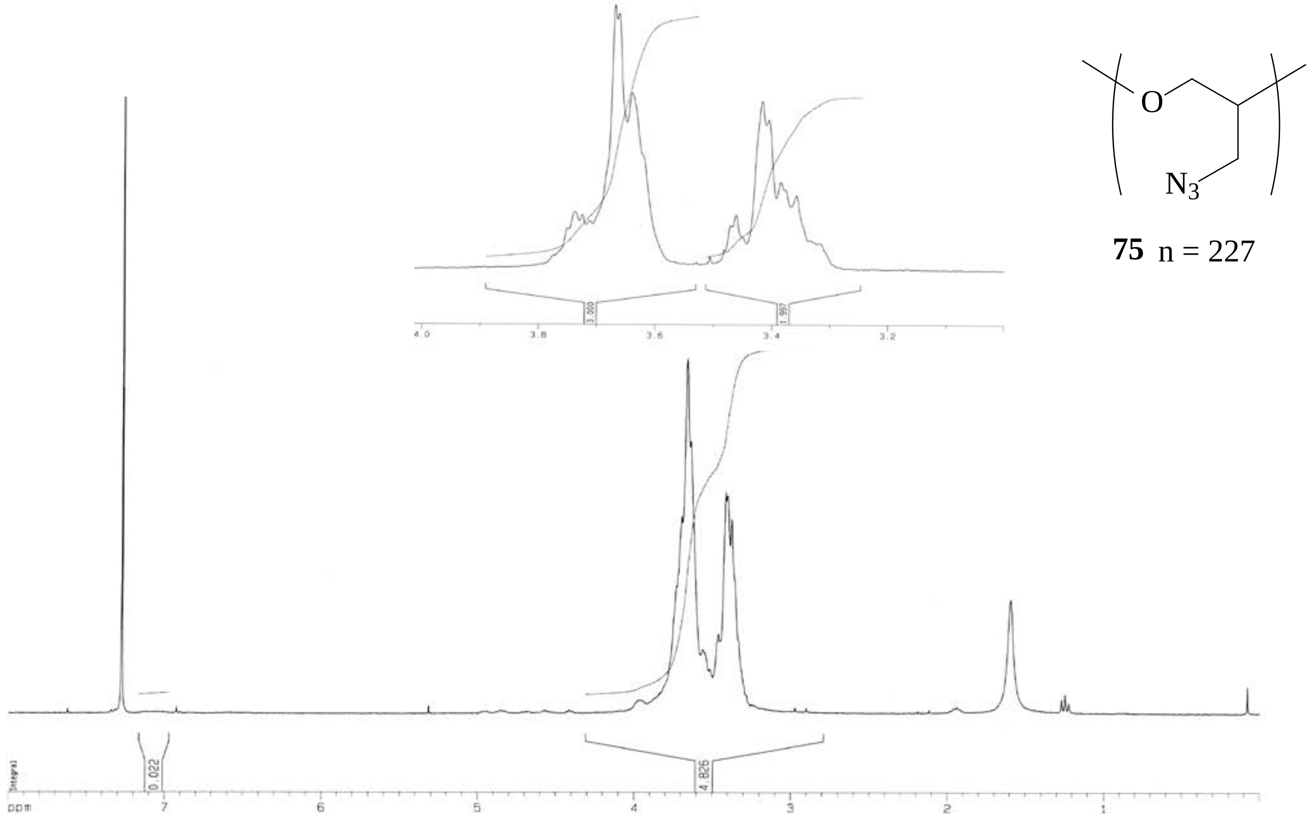


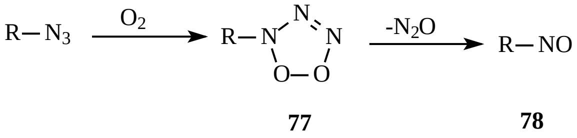
Figure 3.5: ^{1}H NMR spectrum of poly(glycidyl azide) (GAP, 75) in $CDCl_3$.

Unlike **72**, where the ^{1}H NMR spectrum showed the two signals corresponding to the five protons of the repeating epichlorohydrin unit almost overlapping, the protons in the ^{1}H NMR spectrum of **75** were now represented by two clearly separated signals in the same region. The first signal at 3.19 – 3.50 ppm represents the two protons of the methylene spacer attached to the side chain of the polymer and directly bound to the $–N_3$ functional group, i.e. $\text{-C}\underline{\text{H}}_2\text{N}_3$, while the other signal in the region 3.50 – 3.93 ppm represented the three protons of the ethylene unit in the polymeric backbone, i.e. $–C\underline{H}C\underline{H}_2O$-. The infrared transmission peak at 2091 cm^{-1}, as shown in Figure 3.8, p. 62, confirmed the presence of $–N_3$.

Molecular mass determinations by ^1H NMR on **74** and **75** showed that the smaller molecular mass derivative **(74)** did not suffer from polymer backbone degradation, but the larger molecular mass derivative possibly underwent slight backbone degradation, because the number of the repeating units decreased from 294 in **72** to 227 in **75**. However, this tentative result must be seen in the context of ^1H NMR accuracy when comparing the integral values for the five phenyl ring protons at *ca*. 7 ppm with that of the integral values of $(-C\underline{H}(C\underline{H}_2Cl)C\underline{H}_2O-)$, i.e. 1 135 protons, at 3 – 4 ppm (Figure 3.3 and 3.5).

The reaction conditions applied to obtain polymer **74** and **75** were also used to re-functionalise commercially available dihydroxy terminated polyepichlorohydrin **(73)** (Sigma-Aldrich product) with molar mass of 700 000 g mol^{-1}. The reaction led to a successful preparation of polymer **76**, as shown in Scheme 3.9, p. 50, in a yield (95 %) comparable to the yields obtained for polymer **74** and **75**. Polymer **76** was obtained as a yellow rubbery material.

During the first preparations of glycidyl azide polymers **(74)**, **(75)** and **(76)**, it was found that when the reaction was conducted in the presence of air, the molecular mass of the polymers was somehow reduced. The reason for this decrease in molecular mass was thought, at least in part, to be due to the reaction between alkyl azide side chain of the polymer and oxygen. When alkyl azides react with oxygen, the type of reaction shown in Scheme 3.10 occurs. Such side reactions result in the formation of compounds like **77** which subsequently loses N_2O and give **78** as a by-product of the reaction. To prevent such unwanted side reaction from happening, all the reactions were performed under nitrogen atmosphere, i.e. in the absence of air.

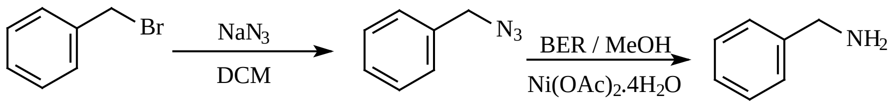


Scheme 3.10: Formation of 77 and 78 as possible by-products when preparing 74, 75, and 76 in the presence of air.

3.3.3 Amine polymer synthesis

After successful preparation of azide-containing polymers, the next step was to convert the azide-containing polymers to amine-containing polymers. Amines are organic derivatives of ammonia, NH_3. Like ammonia, amines contain a nitrogen atom with a lone pair of electrons, making amines both basic and nucleophilic.

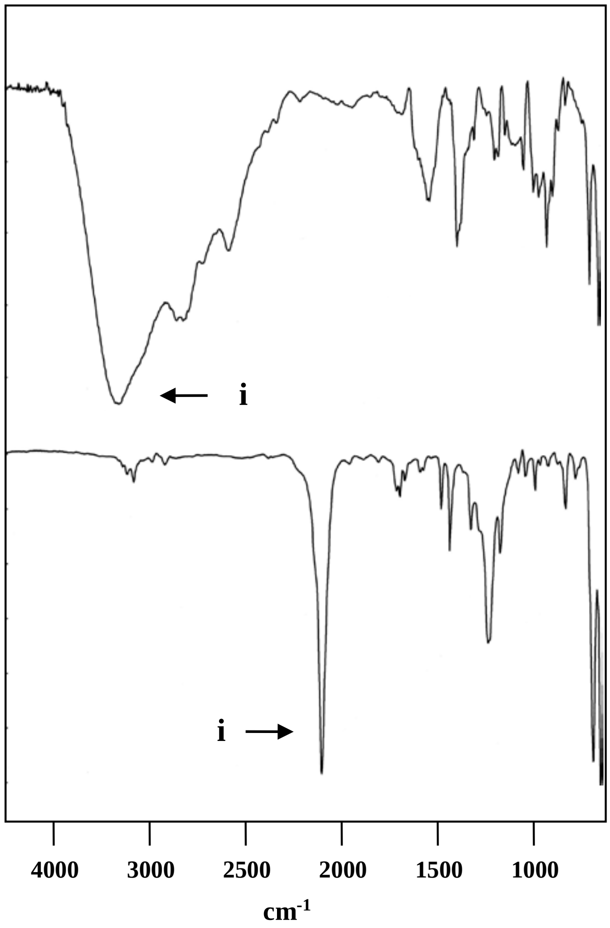
Although azides can be reduced to amines using various methods, as indicated in Section 2.2.3.3, p. 15, initially reduction of azides to amines was planned around the use of borohydride exchange resin (BER), i.e. polymer-supported BH_4^- anion, as a reducing reagent. To establish the technique needed in carrying out reduction with this reducing reagent, attention was first focused on a model reaction whereby benzyl azide **(80)** was reduced to benzylamine **(81)**. When using BER as a reducing agent, benzylamine **(81)** can be prepared in a one pot synthesis from benzyl bromide **(79)**.[35] For this study, benzyl azide **(80)** was first prepared from benzyl bromide **(79)** by S_N2 displacement of bromide ion with azide ion using the same reaction conditions for the synthesis of polymer **74**, **75** and **76** (see p. 50), except that dichloromethane was used as a solvent rather than DMF.



79 **80** **81**

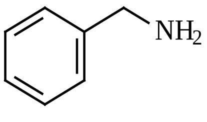
Scheme 3.11: Two step synthesis of benzylamine (81) from benzyl azide (80) prepared from benzyl bromide (79).

After the successful displacement of the bromide ion from benzyl bromide **(79)** to give benzyl azide **(80),** as an oily compound obtained in 91 % yield, benzyl azide **(80)** was subsequently reduced to benzylamine, as shown in Scheme 3.11. Benzyl azide **(80)** was reduced to benzylamine **(81)** by stirring with BER in methanol for 1 hour at room temperature. Following extraction with dichloromethane and solvent removal, benzyl amine **(81)** was obtained as a yellow solid melting into a yellow oil at 10 ^{0}C. In this type of BH_4^- anion reduction reactions, methanol is used as a solvent because it makes available H^+ ions in solution which are needed to trigger polymer-supported BH_4^- anion activation to liberate hydrogen gas. The product was characterised by both ^1H NMR spectrum (Spectrum A.11) and IR spectrum. The IR spectrum showed the disappearance of $–N_3$ peak that was observed at 2 091 cm^{-1} and the emergence of $–NH_2$ peak in the region 2 800 - 3 600 cm^{-1} as shown in Figure 3.6.



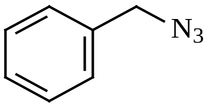
Peak Assignment

i. 3 350 (-NH2)



81

i. 2 091 (-N3)

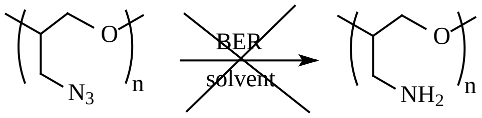


80

Figure 3.6: IR spectrum (relative % transmission *versus* wavenumber) of 80 and 81 showing the disappearance of the azide peak when 80 is reduced to 81 with BER.

Following successful preparation of benzylamine **(81)** under the above mentioned reaction conditions; the next step was to reduce the azide functionality, $-N_3$, in polymers **74**, **75** and **76** using similar reaction conditions as in the above model reaction to obtain polymers which have the amine functionality, $-NH_2$.

The first polymeric azide reduction by BER, using similar reaction conditions, as described above (Scheme 3.11, p. 53) for benzyl azide reduction, was attempted on polymer **76**, hoping to get polymer **83**, as shown in Scheme 3.12, p. 55. The reaction was, however, completely unsuccessful. Polymer **76** was found to be completely insoluble in methanol. The polymer **(76)** is a high molecular mass rubber and poor solubility in almost every solvent indicates an appreciable amount of crosslinking within the polymer. When **76** was found to be insoluble in methanol, it was thought to be due to this possible high degree of crosslinking. The decision was then made to abandon pursuing further re-functionalisation of polymer **76**. The decision came about as further re-functionalisation of polymer **76** side chains to more reactive functional groups like –NCO, i.e. isocyanate functional group, also failed due to drastic solubility problems.



75 n = 227
76

82 n = 227
83

Scheme 3.12: An attempted reduction of 75 and 76 to 82 and 83 respectively with BER as a reducing reagent. Many attempts were done to get this reaction working, see Table 3.1, but none of the attempted methods worked.

Reduction of **75** to **82** was then attempted (Scheme 3.12). However, polymer **75** was also found to be insoluble in methanol. This indicated that crosslinking of polymer **76** was perhaps not the only problem causing insolubility in methanol, but perhaps methanol was not the right solvent for the polymers and its use as a solvent needed to be reconsidered. Unfortunately, although several solvents and a variety of methods were investigated, see Table 3.1, p. 56, none of the attempted methods were successful in reducing **75** with BER to give amine-functionalised polymer **(82)**. This came about as a result of the polymer being insoluble in the solvent and in some cases if the polymer was soluble in the solvent, the solvent was not good enough in providing a strong enough H^+ ion concentration in solution needed to trigger polymer-supported BH_4^- anion activity to liberate hydrogen gas.

Table 3.1: The reaction conditions used for attempted reduction of 75 to 82 with BER as a reducing reagent.

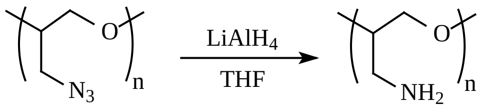
Reaction number	Reaction conditions	Results
1	BER / MeOH / 5 hours	No product, starting material could not dissolve
2	BER / MeOH:DMSO / 4 hours	No product, starting material could not dissolve
3	BER / 9 MeOH:1 THF / 4 hours	No product, starting material could not dissolve
4	BER / ButOH / 4hours	No product, starting material could not dissolve
5	BER / Methylene glycol / 4 hours	Starting polymer dissolved, BH_4^- anion not activated to liberate hydrogen gas.
6	BER / 5 THF: 5 MeOH / 4 hours	Starting polymer dissolved but no reduction was observed.

Having had no success with BER as a reducing reagent, alternative reducing reagents were considered and reduction with hydrogen gas in the presence of 10 % palladium-carbon, as shown in Scheme 3.13, was considered. In the first experiment, after 24 hours of reaction only 20 % reduction, as judged by IR peak measurements, was found to have taken place. This led to increased reaction time (48 hours). Although the reaction seemed to have worked better, after prolonged reaction time, the product was not so easy to recover from the reaction mixture and low yields were obtained.

75 n = 227, Mr = 22 473 **85** a + b = n = 227

Scheme 3.13: Attempted reduction of 72 with hydrogen gas in the presence of palladium-carbon to give 85 with n = a + b and a ≈ 0.20n.

As a result, reduction with aluminium hydride ($LiAlH_4$) was decided upon. As mentioned in Section 2.2.3.3, p. 15, reduction of azides to amines with $LiAlH_4$ represents an important tool in organic synthesis.[33]



74 n = 20, Mr = 1 981
75 n = 227, Mr = 22 473

84 n = 20, Mr = 1 460
82 n = 227, Mr = 16 571

Scheme 3.14: Synthesis of amine-containing polymer (82) and (84), by reduction of azide-containing poly(glycidyl azide) (74) and (75) with $LiAlH_4$.

The first attempt to prepare **82** from **75** with $LiAlH_4$ as a reducing was made by refluxing in tetrahydrofuran (THF) for 4 hours (Scheme 3.14). This resulted in **82a**, see Table 3.2, which was found to contain only 20 % of the amine functional groups and about 80 % azide functional groups as judged by IR measurements. Towards obtaining polymer **82** with high amine functional group content, the reaction was attempted several times by increasing the reaction time, as indicated in Table 3.2, while keeping the reaction conditions the same. Ultimately, poly (glycidyl azide) **(75)** was successfully reduced to amine-functionalised polymer **82d** by $LiAlH_4$ after refluxing for 48 hours in THF. Polymer **82d** was obtained in 34 % yield as a yellow sticky solid. Its ^1H NMR in D_2O (Spectrum A.8) showed signals in the region 2.80 – 3.18 ppm (2H, $-C\underline{H_2}NH_2$) and in the region 3.32 – 3.92 ppm (3H, $-C\underline{H}C\underline{H_2}O-$). The molecular mass of **82** was also determined using ^1H NMR as described in Section 3.3.1, p. 49. No noticeable polymer backbone degradation was observed, molecular masses can be found in Scheme 3.14. The infrared of **82d** showed a broad transmission peak associated with the $-NH_2$ in the region 2 800 – 3 400 cm^{-1} and no $-N_3$ peak at 2 091 cm^{-1} (Figure 3.8, p. 62).

Table 3.2: The conditions employed to obtain amine-containing polymer 82.

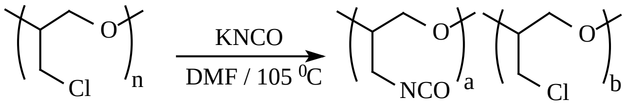
Compound	**Reaction time**	**Percentage amine ($-NH_2$) reduced**
82a	4 hours	≈ 20 %
82b	24 hours	≈ 60 %
82c	36 hours	≈ 85 %
82d	48 hours	≈100 %

Amine-containing polymer **82d** was found as a yellow sticky solid insoluble in most organic solvents, but readily soluble in water. On long standing, polymer **82d** tends to absorbs lots of moisture and form a yellow tarry compound. The presence of amine functional groups makes it possible for polymer **82d** to react with other functionalities to form an amide or urea covalent bond.

3.3.4 Isocyanate polymer synthesis

Alkyl isocyanates can be prepared by many different methods, as described in Section 2.2.3.2, p. 14, including treatment of the appropriate halides with the isocyanate ion. When alkyl halides are treated with NCO ion, alkyl isocyanates can be prepared directly.

For this research program, preparation of isocyanate-functionalised polymers **(86)** and **(87)** was first attempted, as shown in Scheme 3.15, by heating polymer **71** and **72** with potassium isocyanate in DMF for 16 hours at 105 ^{0}C in the presence of potassium carbonate and tetrabutylammonium bromide as a phase-transfer catalyst. After precipitation with hexane, polymer **86** and **87** were obtained. These polymers were found to contain only 15 % NCO group, as judged by IR measurements.

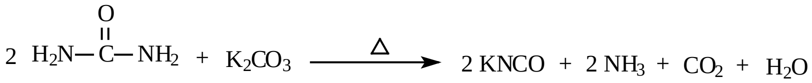


71 n = 20
72 n = 294

86 n = 20
87 n = 294

Scheme 3.15: Preparation of isocyanate-functionalised polymer from polyepichlorohydrin by an isocyanate ion to give polymers with n = a + b and a ≈ 0.15n.

The poor conversion of halide to isocyanate in the reaction was thought to be the result of potassium isocyanate which might have been partially decomposed. Ultimately, fresh potassium isocyanate was prepared in-house according to Scheme 3.16, p. 59. However, after the reaction was conducted with this freshly prepared potassium isocyanate, the results obtained were similar to those obtained using commercially available potassium isocyanate.



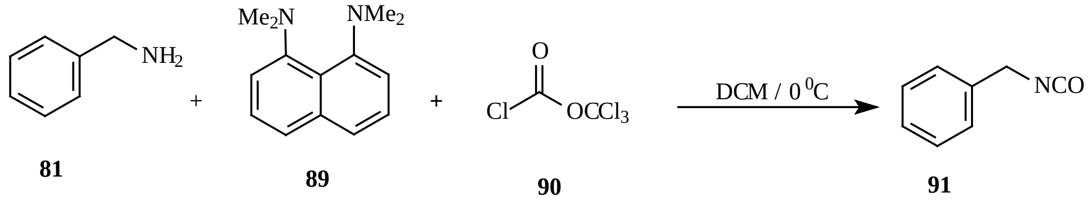
$$2\ H_2N-\overset{\overset{O}{\|}}{C}-NH_2 + K_2CO_3 \xrightarrow{\Delta} 2\ KNCO + 2\ NH_3 + CO_2 + H_2O$$

Scheme 3.16: Preparation of potassium isocyanate from potassium carbonate and urea.

In the end, potassium isocyanate was substituted with silver isocyanate (AgNCO). This change came about as it was thought that silver chloride, which forms as a by-product of the reaction, will precipitate from the reaction mixture. It was hoped that this precipitation would drive the reaction to completion. Nonetheless, the reaction with silver isocyanate formed a dark brown reaction mixture from which the desired product could not be recovered. This observation was thought to result from the silver cation which possibly came into contact with light. Silver cation is light sensitive and all the reactions involving its use need to be conducted a dark place.

As a result, re-functionalisation of polyepichlorohydrin **(72)** to isocyanate-functionalised polymer was considered starting from the amine-functionalised polymer **(82d)** in a completely new and different route. Various methods for conversion of amines to isocyanates were investigated. The reaction of aliphatic amines with trichloromethyl chloroformate (diphosgene, **90**) at 0 ^{0}C, in the presence of the nucleophilic base 1,8-bis(dimethylamino)-naphthalene **(89)**, affords isocyanates in good to excellent yields.[117] The reaction proceeds *via* formation of chloroformamides (ClCONHR), which loose HCl to give isocyanates (RNCO).[30]**Error! Bookmark not defined.** This type of reaction was considered for further preparation of isocyanate from amines in this study.

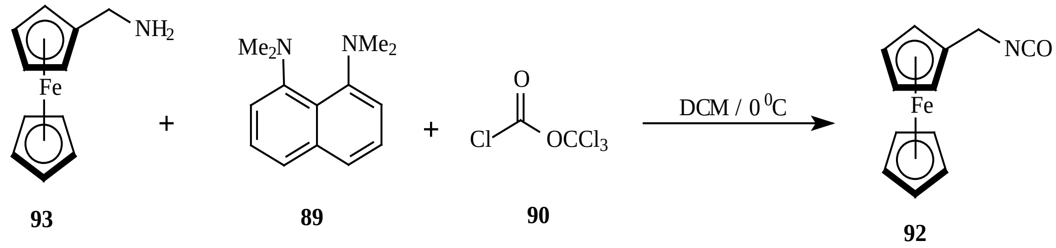
Before an attempt was made to prepare isocyanate-functionalised polymer **(88)** with diphosgene **(90)**, a model isocyanate preparation reaction was performed. The reaction involved conversion of benzylamine **(81)** to benzyl isocyanate **(91)**, as shown in Scheme 3.17, p. 60.



Scheme 3.17: Preparation of benzyl isocyanate (91) from benzylamine (81) with the diphosgene derivative, trichloromethyl chloroformate (90).

Unlike in most procedures for preparation of isocyanates which rely on distillation for purification of products,[118,119,120] the product from this reaction was obtained in 95 % purity without additional purification. This crude material was of sufficient quality to use in follow-up reactions. Benzyl isocyanate **(91)** was obtained as a colourless liquid (86 % yield) and characterised with ^{1}H NMR spectra (Spectrum A.12).

Following the successful preparation of **91**, similar reaction conditions were used to prepare the isocyanate-containing ferrocene derivative **(92)** from ferrocylamine **(93)**, as shown in Scheme 3.18. Ferrocyl isocyanate **(92)** was obtained as a reddish-orange liquid in 68 % yield after 30 minutes of reaction. To the knowledge of the author, ferrocyl isocyanate **(92)** was not synthesised before. This study represent the first time its synthesis has ever been recorded.



Scheme 3.18: Preparation of ferrocyl isocyanate (92) from ferrocyl amine (93) with the diphosgene derivative (90). (Ferrocyl = ferrocenyl = Fc-CH$_2$)

Figure 3.7, p. 61, shows the IR spectrum of **92** and a peak at 2 149 cm^{-1} indicates the presence of an isocyanate group.

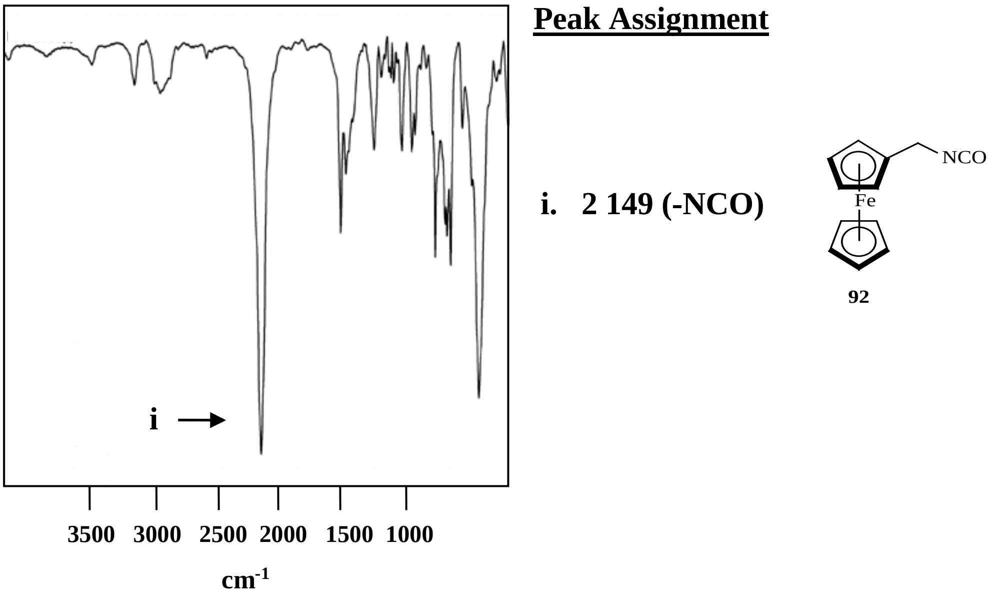


Figure 3.7: IR spectrum (relative % transmission *versus* wavenumber) of ferrocyl isocyanate (92).

The reaction of **92** with 4’-(hydroxymethyl)benzo-15-crown-5 **(69)** is described on p. 63. Further characterisation of ferrocyl isocyanate **(92)** (e.g. electrochemical properties) was not done in this research program. It will be the topic of research in another follow-up research program.

After benzyl isocyanate **(91)** and ferrocyl isocyanate **(92)** were efficiently prepared in good yield, the reaction conditions were adapted for preparation of an isocyanate-functionalised polymer **(88)**. The reaction was performed in DMSO, as indicated in Scheme 3.19, because polymer **82d** was found to be insoluble in dichloromethane and diphosgene **(90)** reacted with DMF to form an unwanted side product. Following extraction of DMSO and precipitation of the product with hexane, the polymer **(88)** was obtained in high yield (90 %). Conversion of amines to isocyanates utilising this technique was almost quantitative (> 90 %).

82d n = 227, Mr = 22 686 **88** n = 227, Mr = 22 686

Scheme 3.19: Preparation of isocyanate-functionalised polymer (88) from amine-functionalised polymer (82d).

Infrared spectroscopy showed a sharp peak at 2 149 cm^{-1} indicating the presence of NCO group (Figure 3.8).

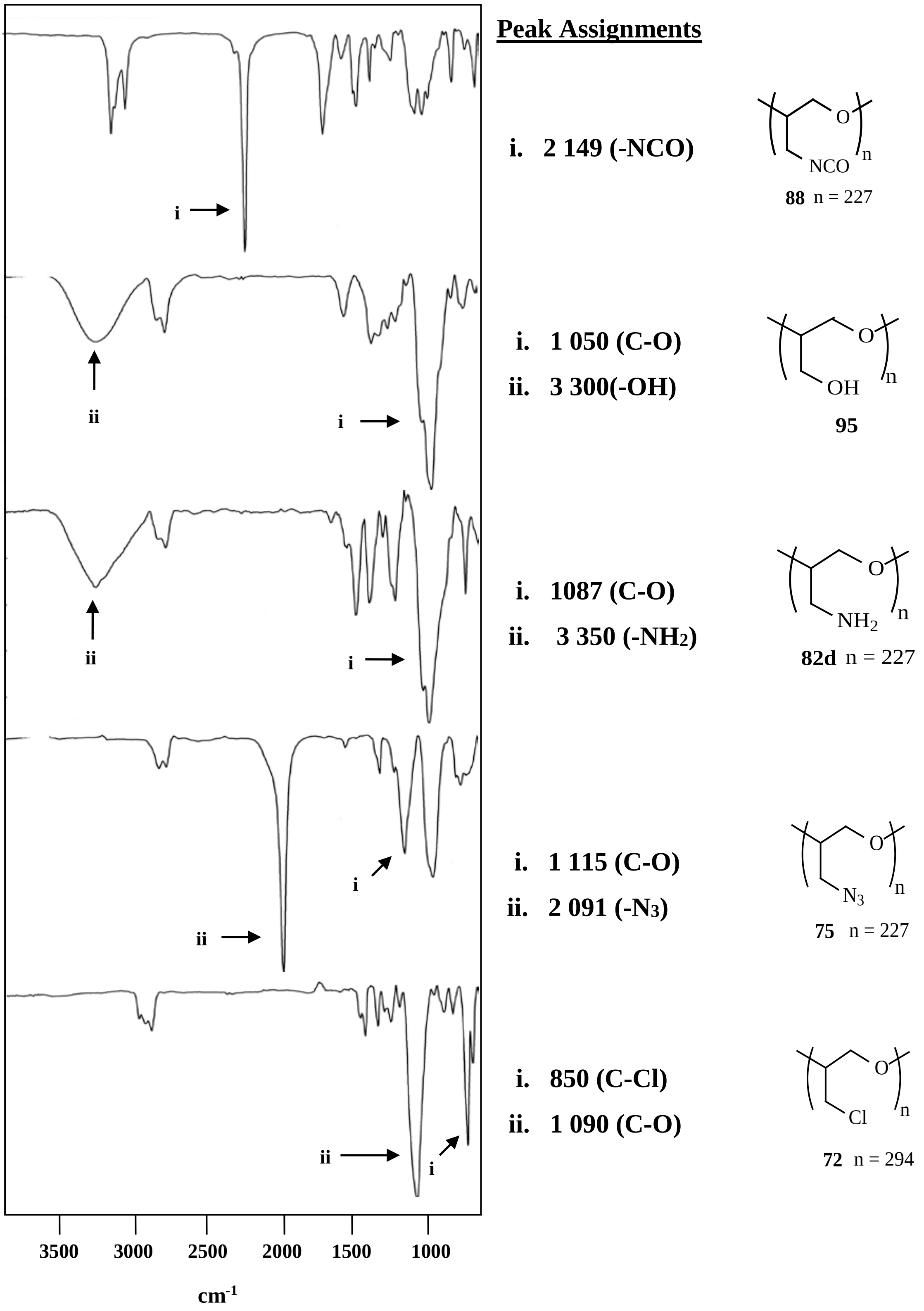
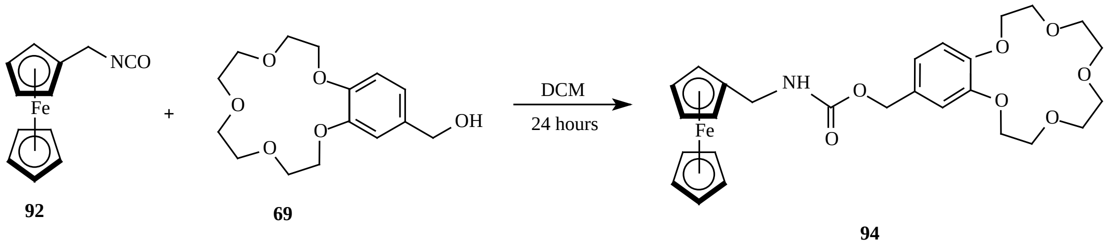


Figure 3.8: IR spectra showing the change in peak transmission as the side chain of polyepichlorohydrin (72) is re-functionalised into different functional groups.

The aim behind preparation of polymer **88** was to ultimately anchor onto it hydroxy-functionalised crown ether derivative such as 4'-(hydroxymethyl)benzo-15-crown-5 **(69)**. However, anchoring of hydroxy-functionalised crown ether derivatives onto polymer **88** did not fall within the scope of this research program. Due to time constraints, in this study program only a model anchoring reaction was performed whereby the hydroxy-functionalised crown ether derivative **(69)** (p. 43, Scheme 3.7) was reacted with ferrocyl isocyanate **(92)**. The coupling experiment was performed by stirring **92** and **69** in dichloromethane for 24 hours at room temperature, as shown in Scheme 3.20. Subsequent to reaction work-up and column chromatography, the crown ether-containing ferrocene derivative **(92)** was obtained as a yellow wax-like solid in 98 % yield.

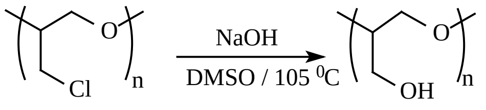


Scheme 3.20: Coupling of 4'-(hydroxymethyl)benzo-15-crown-5 (69) with ferrocyl isocyanate (92) to give the crown ether-containing ferrocene derivative (94).

The ferrocene-crown ether conjugate **(94)** is also a hitherto unknown compound, and further investigations on its physical and chemical properties may well open-up a complete new research program.

3.3.5 Hydroxy polymer synthesis

In conclusion of goal 2 of this study, as stated in Chapter 1, the hydroxy-functionalised polymer **95** was synthesised. Hydroxide ions are usually required to hydrolyse alkyl halides to alcohols. Sometimes halides can also be hydrolysed by water depending on the solvent used.[121]



72 **95**

Scheme 3.21: Hydrolysis of polyepichlorohydrin (72) with NaOH to prepare hydroxy-functionalised polymer (95).

Polymer **72** was converted to **95** by S$_N$2 displacement of chloride anion with hydroxy anion. The reaction was conducted by reacting polymer **72** with saturated sodium hydroxide (NaOH) for 16 hours in DMSO, as shown in Scheme 3.21, in the presence of potassium carbonate (K_2CO_3) and a phase transfer catalyst (tetrabutylammonium bromide). Polymer **95** was obtained in 45 % yield as a dark-brown solid and characterised with both ^1H NMR (Figure 3.9) and IR spectroscopy. IR spectrum showed a broad peak in the region 3 050 – 3 500 cm^{-1} (Figure 3.8, p. 62).

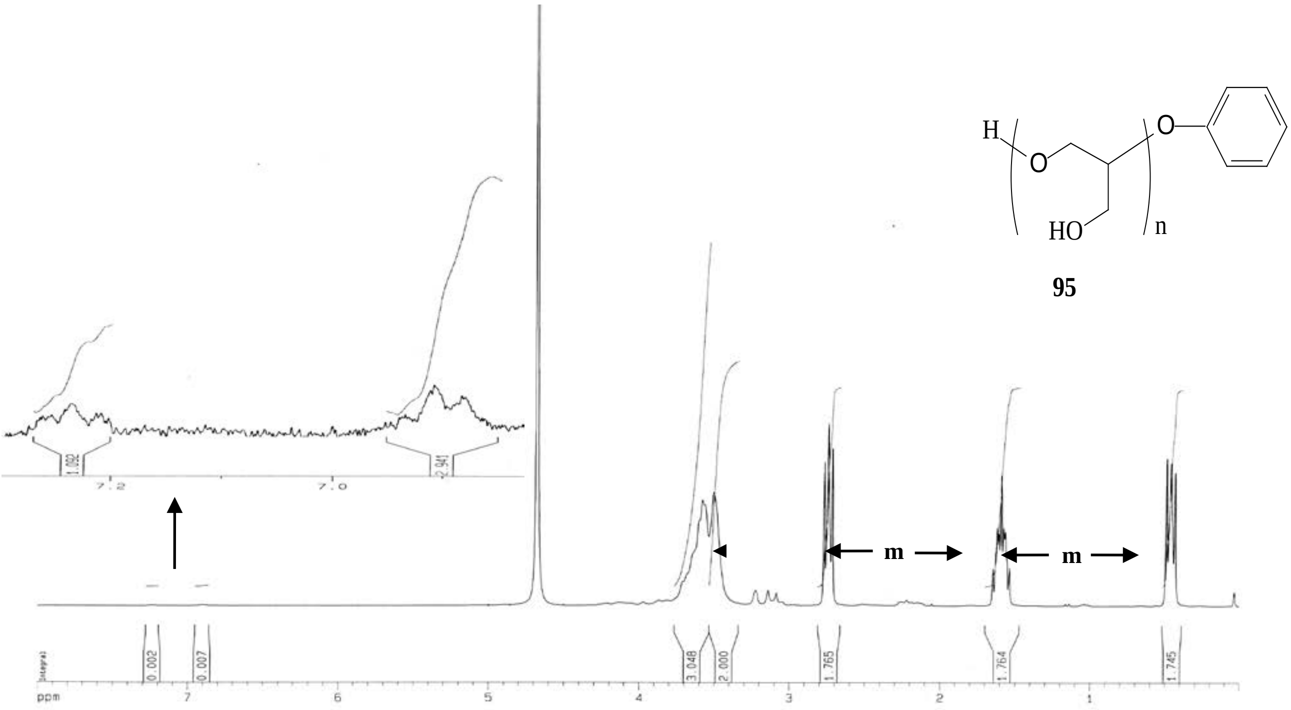


Figure 3.9: ^1H NMR spectrum of hydroxy-functionalised polymer (95) in D_2O. The peaks labelled m are due to the internal marker, 3-(trimethylsilyl)propionic-2,2,3,3-d$_4$ acid, sodium salt, in the solvent. [$(CH_3)_3Si-CD_2-CD_2-COONa^+$]

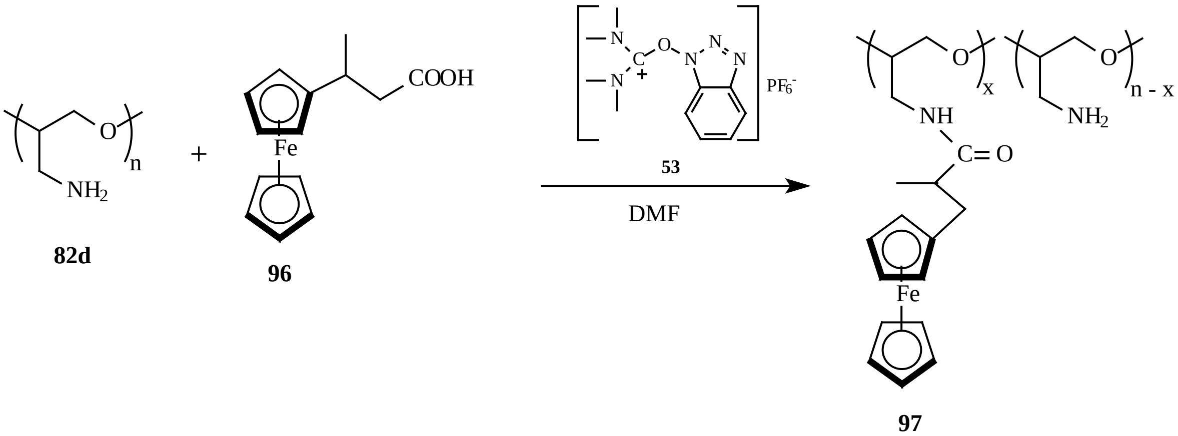
As seen from Figure 3.9, when the hydroxy functional group is introduced into alkyl side chain of polymer **72**, the signals representing the phenyl protons that were observed in the region 6.89 – 7.02 ppm (Figure 3.3, p. 48) become split into two signals at 6.90 ppm and 7.22 ppm.

Polymer **95** was found to be highly soluble in water and if not stored in moisture free area, it tends to absorb moisture very quickly. The presence of hydroxy functional group in polymer **95** makes it possible for the polymer to react with isocyanate- and acid-functionalised compounds to form urethane and ester bond respectively.

3.4 Anchoring Experiments

3.4.1 The anchoring of carboxylic acid-containing ferrocene derivatives onto amine-functionalised polymer (82d)

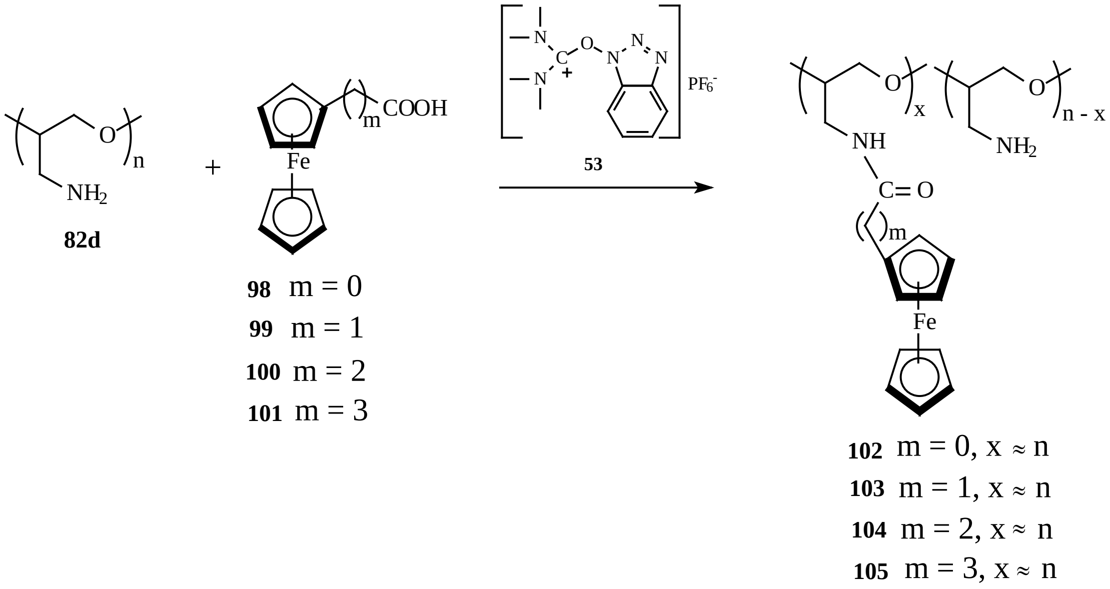
Following the successful preparation of polymer **82d** (see Table 3.2, p. 57), the reactivity of the amine group on **82d** towards carboxylic acids was investigated by anchoring a series of carboxylic acid-containing ferrocene derivatives onto it. The reactions involved to attain this are shown in Scheme 3.23, p. 67. To establish the reaction conditions of this ferrocene derivative anchoring step onto polymer **82d**, attention was first focused on the synthesis of polymer **97**, as shown in Scheme 3.22. The author thanks J. C. Swarts for supplying compound **96**.



Scheme 3.22: Anchoring of carboxylic acid-containing ferrocene derivative (96) onto amine-functionalised polymer (82d) with coupling reagent *O*-benzotriazolyl-*N,N,N',N'*-tetramethyluronium hexafluorophosphate to give polymer 97.

In the first anchoring experiment, amine-functionalised polymer **(82d)** was reacted in stoichiometric amounts with **96** by stirring in DMF at room temperature for 1 hour in the presence of a coupling reagent (*O*-benzotriazolyl-*N,N,N',N'*-tetramethyluronium hexafluorophosphate **(53)**. Extraction with dichloromethane afforded crude product that was supposed to be polymer **97**. With the use of ^{1}H NMR spectrum, it was established that anchoring was only 40 % successful, i.e. $x = 0.4n$. Another attempt of the same anchoring reaction was conducted whereby the reaction time was increased to 5 hours. After extraction with dichloromethane and fractional precipitation with pentane, polymer **97** was obtained in 70 % yield as a dark-orange solid. ^{1}H NMR spectra of **97** from the second attempt showed 1:1 coupling of **96** onto **82d** (Spectrum A.14). This meant that $x \approx n$ and $n - x \approx 0$.

Having established a simple, quick and highly effective procedure for anchoring of carboxylic acid-containing ferrocene derivative onto amine-functionalised polymer **(82d)**, a series of experiments, as shown in Scheme 3.23, was conducted to anchor other carboxylic acid-containing ferrocene derivatives to obtain polymers **102**, **103**, **104** and **105**. The author thanks P. T. N. Nonjola, R. F. Shago, E. Erasmus and W. L. Davis for supplying sufficient quantities of compounds **98** through **101** to conduct this research.



Scheme 3.23: Anchoring of carboxylic acid-containing ferrocene derivatives 98 - 101 onto amine-functionalised polymer (82d) with the coupling reagent *O*-benzotriazolyl-*N,N,N',N'*-tetramethyluronium hexafluorophosphate to give polymer 102 - 105.

In the first reactions performed for anchoring of **98**, **99**, **100** and **101**, it was found that ferrocene anchoring onto **82d** took place, but the anchoring process was not really quantitative. Anchoring was established by ^{1}H NMR spectroscopy to be between 15 and 70 %. After several experiments were done to determine the cause of this poor anchoring, it was found that the trouble was caused by poor solubility of polymer **82d** in DMF. This resulted in **98**, **99**, **100**, and **101** reacting with **82d** in unequal molar amounts. It was found that aging of **82d** was also detrimental to ferrocene anchoring. Freshly synthesised polymer had the highest success rate in these anchoring experiments. To overcome the solubility of **82d** in DMF, a small amount of water and/or THF was added to the reaction mixture. When water:DMF was mixed in a ratio of 1:6, polymer **82d** was found to be much more soluble. However, the carboxylic acid-containing ferrocene derivatives **(98 - 101)** were less soluble in this mixed solvent system. This limited solubility of carboxylic acid-containing ferrocene derivative, as can clearly be seen in the experiments involving anchoring of acids **98** and **101** onto **82d**. Even though acids **98** and **101** were effectively anchored onto **82d**, the yields of polymer **102** and **105** were drastically reduced. To explain the reduced yields it is instructive to note that **102** to **105** with x ≈ n became soluble in dichloromethane. By adding dichloromethane to the reaction mixture followed by washing with copious amounts of water, one recovers only that fraction of ferrocene-containing polymer product which has very high ferrocene content. All the other material is washed away in the water. Eventually, when a small amount of THF was added to the reaction mixture to enhance carboxylic acid-containing ferrocene derivatives solubility in water/DMF mixture, following extraction with hexane and washing with water and acetone polymer **103** and **104** were obtained in reasonable yields as shown in Table 3.3.

Table 3.3: Yields of obtained for polymer 102 – 105 when the reaction was done in different solvent mixtures.

Compound	Reaction mixture	% Yield
102	2 cm^3 H_2O and 6 cm^3 DMF	2 %
103	2 cm^3 H_2O, 6 cm^3 DMF and 2 cm^3 THF	42 %
104	2 cm^3 H_2O, 6 cm^3 DMF and 2 cm^3 THF	45 %
105	2 cm^3 H_2O and 6 cm^3 DMF	4 %

For polymer **104**, ^{1}H NMR spectra were taken in two different ^{1}H NMR solvents, i.e. $CDCl_3$ and deuterated DMSO, as shown in Figure 3.10, p. 69. The ^{1}H NMR spectrum taken in $CDCl_3$ showed four broad signals, the first signal integrating for 9 and corresponding to the nine protons of ferrocene was found in the region 4.07 – 5.03 ppm, the second signal integrating for 5 and representing the protons of polymer **82d** repeating units was found in the region 2.98 – 3.87, the third signal which integrated for 4 and representing the 4 protons of the ethylene spacer from the functionalised arm of the ferrocene derivative was found in the region 2.23 – 2.79 ppm and the fourth unidentified signal which integrated for 2 was found in the region 1.89 – 2.13 ppm. When ^{1}H NMR spectrum of **104** was taken in deuterated DMSO, two signals representing the protons of polymer **104** were observed, see Figure 3.10. The one signal corresponding to the protons of ferrocene showed a multiplet signal integrating for 5 at 4.15 ppm and integrating for 2 at 4.08 and 2 at 4.00 ppm. The second signal which integrated for 2 and represented two protons of the ethylene spacer was observed in the region 2.29 – 2.48 ppm. In this ^{1}H NMR spectrum the signals corresponding to the two protons of the other ethylene spacer and five protons of polymer **82d** repeating unit could not be observed because they were under the signals of the ^{1}H NMR solvent, DMSO.

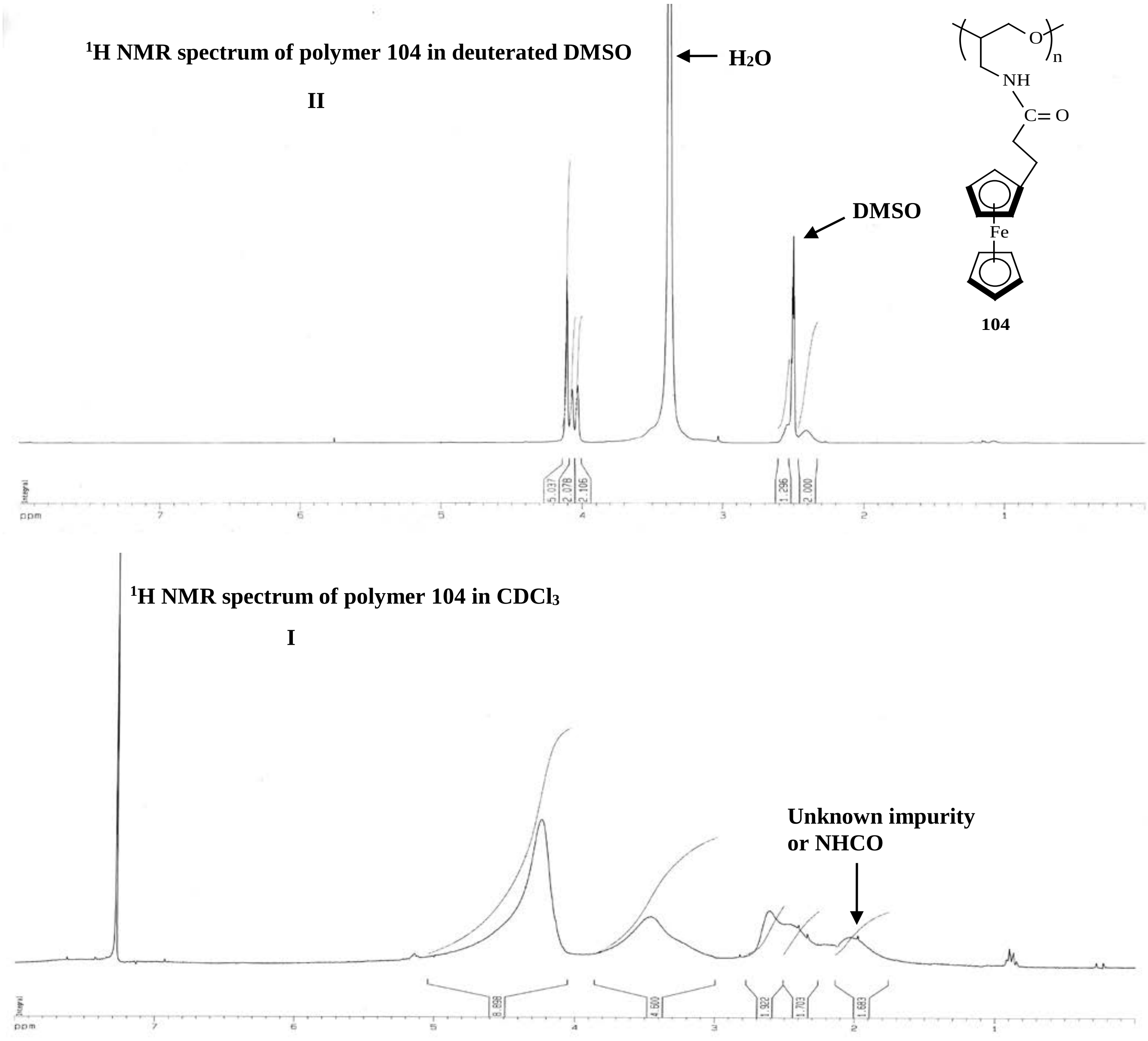


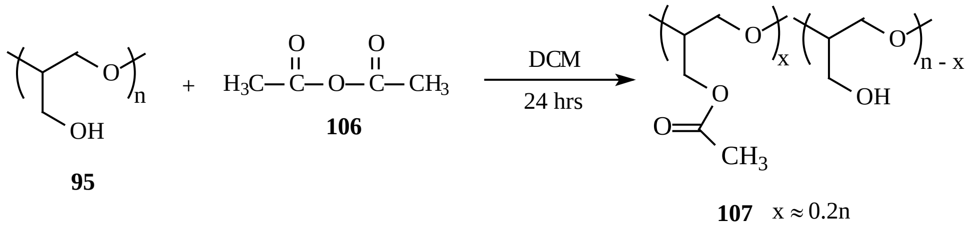
Figure 3.10: ^{1}H NMR spectrum comparison of polymer 104 in different ^{1}H NMR solvents.

From the obtained results, it became apparent that the reactivity of amine-functionalised polymer **82d** with carboxylic acid functional groups is very high. Therefore, the introduction of amine functionality in polyepichlorohydrin opens up a new dimension in anchoring a variety of functional groups onto polyepichlorohydrin type polymers. Isocyanate- and carboxylic acid-functionalised molecules may be anchored with high efficiency on this new polymeric carrier.

3.4.2 Anchoring experiment including hydroxy-functionalised polymer (95)

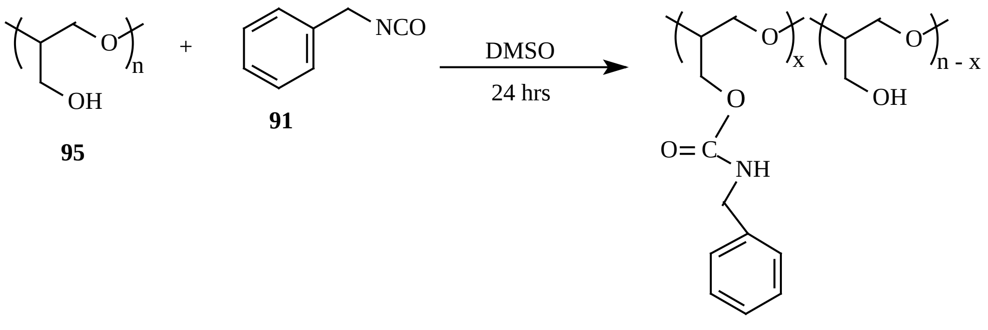
Hydroxy-functionalised compounds do not only react with isocyanates to form urethane bonds, they also react with carboxylic acids (or its activated forms) to form an ester bond.

The first attempt to anchor a compound onto hydroxy-functionalised polymer **(95)** was made with acetic anhydride. Acetic anhydride was reacted with polymer **95** by stirring in dichloromethane for 24 hours at room temperature, as shown in Scheme 3.24. Following evaporation of dichloromethane and other volatile material, what was expected to be polymer **107** was obtained. With the use of IR spectrum it was established that only 20 % ester formation on polymer **91** had occurred. The reason for this poor anchoring was partially attributed to the poor solubility of polymer **95** in dichloromethane. Due to the time limit of this study, further anchoring attempts of acetic anhydride **(106)** onto polymer **91** was not pursued.



Scheme 3.24: Anchoring of acetic anhydride (106) onto hydroxy-functionalised polymer (95).

Finally, benzyl isocyanate **(91)** was anchored onto hydroxy-functionalised polymer **(95)**. The reaction was conducted by adding benzyl isocyanate **(91)** to a solution of polymer **(95)** in DMSO and stirring at room temperature for 24 hours, as shown in Scheme 3.25, p. 71. Polymer (**108)** was obtained in 88 % yield as a colourless solid. ^{1}H NMR (Spectrum A.21) was used to characterise polymer **108**. It was found that **95** had reacted for all practical purposes quantitatively with benzyl isocyanate **(91)**.



108 x ≈ n

Scheme 3.25: Anchoring of benzyl isocyanate (91) onto hydroxy-functionalised polymer (95) to give polymer 105.

The ease of the reaction shown Scheme 3.25 showed just how reactive the hydroxy functional groups in polymer **95** are towards an isocyanate group, as the reaction did not require any form of energy nor catalyst to give the product in high yield. The successes of these reactions open up an entirely new avenue of research with the aim of anchoring many different isocyanate-functionalised compounds onto polyethers bearing hydroxy-functionalised side chains.

3.5 Conclusion

In Chapter 1, the problem surrounding the decline in water quality due to contamination was outlined. The recently patented device that may be used to combat this problem by removing metal cations, especially Na^+ ions from industrial wastewater effluents, and its shortcomings was also described. To address the shortcoming of the described device, highly reactive well characterised polymeric spacers are needed. In this study, some new highly reactive polymers were developed by polymerising epichlorohydrin to polyepichlorohydrin. Subsequently, the chloro-containing alkyl side chains of polyepichlorohydrin were re-functionalised to have $–N_3$, $-NH_2$, -NCO and –OH groups. The reactivity of these polymers proved to be very high as they all showed very good results in anchoring different compounds onto them.

This study has developed potential polymeric spacers needed to enhance the efficiency of the Na^+ ion-scavenging device mentioned in Chapter 1 and 2.

While testing the reactivity of these functionalised polymers, new polymer-bound ferrocene compounds with possible bioactivity were synthesised. Additional research into these polymer-bound ferrocene derivatives will determine their importance in, for example, anticancer research and any other advantages offered by this type of polymers in ferrocene chemistry.

---

[112] J. March, *Advanced Organic Chemistr,* 4th Ed., Wiley: New York, **1992,** pp. 326

[113] C. C. Lee, J. W. Clayton, D. G. Lee, A. J. Finlayson, *Tetrahedron*, **18 (1962),** 1395

[114] J. McMurry, *Organic Chemistry*, 5th Ed., p. 991

[115] R. J.Lewis, Sr., *Hazardous Chemicals, Desk reference*, 3rd Ed., Van Nostrand Reinhold: New york, **1993,** p. 1148

[116] S. E. Maree, Unpublished Results

[117] S. T. Sigurdsson, B. Seeger, U. Kutzke, F. Eckstein, J. Org. Chem, **61 (1996)**, 3883

[118] C. V Wilson, *Org. Chem. Bull.*, **35 (1963)**, 1

[119] S. Ozaki, *Chem. Rev.*, **72 (1972)**, 457

[120] J. H. Saunders, R. Slocombe, *J. Chem. Rev.*, **43 (1948)**, 203

[121] Hutchins and Taffer, *J. Org. Chem.*, **48 (1983)**, 1360

4.1 Materials

Solid reagents (Merck, or Sigma-Aldrich) were used without further purification. Liquid reactants and solvents were distillled prior to use, water was double distilled. Dry, air-free tetrahydrofuran (THF) was obtained by refluxing under nitrogen over sodium wire for 3 hours.

4.2 Techniques and apparatus

4.2.1 Infrared (IR) spectroscopy

IR-spectroscopy was conducted on Digilab-Menlin 3.0 spectrometer with data processor. Both solids and liquids samples were recorded by placing a small amount of the product on the machine. This machine does not need a liquid solvent or a KBr matrix to support samples when obtaining IR spectra.

4.2.2 Nuclear Magnetic Resonance (NMR) spectroscopy

Proton ^{1}H NMR spectra at 298 K were recorded on a 300 MHz Bruker AMT-300 FT-instrument with deuterated solvents as internal standards, while chemical shifts are presented as δ-value referenced to $SiMe_4$ at 0.00 parts per million (ppm).

4.2.3 Determination of the melting points (m.p.)

Melting points were determined with Reichet Thermopan microscope, with a Koffler hot stage and are uncorrected. This instrument can only detect melting points lower than 200 ^{0}C.

4.2.4 Dialysis and freeze drying of polymers

Dialysis were performed against running tap water in 3 000 molecular mass cut-off cellulose membrane tubing followed by freeze drying on an EZ-DRY 550Q instrument at -43 ^{0}C and 63 Torr (1 Torr = 1mmHg = 133.32 Pa).

4.2.5 Column chromatography

Merck silica gel 60 (particle size 0.040 – 0.063 mm) was used for column chromatography, and aluminium coated sheets with silica gel 60 F_{254} were used for thin layer chromatography.

4.3 Synthesis and functionalisation of crown ethers

4.3.1 Synthesis of 1,11-dichloro-3,6,9-trioxaundecane (59)[64] [Scheme 3.1, p. 39]

In a clean two-neck 1 000 cm^3 round-bottom flask, tetraethylene glycol (**58**, 120.00 cm^3, 134.34 g, 0.6920 mol) was added to toluene (600 cm^3) and pyridine (122.90 cm^3, 120.42 g, 1.522 mol), and heated to *ca*. 110 ^{0}C. Thionyl chloride (110.40 cm^3, 181.07 g, 1.522 mol) was added over a period of 3 hours. The colour changed to dark-brown, and heating was continued overnight (16 hours). After the reaction 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 precipitated hydrochloride salt was seperated by filtration and the organic liquid phase washed with distilled water and dried with $MgSO_4$. Removal of the solvent under reduced pressure yielded a brown-yellow liquid, 1,11-dichloro-3,6,9-trioxaundecane **(59)** (118,85 g, 74. 32 %). δ_H ($CDCl_3$, Spectrum A.1): 3.63 – 3.81 (16 H, m, $OC\underline{H}_2C\underline{H}_2O$). IR /$cm^{-1}$: 664 – 714 (C-Cl), 1 016 – 1 201 (C-O-C).

4.3.2 Synthesis of benzo-15-crown-5 (29)[64] [Scheme 3.4, p. 41]

Catechol (**64**, 51.34 g, 0.4663 mol) was added to 1-butanol (500 cm^3) in a 1 000 cm^3 two-neck round-bottom flask. After the mixture was degassed with nitrogen, NaOH (41.04 g, 1.293 mol) was added and the solution was allowed to stir for 5 minutes at room temperature. 1,11-Dichloro-3,6,9-trioxaundecane(**59**, 107.77 g, 0.4663 mol) was added to the solution and the reaction mixture was heated for 30 hours at 117 ^{0}C. The reaction mixture was cooled to room temperature, acidified with concentrated hydrochloric acid, filtered and the residue washed with methanol (250 cm^3). The filtrate was concentrated under reduced pressure to give a dark black viscous liquid. Continuous extraction and recrystallisation with hexane gave benzo-15-crown-5 **(29)** as white needles, (47.61 g, 38.05 %); m.p. 75 – 78 ^{0}C. δ_H ($CDCl_3$, Spectrum A.2): 3.72 – 3.84 (8 H, s, $OC\underline{H_2}C\underline{H_2}O$), 3.88 – 3.99 (4 H, m, $PhOCH_2C\underline{H_2}O$), 4.12 – 4.21 (4 H, m, $PhOC\underline{H_2}OCH_2$), 6.86 – 6.97 (4 H, d, $Ar\underline{H}$). IR /cm^{-1}: 1 077 – 1 239(C-O-C), 1 458 – 1 593 (Ar), 2 872 – 2 914 (ArH).

4.3.3 Synthesis of 4'-formylbenzo-15-crown-5 (68)[42] [Scheme 3.6, p. 43]

Phosphoryl chloride (4.572 g, 0.02982 mol) was added to N-methylformanalide (**67**, 4.031 g, 0.02982 mol) and the resulting mixture was put aside for 20 minutes. The reaction was proceeded by addition of benzo-15-crown-5 (**29**, 2.00 g, 0.007454 mol) and heating at ca. 90 ^{0}C for 4 hours. After cooling, the solution was diluted with water (12.00 cm^3) and extracted with dichloromethane (4 x 100 cm^3). The dichloromethane phase was dried over $MgSO_4$ and evaporated under reduced pressure to give residual brown oil. Following extraction and recrystallisation of this oil with hexane, a white solid was obtained as 4'-formylbenzo-15-crown-5 **(68)** (1.45 g, 65.70 %), m.p. 79 -81 ^{0}C. δ_H ($CDCl_3$, Spectrum A.3): 3.72 – 3.84 (8 H, s, $OC\underline{H_2}OC\underline{H_2}O$), 3.91 – 4.00 (4 H, m, $OPhOCH_2OC\underline{H_2}$), 4.15 – 4.18 (4 H, m, $OPhOC\underline{H_2}OCH_2$), 6.89 – 6.97 (1 H, d, $J_{a'b'}$ = 8 Hz, $Ar\underline{H_{a'}}$), 7.35 – 7.42 (1 H, d, $J_{b'c'}$ = 2 Hz, $Ar\underline{H_{c'}}$), 7.42 – 7.48 (1 H, dd, $J_{a'b'}$ = 2 Hz, $Ar\underline{H_{b'}}$). IR /cm^{-1}: 1 050 – 1 131 (C-O-C), 1 509 – 1 599 (Ar), 1 686 (C = O), 2 872 – 2 932 (ArH).

4.3.4 Synthesis of 4'-(hydroxymethyl)benzo-15-crown-5 (69) [Scheme 3.7, p. 43]

To a freshly prepared and ice-cooled suspension of sodium borohydride (1.36 g, 0.03604 mol) in a mixture of THF (2 cm^3) and ethanol (8 cm^3) was added 4'-formylbenzo-15-crown-5 (**68**, 5.34 g, 0.01802 mol) dissolved in a mixture of THF (10 cm^3) and ethanol (40 cm^3). Subsequent to stirring the reaction at room temperature (< 30 ^{0}C) for 5 hours, the reaction mixture was added to ice, filtered and the filtrate extracted with dichloromethane (3 x 100 cm^3). The organic phase was dried over $MgSO_4$ and removed under reduced pressure to give 4'-(hydroxymethyl)benzo-15-crown-5 **(69)** as a white solid, (4.97 g, 92.45 %) m.p. 45 – 47 ^{0}C. δ_H ($CDCl_3$, Spectrum A.4): 3.65 – 3.83 (8 H, s, $OC\underline{H_2}OC\underline{H_2}$), 3.83 – 3.99 (4 H, m, $PhOCH_2OC\underline{H_2}$), 4.05 – 4.24 (4 H, m, $PhOC\underline{H_2}OCH_2$), 4.50 – 4.57

(2 H, s, PhC$\underline{H}_2$OH), 6.78 – 6.97 (3 H, m, Ar$\underline{H}$). IR /cm^{-1}: 1 044 – 1 122 (C-O-C), 1 458 – 1 596 (Ar), 2 878 (ArH), 3328 – 3430 (O-H).

4.4 Polymer synthesis and re-functionalisation

4.4.1 Synthesis of polyepichlorhydrin (71) with Mr = 2 000 [Scheme 3.8, p. 47]

Phenol (**70**, 0.9411 g, 0.010 mol) was added to a mixture of pentane (10 cm^3) and hexane (10 cm^3) in a 500 cm^3 three-neck round-bottomed flask, equiped with an overhead stirrer. A solution containing epichlorohydrin (**1**, 18.84 g, 0.2036 mol) in hexane (40 cm^3) was prepared, placed in a dropping funnel and mounted on the three-neck flask. From this solution 0.5 cm^3 was added to the three-neck round-bottom flask. The internal temperature of the reaction mixture was then set to 25 ^{0}C and freshly distilled $BF_3.O(C_2H_6)_2$ complex (0.8 cm^3) was added to it under stirring. The remainder of the epichlorohydrin solution in the dropping funnel was the added over a period of 24 hours, while maintaining the temperature between 24 – 27 ^{0}C. Subsequent to addition, the reaction mixture was stirred for a further 30 minutes. The hexane phase was decanted and water (100 cm^3) was added. After stirring for 30 minutes, the water was decanted and the precipitate was dissolved in dichloromethane (100 cm^3). The dichloromethane phase was thoroughly washed with water (6 x 100 cm^3), dried over $MgSO_4$ and removal of the solvent under reduced pressure gave colourles highly viscous liquid as polyepichlorohydrin **(71)** (13.65 g), Mr = 2 083 g mol^{-1}. δ_H ($CDCl_3$): 3.48 – 3.68 (2 H, m, C$\underline{H}_2$Cl), 3.68 – 3.78 (3 H, m, C$\underline{H}$C$\underline{H}_2$O), 6.79 – 7.04 (Ar$\underline{H}$). IR /cm^{-1}: 1 100 (C-O), 850 (C-Cl).

4.4.2 Synthesis of polyepichlorohydrin (72) with Mr = 20 000 [Scheme 3.8, p. 47]

Phenol (**70**, 0.09411 g, 0.0010 mol) was added to a mixture of pentane (10 cm^3) and hexane (10 cm^3) in a 500 cm^3 three-neck round-bottom flask, equiped with an overhead stirrer. A solution of epichlorohydrin (**1**, 18.84 g, 0.2036 mol) in hexane (40 cm ^{3}) was prepared, placed in a dropping funnel and mounted on the three-neck flask. From this solution 0.5 cm^3 solution was added to the flask from the dropping funnel. After the internal temperature of the reaction mixture was set to 25 ^{0}C, freshly distilled $BF_3.O(C_2H_6)_2$ complex (0.08 cm^3) was added to the stirring solution. The remainder epichlorohydrin solution in the dropping funnel was then added over a period of 24 hours, while maintaining the temperature between 24 – 27 ^{0}C. Subsequent to addition, the reaction mixture was stirred for a further 30 minutes. The hexane phase was decanted and water (100 cm^3) was added. After stirring for 30 minutes, the water was decanted and the precipitate was dissolved in dichloromethane (100 cm^3). Following thorough washing of the dichloromethane phase with water (6 x 100 cm^3), the organic phase was dried over $MgSO_4$ and removal of the solvent under reduced pressure gave colourless, highly vicous liquid as polyepichlorohydrin **(72)** (11.07 g), M_r = 27 296 g mol^{-1}. δ_H ($CDCl_3$, Spectrum A.5): 3.48 – 3.68 (2 H, m, $C\underline{H_2}Cl$), 3.68 – 3.78 (3 H, m, $C\underline{H}C\underline{H_2}O$), 6.79 – 7.04 (Ar$\underline{H}$). IR /cm^{-1}(Figure 3.8, p. 62): 1 090 (C-O), 850 (C-Cl).

4.4.3 Azide-functionalised polymer (74) synthesis [Scheme 3.9, p. 50]

To a DMF (100 cm^3) solution of polyepichlorohydrin (**71**, 1.00 g, 0.1081 mol repeating units) in a two-neck round-bottom flask was added potassium carbonate (7.469 g, 0.05404 mol), tetrabutylammonium bromide (0.3484 g, 0.001081 mol) and sodium azide (7.028 g, 0.1081 mol). The reaction mixture was heated at 105 ^{0}C for 16 hours. Subsequent to cooling, the solution was diluted with dichloromethane (70 cm^3) and filtered. After the organic phase was washed with water (5 x 100 cm^3) and dried over $MgSO_4$, the solvent was evaporated under reduced pressure to give a yellow viscous liquid as poly (glycidyl azide) **(74)** (0.95 g, 95.00 %), M_r = 1 981 g mol^{-1}. δ_H ($CDCl_3$): 3.19 – 3.50 (2 H, m, $C\underline{H_2}N_3$), 3.50 – 3.93 (3 H, m, $C\underline{H}C\underline{H_2}O$), 6.89 – 7.01 (5 H, m, Ar$\underline{H}$). IR /cm^{-1}: 2 091 ($-N_3$).

4.4.4 Azide-functionalised polymer (75) synthesis [Scheme 3.9, p. 50]

To a DMF (100 cm^3) solution of polyepichlorohydrin (**72**, 5.00 g, 0.05404 mol repeating units) in a two-neck round-bottom flask was added potassium carbonate (3.734 g, 0.02702 mol), tetrabutylammonium bromide (0.1742 g, 0.0005404 mol) and sodium azide (3.5131 g, 0.05404 mol). The reaction mixture was heated at 105 ^{0}C for 16 hours. Subsequent to cooling, the solution was diluted with dichloromethane (70

cm^3) and filtered. After the organic phase was washed with water (5 x 100 cm^3) and dried over $MgSO_4$, the solvent was evaporated under reduced pressure to give a yellow viscous liquid as poly(glycidyl azide) **(75)**, M_r = 22 473 g mol^{-1} (4.92 g, 98.40 %). δ_H ($CDCl_3$, Spectrum A.6): 3.19 – 3.50 (2 H, m, $C\underline{H_2}N_3$), 3.50 – 3.93 (3 H, m, $C\underline{H}C\underline{H_2}O$), 6.89 – 7.01 (5 H, m, $Ar\underline{H}$). IR /cm^{-1} (Figure 3.8, p. 62): 2 091 ($-N_3$)

4.4.5 Azide-functionalised polymer (76) synthesis [Scheme 3.9, p. 50]

To a DMF (100 cm^3) solution of polyepichlorohydrin (**73**, 1.00 g, 0.01081 mol repeating units) in a two-neck round-bottom flask was added potassium carbonate (0.7470 g, 0.005405 mol), tetrabutyl ammonium bromide (0.03484 g, 0.0001081 mol) and sodium azide (0.7028 g, 0.01081 mol). The reaction mixture was heated for 16 hours at 105 ^{0}C. The cooled solution was diluted with dichloromethane (70 cm^3) and filtered. After the organic phase was thoroughly washed with water and dried over $MgSO_4$, the solvent was evaporated under reduced pressure to give a yellow rubbery-solid as poly(glycidyl azide) **(76)** (0.95 g, 95.00 %), M_r = 1 981 g mol^{-1}. δ_H ($CDCl_3$, Spectrum A.7): 3.25 – 3.52 (2 H, m, $C\underline{H_2}Cl$), 3.54 – 3.89 (3 H, m, $C\underline{H}C\underline{H_2}O$), 6.89 – 7.01 (5 H, m, $Ar\underline{H}$). IR /cm^{-1}: 2 091 ($-N_3$).

4.4.6 Attempted synthesis of amine-functionalised polymer (82) with BER method [Scheme 3.12, p. 55]

In a clean and dry two-neck round-bottom flask flushed with nitrogen gas, a solution of $Ni(OAc)_2.4H_2O$ (0.224 g, 0.0008987 mol) and poly(glycidyl azide) (**75**, 1.00 g, 0.01081 mol repeating units) in methanol (100 cm^3) was prepared. After 5 hours of stirring at room temperature the polymer was found to be insoluble in methanol. Reaction number **2**, **3**, and **4**, as shown in Table 3.1, p. 56, were ultimately attempted but the polymer was still found to be insoluble in the solvents. Eventually the polymer reaction was performed according to reaction conditions for Reaction number **5**, shown in Table 3.1, after stirring at room temperature for 1 hour the polymer had dissolved in the solvent. BER (15.82 g) was added to the reaction mixture and the reaction stirred for 4 hours at room temperature. The solution was filtered and the solvent removed under reduced pressure to give a yellow liquid residue. ^{1}H NMR indicated the yellow residue to be unreacted poly(glycidyl azide) **(75)**.

4.4.7 Preparation of Borohydride Exchange Resin (BER)[35]

An aqueous solution of sodium borohydride (1 M, 250 cm^3) was stirred with 50 g of wet chloride-form anion exchange resin (Amberlite IRA-400 [20 – 50 mesh]) for 1 hour. The resulting resin was washed thoroughly with distilled water until free of excess $NaBH_4$. The borohydride form anion exchange resin was then dried under reduced pressure at 60 ^{0}C for 5 hours. Subsequent to drying, the resin was analysed for borohydride content by hydrogen evolution on acidification with 2 M HCl and the average capacity of BER was found to be 2.5 mmol BH_4^- per gram. The dried resin was stored under nitrogen in refrigerator (~ 4 ^{0}C).

4.4.8 A ttempted amine-functionalised polymer (85) synthesis with H_2 in the presence of 10 % palladium-carbon [Scheme 3.13, p. 56]

To a flask containing poly(glycidyl azide) (**75**, 0.100 g, 0.001009 mol repeating units) dissolved in THF (4 cm^3) was added 10 % palladium-carbon (0.0400 g) and ethanol (16 cm^3). Hydrogen was bubbled through the mixture for 48 hours, while maintaining the volume of the reaction at 20 cm^3. The reaction mixture was separated from the palladium-carbon by decantation and the solvent removed under reduced pressure to give polymer **85**. Polymer **85** was found to contain small amounts of palladium-carbon and material could only be recoverd in small quantities.

4.4.9 Amine-functionalised polymer (82d) synthesis with $LiAlH_4$ [Scheme 3.14, p. 57]

Poly(glycidyl azide) (**75**, 2.00 g, 0.02018 mol repeating units) dissolved in anhydrous THF (50 cm^3) was slowly added to anhydrous THF (100 cm^3) suspension of $LiAlH_4$ (5.765 g, 0.1519 mol) at 0 ^{0}C. The solution was allowed to stir at room temperature for 48 hours. After cooling, unreacted $LiAlH_4$ was quenched by addition of ice and the solution was filtered through a thick pad of celite. The reaction mixture was dialysed for 48 hours in a 3 000 molecular mass cut-off membrane tubing against a running tap water, followed by freeze drying to give the final product as a yellowish sticky solid polymer **82d** (0.685 g, 34 %), M_r = 16 571 g mol^{-1}. δ_H (D_2O, Spectrum A.8): 2.80 – 3.18 (2 H, m, $C\underline{H_2}NH_2$), 3.32 – 3.94 (3 H, m, $C\underline{H}C\underline{H_2}O$), 6.89 – 7.01 (5 H, m, Ar$\underline{H}$). IR /cm^{-1} (Figure 3.8, p. 62): 1 087 (C-O), 3 350 ($-NH_2$).

4.4.10 Synthesis of isocyanate-functionalised polymer (87) with KNCO [Scheme 3.15, p. 58]

To a DMF solution of polyepichlorohydrin (**72**, 1.00 g, 0.01081 mol repeating units) in a three-neck round-bottom flask was added potassium carbonate (0.7464 g, 0.005405 mol), tetrabutylammonium bromide (0.03484 g, 0.0001081 mol) and potassium isocyanate (0.8765 g, 0.01081 mol). The solution was heated for 16 hours at 105 ^{0}C. After the solution was cooled to room temperature and filtered, hexane was added to the filtrate and the solution stirred at room temperature for 24 hours. The hexane layer was decanted, and the colourless polymer **87** was obtained showing a low NCO content as judged by the intensity of the -NCO peak in the IR spectrum, (0.836 g, 83.6 %). δ_H ($CDCl_3$): 3.19 – 3.40 (2 H, t, $C\underline{H_2}NCO$), 3.40 – 4.01 (5 H, m, $C\underline{H}(C\underline{H_2}Cl)C\underline{H_2}O$), 6.89 – 7.01 (5 H, m, Ar$\underline{H}$). IR /cm^{-1}: 2 149 (-NCO).

4.4.11 Preparation of potassium isocyanate[122] [Scheme 3.16, p. 59]

Finely powdered anhydrous potassium carbonate (35.00 g, 0.2532 mol) was thoroughly mixed with urea (40.00 g, 0.6667 mol) in a porcelain evaporating dish. The mixture, while continuously pressing it down, was heated (under the hood) with a bunsen burner whose flame was gradually increased until full flame was utilised. As soon as the melt was quiescent and the surface was nearly free of bubbles, the flame was turned down and the test for carbonate was made by adding barium chloride. When the melt was found to be carbonate free, i.e. when no barium carbonate precipitate was formed, the molten substance was poured into a dry mortar and swirled until the crystals began to adhere to the sides of the container. Following grinding of the hot product, crude potassium isocyanate was obtained and dissolved in water (50 cm^3). Glacial acetic acid was added until the solution became neutral to phenolpthalein. The warm solution was then quickly filtered into a 250 cm^3 flask, rinsed with warm water (50 ^{0}C) and the filtrate treated with ethanol (150 cm^3). After ethanol was thoroughly mixed with water, the flask was placed overnight in a refrigerator. The formed crystals were then removed on a Büchner funnel and washed with ethanol. Subsequent to drying over barium oxide, potassium isocyanate (41.23 g, 76.24 %) was obtained as white crystals.

4.4.12 Attempted synthesis of isocyanate-functionalised polymer with silver isocyanate (AgNCO)

To a DMSO (120 cm^3) solution of polyepichlorohydrin (**72**, 1.00 g, 0.01081 mol repeating unit) in a three-neck round bottom flask, was added potassium carbonate (0.7464 g, 0.005475 mol), tetrabutylammonium bromide (0.03484 g, 0.0001081 mol) and silver isocyanate (1.6203g, 0.01081 mol). The solution was heated for 16 hours at 105 ^{0}C in a dark room. Subsequent to cooling, the brown reaction mixture was filtered. Hexane was added to the brown filtrate to extract DMSO. After stirring at room temperature for 48 hours the product could still not be recovered by precipitation from a brown solution.

4.4.13 Isocyanate-functionalised polymer (88) synthesisError! Bookmark not defined. [Scheme 3.19, p. 61]

A solution of polymer **82d** (0.500 g, 0.000684 mol repeating unit) and 1,8-bis(dimethylamino)naphthalene (**89**, 0.2928 g, 0.001366 mol) in DMSO (10 cm^3) was added over a period of 5 minutes to a stirred DMSO (10 cm^3) solution of trichloromethyl chloroformate (**90**, 0.0813 g, 0.0004108 mol) at 0 ^{0}C. Subsequent to addition, the mixture was stirred for a further 1 hour, and DMSO was removed by extraction with hexane to leave a white precipitate. The precipitate was dissolved in dichloromethane and dried over $MgSO_4$ and the solvent removed under reduced pressure to give a colourless highly viscous polymer **88** (0.4502 g, 90.04 %), , M_r = 22 686 g mol^{-1}. δ_H ($CDCl_3$): 3.18 –3.40 (2 H, m, $C\underline{H_2}NCO$), 3.40 – 4.01 (3 H, m, $C\underline{H}C\underline{H_2}O$), 6.89 – 7.01 (5 H, m, $Ar\underline{H}$). IR /cm^{-1} (Figure 3.8, p. 62): 2 149 (-NCO).

4.4.14 Hydroxy-functionalised polymer (95) synthesis [Scheme 3.21, p. 64]

To a DMSO (100 cm^3) solution of polyepichlorohydrin (**72**, 1.00 g, 0.01081 mol repeating unit) in a two-neck round-bottom flask was added potassium carbonate (0.7470 g, 0.005404 mol), tetrabutylammonium bromide (0.03485 g, 0.0001081 mol) and a satured solution NaOH (0.8429 g, 0.02152 mol) in water (2 cm^3). The solution was heated for 16 hours at 105 ^{0}C. After the reaction mixture was cooled and filtered, the solution was dialysed for 48 hours in a 3 000 molecular mass cut-off membrane tubing against a running tap water, followed by freeze drying to give the final product as a dark-brown solid polymer **95** (0.4509 g, 45.09 %), . δ_H (D_2O, Spectrum A.9): 3.38 – 3.54 (2 H, m, $C\underline{H_2}OH$), 3.54 – 3.77 (3 H, m, $C\underline{H}C\underline{H_2}O$), 6.85 – 6.97 (3, m, $Ar\underline{H_a}\underline{H_b}\underline{H_c}$), 7.18 – 7.29 (2 H, m, $Ar\underline{H_d}\underline{H_e}$). IR /cm^{-1} (Figure 3.8, p. 62): 1 050 (C-O), 3 300 (-OH).

4.5 Preparation of compounds used as model reactions

4.5.1 Preparation of benzyl azide (80) [Scheme 3.11, p. 53]

To a DMF (20 cm^3) solution of benzyl bromide (**79**, 2.00 g, 0.01169 mol) in a two-neck round-bottom flask, was added potassium carbonate (0.8078 g, 0.005845 mol), tetrabutylammonium bromide (0.03769 g, 0.0001169) and sodium azide (0.7607 g, 0.01169 mol). The reaction mixture was heated for 16 hours at 105 ^{0}C. The cooled solution was diluted with dichloromethane (70 cm^3) and stirred for another 15 minutes. After filtering the solution, the filtrate was washed with water (5 x 100 cm^3), the organic phase dried over $MgSO_4$ and evaporated under reduced pressure to give a yellow liquid, benzyl azide **(80)** (1.90 g, 91.51 %). δ_H ($CDCl_3$, Spectrum A.10): 4.31 – 4.42 (2 H, s, $C\underline{H_2}N_3$), 7.28 – 7.51 (5 H, m, $Ar\underline{H}$). IR /cm^{-1}(Figure 3.6, p. 55): 2 091 ($-N_3$).

4.5.2 Preparation of benzylamine (81)[35] [Scheme 3.11, p. 53]

To the reaction flask containing $Ni(OAc)_2.4H_2O$ (0.25 g, 0.001005) and benzyl azide (**80**, 1.33 g, 0.007488 mol) solution in methanol (100 cm^3), was added

BER (15.20 g, 0.0030 mol). The mixture was stirred for 30 minutes at room temperature to complete the reduction. After the resin was removed by filtration, the filtrate was poured into water (150 cm^3) and extracted with dichloromethane (3 x 100 cm^3). The combined extracts were dried with $MgSO_4$ and evaporated under reduced pressure to give a yellow solid, benzylamine **(81)**, (1.37 g, 96 %), m.p. 10 ^{0}C. δ_H (D_2O, Spectrum A.11): 5.25 – 5.37 (2 H, s, $C\underline{H_2}N\underline{H_2}$), 7.27 – 7.38 (Ar$\underline{H}$). IR /$cm^{-1}$ (Figure 3.6, p. 55): 3 350 ($-NH_2$).

4.5.3 Preparation of benzyl isocyanate (91)[123] [Scheme 3.17, p. 60]

A solution of benzylamine (**81**, 0.3218 g, 0.001293 mol) and 1,8-bis(dimethylamino)naphthalene (**89**, 0.5536 g, 0.002583 mol) in dichloromethane (10 cm^3), was added dropwise to a stirred dichloromethane (10 cm^3) solution of trichloromethyl chloroformate (**90**, 0.1536 g, 0.0007765 mol) at 0 ^{0}C over a period of 5 minutes. Following a further 20 minutes of stirring at room temperature, the volatiles were evaporated under reduced pressure. The residue was partitioned between dichloromethane (20 cm^3) and 1M hydrochloric acid. Subsequently, the organic phase was separated and washed successively with 1 M hydrochloric acid (3 x 10 cm^3) and 1 M NaOH (10 cm^3). After the separated organic phase was dried over $MgSO_4$, the solvent was removed under reduced pressure to yield colourless liquid, benzyl isocyanate **(91)**, (0.240 g, 86 %). δ_H ($CDCl_3$, Spectrum A.12): 4.48 – 4.59 (2 H, s, $C\underline{H_2}NCO$), 7.27 – 7.60 (5 H, m, Ar$\underline{H}$). IR /cm^{-1}: 2 149 (-NCO).

4.5.4 Preparation of ferrocyl isocyanate (92)[123] [Scheme 3.18, p. 60]

A solution of ferrocylamine (**93**, 0.020 g, 0.00009299 mol) and 1,8-bis(dimethylamino)naphthalene (**89**, 0.0390 g, 0.0001857 mol) in dichloromethane (5 cm^3) was added dropwise to a stirred dichloromethane (5 cm^3) solution of trichloromethyl chloroformate (**90**, 0.01105 g, 0.00005584 mol) at 0 ^{0}C over a period of 5 minutes. The reaction mixture was then stirred for a further 20 minutes at room temperature before evaporation of the volatiles under reduced pressure. Subsequently, the residue was partitioned between dichloromethane (10 cm^3) and 1 M hydrochloric acid (5 cm^3) followed by a successive wash of the organic phase with 1 M hydrochloric acid (3 x 10 cm^3) and 1 M NaOH (10 cm^3). After the organic phase was dried over $MgSO_4$, the solvent was removed under reduced pressure to yield a reddish-orange liquid isocyanate-containing ferrocene derivative **(92)**, (0.0153 g, 68.24 %). IR /cm^{-1} (Figure 3.7, p. 61): 2 149 (-NCO).

4.5.5 Coupling of ferrocyl isocyanate (92) with 4'-(hydroxymethyl)benzo-15-crown-5 (69) [Scheme 3.20, p. 63]

To a solution of **92** (0.010 g, 0.00004148 mol) in dichloromethane (10 cm^3) was added 4'-(hydroxymethyl)benzo-15-crown-5 (**69**, 0.01233 g, 0.00004148 mol). The resulting mixture was stirred at room temperature for 24 hours. The solvent was removed under reduced pressure to yield crude product. After the crude product was cleaned with column chromatography using a mixture of methanol and aqueous ammonia in 95:5 (v/v) ratio, **94** was obtained as yellow-orange wax-like solid, (0.02188 g, 98.21 %). δ_H ($CDCl_3$, Spectrum A.13): 3.69 – 3.84 (8 H, m, $OC\underline{H_2}OC\underline{H_2}$), 3.88 – 3.98 (4 H, m, $PhOCH_2OC\underline{H_2}$), 3.98 – 4.11 (2 H, m, Fc-$C\underline{H_2}NHCOCH_2Ph$), 4.11 – 4.40 (13 H, m, $PhOC\underline{H_2}$ and Fc-$\underline{H}$), 5.01 – 5.14 (2 H, m, Ph-$C\underline{H_2}OCNHCH_2Fc$). IR /$cm^{-1}$: 1 100 (C-O), 1 500 (C=O), 3 000 – 3 400 (NH).

4.6 Anchoring experiments

4.6.1 The anchoring of carboxylic acid-containing ferrocene derivative (96) onto polymer (82d) [Scheme 3.22, p. 65]

To a solution of amine-functionalised polymer (**82d**, 0.05 g, 0.000684 mol repeating unit) dissolved in DMF (2 cm^3), was added triethylamine (0.070 g, .00070 mol) followed by a DMF (2 cm^3) solution of **96** (0.1861 g, 0.000684 mol) and then *O*-benzotriazolyl-*N*,*N*,*N'*,*N'*-tetramethyluronium hexafluorophosphate (**53**, 0.227g, 0.0006 mol). The mixture was stirred for 5 hours at room temperature. The resulting reaction mixture was diluted with dichloromethane (100 cm^3), washed with water (3 x 100 cm^3) and 1 M NaOH (2 x 100 cm^3). The dichloromethane phase was dried over $MgSO_4$, and removed under reduced pressure to give crude polymer **97**. Following fractional precipitation with pentane, polymer **97** was obtained as brown-orange solid, (0.1653 g, 70 %). δ_H ($CDCl_3$, Spectrum A.14): 1.23 – 1.34 [3 H, s, $CH(C\underline{H_3})$], 2.11 – 2.69 (2 H, m, $C\underline{H_2}CH$), 2.97 – 3.15 (1 H, m, $CH[C\underline{H_a}$-NHCOCH2CH(CH_3)-

Fc]CH_2O, 3.27 – 3.69 (4 H, m, $C\underline{H}[C\underline{H}_{\underline{b}}$- NHCOCH2CH($CH_3$)-Fc]$C\underline{H}_{\underline{2}}O$), 3.98 – 4.36 (9 H, m, Fc-$\underline{H}$). IR /cm^{-1}: 990 – 1 100 (C-O), 1 650 (C=O), 3 100 – 3 650 (-NH).

4.6.2 Anchoring of carboxylic acid-containing ferrocene derivative 101 onto polymer 82d [Scheme 3.23, p. 67]

To a solution of polymer **82d** (0.1090 g, 0.00149 mol repeating unit) dissolved in a mixture of DMF (6 cm^3) and water (2 cm^3), was added triethylamine (0.200 g, 0.00198 mol) followed by **101** (0.4085 g, 0.00150 mol) and *O*-benzotriazolyl-*N*,*N*,*N'*,*N'*-tetramethyluronium hexafluorophosphate (**53**, 0.227 g, 0.0006 mol). The solution was stirred for 5 hours at room temperature, after which it was filtered and the filtrate precipitated with hexane. The precipitate was washed with water (2 x 100 cm^3) and then acetone (2 x 100 cm^3). After washing, the precipitate was dissloved in dichloromethane, dried over $MgSO_4$ and the solvent removed under reduced pressure to yield polymer **105**, (0.022 g, 4.25 %). The low yield was taken to imply anchoring was not effective, thus the polymer was mostly washed away with water. The ferrocene-containing polymer with high ferrocene content dissolves poorly in water. δ_H ($CDCl_3$, Spectrum A.15): 1.01 – 1.39 (2 H, m, pol-$NHCOC\underline{H}_{\underline{2}}CH_2CH_2Fc$), 2.10 – 2.78 (4 H, m, pol-$NHCOCH_2C\underline{H}_{\underline{2}}C\underline{H}_{\underline{2}}Fc$), 2.78 – 3.95 (5 H, m, $C\underline{H}[C\underline{H}_{\underline{2}}$-$NHCOCH_2CH_2CH_2Fc]C\underline{H}_{\underline{2}}O$), 3.95 – 5.09 (9 H, m, Fc-$\underline{H}$). δ_H (deuterated DMSO, Spectrum A.16): 1.67 – 1.79 (2 H, m, pol-$NHCOC\underline{H}_{\underline{2}}CH_2CH_2Fc$), 2.14 – 2.27 (4 H, m, pol-$NHCOCH_2C\underline{H}_{\underline{2}}C\underline{H}_{\underline{2}}Fc$), 3.93 – 4.22 (9 H, m, Fc-$\underline{H}$).

The same reaction procedure was followed for anchoring of **98** (0.3451 g, 0.001500) onto polymer **82d** (0.109 g, 0.00149 mol repeating unit) to give polymer **102**, (0.0109 g, 2.40 %). δ_H ($CDCl_3$, Spectrum A.17): 2.78 – 3.36 (3 H, m, $C\underline{H}C\underline{H}_{\underline{2}}O$), 3.36 – 3.87 (2 H, m, $C\underline{H}_{\underline{2}}$-NHCOFc), 4.16 – 4.55 (5 H, m, $C_5\underline{H}_{\underline{5}}$), 4.58 – 4.74 ($C_5\underline{H}_{\underline{a}}\underline{H}_{\underline{b}}$), 4.74 – 5.29 ($C_5\underline{H}_{\underline{c}}\underline{H}_{\underline{d}}$).

4.6.3 Anchoring of carboxylic acid-containing ferrocene derivative 100 onto polymer 82d [Scheme 3.23, p. 67]

To a solution polymer **82d** (0.1090 g, 0.00149 mol repeating unit) dissolved in a mixture of DMF (6 cm^3) and water (2 cm^3), was added triethylamine (0.200 g, 0.00198 mol) followed by a THF (2 cm^3) solution of **100** (0.3872 g, 0.00150 mol) and *O*-benzotriazolyl-*N,N,N',N'*-tetramethyluronium hexafluorophosphate (**53**, 0.2270 g, 0.0006 mol). The reaction mixture was stirred at room temperature for 5 hours, afterwhich it was filtered and the filtrate precipitated with hexane. The precipitate was washed with water (2 x 100 cm^3) and then acetone (2 x 100 cm^3). After washing, the precipitate was dissolved in dichloromethane, dried over $MgSO_4$ and the solvent removed under reduced pressure to give polymer **104**, (0.223 g, 44.94 %). δ_H ($CDCl_3$, Spectrum A.18): 2.23 – 2.40 (2 H, m, pol-$NHCOC\underline{H_2}CH_2Fc$), 2.40 – 2.79 (2 H, m, pol-$NHCOCH_2C\underline{H_2}Fc$), 2.98 – 3.87 (5 H, m, $C\underline{H}[C\underline{H_2}$-$NHCOCH_2CH_2Fc]C\underline{H_2}O$), 4.07 – 5.03 (Fc-$\underline{H}$). δ_H (deuterated DMSO, Spectrum A.19): 2.29 – 2.48 (2 H, m, pol-$NHCOC\underline{H_2}CH_2Fc$), 3.94 – 4.19 (9 H, t, Fc-$\underline{H}$).

The same procedure was followed for anchoring of **99** (0.3661 g, 0.00150 mol repeating unit) onto polymer **82d** to give polymer **103** (0.3050 g, 64.19 %). δ_H ($CDCl_3$, Spectrum A.20): 2.51 – 3.94 (7 H, m, $C\underline{H}[C\underline{H_2}$-$NHCOC\underline{H_2}Fc]C\underline{H_2}O$), 3.96 – 5.78 (9 H, m, Fc-$\underline{H}$).

4.6.4 Attempted anchoring of acetic anhydride (106) onto polymer 95 [Scheme 3.24, p. 70]

Acetic anhydride (**106**, 0.02794 g, 0.0002737 mol) was added to a dichloromethane (10 cm^3) solution of polymer **95** (0.0100 g, 0.0001369 mol repeating unit). The mixture was allowed to stir for 24 hours at room temperature. The solution was concentrated by removing the solvent under reduced pressure to give polymer **107**. From IR spectrum, polymer **107** was found to have only low acetyl content.

4.6.5 Anchoring of benzyl isocyanate (91) onto polymer 95 [Scheme 3.25, p. 71]

To a DMSO (10 cm^3) solution of hydroxy polymer **95** (0.0200 g, 0.0002737 mol repeating unit) was added benzyl isocyanate (**91**, 0.07178 g, 0.0005474 mol). The mixture was stirred for 24 hours at room temperature. The reaction mixture was diluted with dichloromethane (100 cm^3) and washed with water (5 x 100 cm^3). After the dichloromethane phase was dried over $MgSO_4$, the solvent was removed under reduced pressure to give polymer **108** as a colourless solid, (0.08081 g, 88.05 %). δ_H

($CDCl_3$, Spectrum A.21): 3.16 - 3.84 (3 H, m, $C\underline{H}C\underline{H_2}O$), 3.84 – 4.32 (2 H, m, $C\underline{H_2}OOCNHCH_2Ph$), 4.32 – 4.41 (2 H, s, $CH_2OOCNHC\underline{H_2}Ph$), 7.22 – 7.44 (5 H, m, $Ar\underline{H}$). IR /cm^{-1}: 1 087 – 1 320 (C-O), 1720 (C=O), 3 300 – 3 400 (-NH).

---

[122] *Inorganic Syntheses*, **vol. 2**, **1946**, pp. 88

5.1 Summary

The main aim of this study was to develop highly reactive polymeric spacer systems capable of acting as a linking unit between an elastomeric solid support and a metal ion scavenging ligand, as mentioned in Chapter 1 and 2.

During this study, benzo-15-crown-5 was synthesised as a sodium cation-scavenging ligand. This crown ether moiety was then functionalised to give 4’-formylbenzo-15-crown-5 and 4’-(hydroxymethyl)benzo-15-crown-5. The first synthesis of ferrocyl isocyanate is reported. The reaction between this compound and 4’-(hydroxymethyl)benzo-15-crown-5 provided a new benzo-15-crown-5 / ferrocene conjugate.

Polyepichlorohydrin and its derivatives were focused on for the development of suitable polymeric spacer linking units between a solid support and the crown ether sodium cation-scavenging ligand. Consequently, epichlorohydrin was polymerised to polyepichlorohydrin derivatives having molar masses of 2 000 and 20 000 g mol^{-1} following a cationic ring-opening process and utilising the BF_3 / phenol initiator system. The chloro-containing alkyl side chains of polyepichlorohydrin were re-functionalised to $-N_3$ in the presence of phase transfer catalyst (tetrabutylammonium bromide) by reacting polyepichlorohydrin with sodium azide in DMSO at 110 ^{0}C. The azide polymer was converted to an amine polymer in high yields utilising $LiAlH_4$ as a reducing reagent. Polymer supported BH_4^- (BER) in the presence of nickel acetate as a catalyst failed to promote this reaction. Hydrogen gas in the presence of 10 % palladium-carbon induced azide reduction, however, the yields obtained were much lower than the yields obtained using $LiAlH_4$. The amine-containing polymer was converted to an isocyanate polymer with the diphosgene derivative, trichloromethyl chloroformate. The hydroxy-functionalised polymer was obtained by reacting polyepichlorohydrin with NaOH in the presence of a phase transfer catalyst.

The reactivity of the $-NH_2$, -NCO and -OH functional groups on these polymers was tested through various model reactions. This included anchoring of carboxylic acid-containing ferrocene series, Fc-$(CH_2)_n$COOH with n = 0 – 3, onto the amine-functionalised polymer under the influence of the coupling reagent, *O*-benzotriazolyl-*N*,*N*,*N’*,*N’*-tetramethyluronium hexafluorophosphate. The newly obtained polymer-bound ferrocene derivatives may have appreciable anticancer activity. The reactivity of the isocyanate functional groups was tested by reacting with alcohol functional groups.

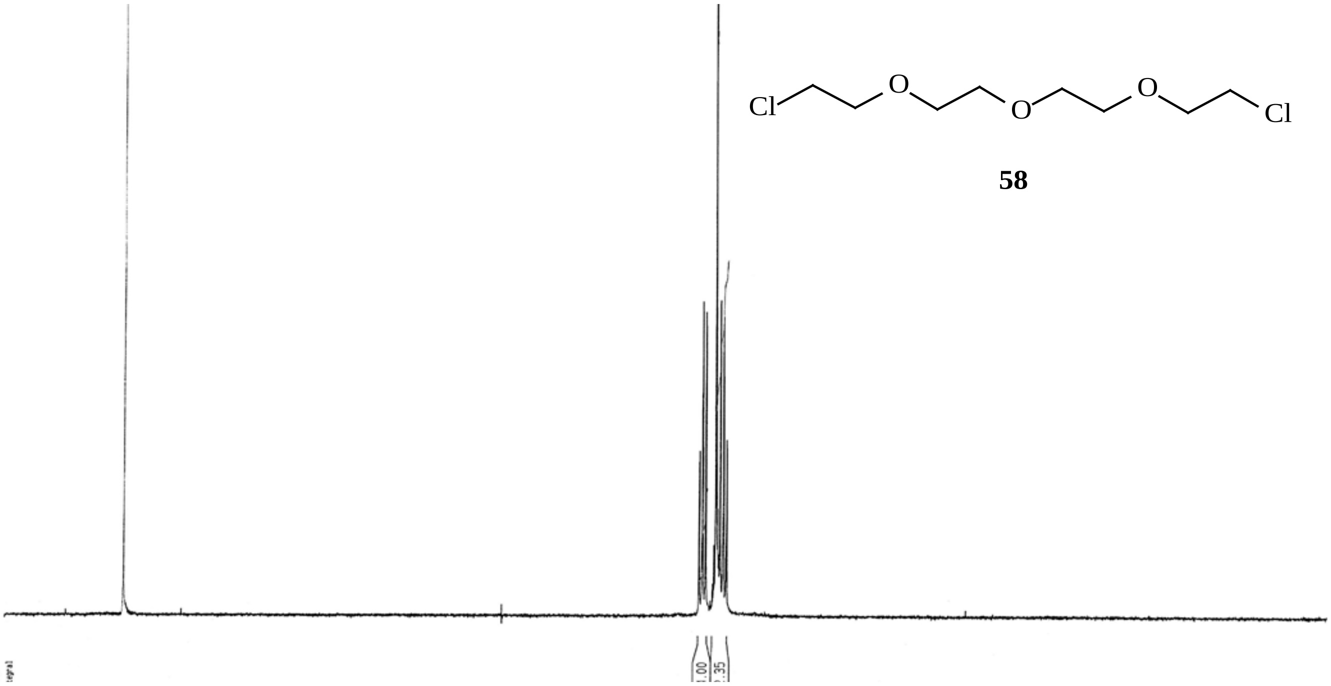
Through the course of this study eleven hitherto unknown compounds were synthesised. These include three highly reactive polymeric derivatives of polyepichlorhydrin, five polymer-bound ferrocene derivatives, a polymer-bound phenyl derivative, ferrocyl isocyanate and a ferrocene-crown ether conjugate. All the compounds were characterised utilising *inter alia* techniques such as melting point determination, IR spectroscopy and ^{1}H NMR spectroscopy.

5.2 Future perspectives

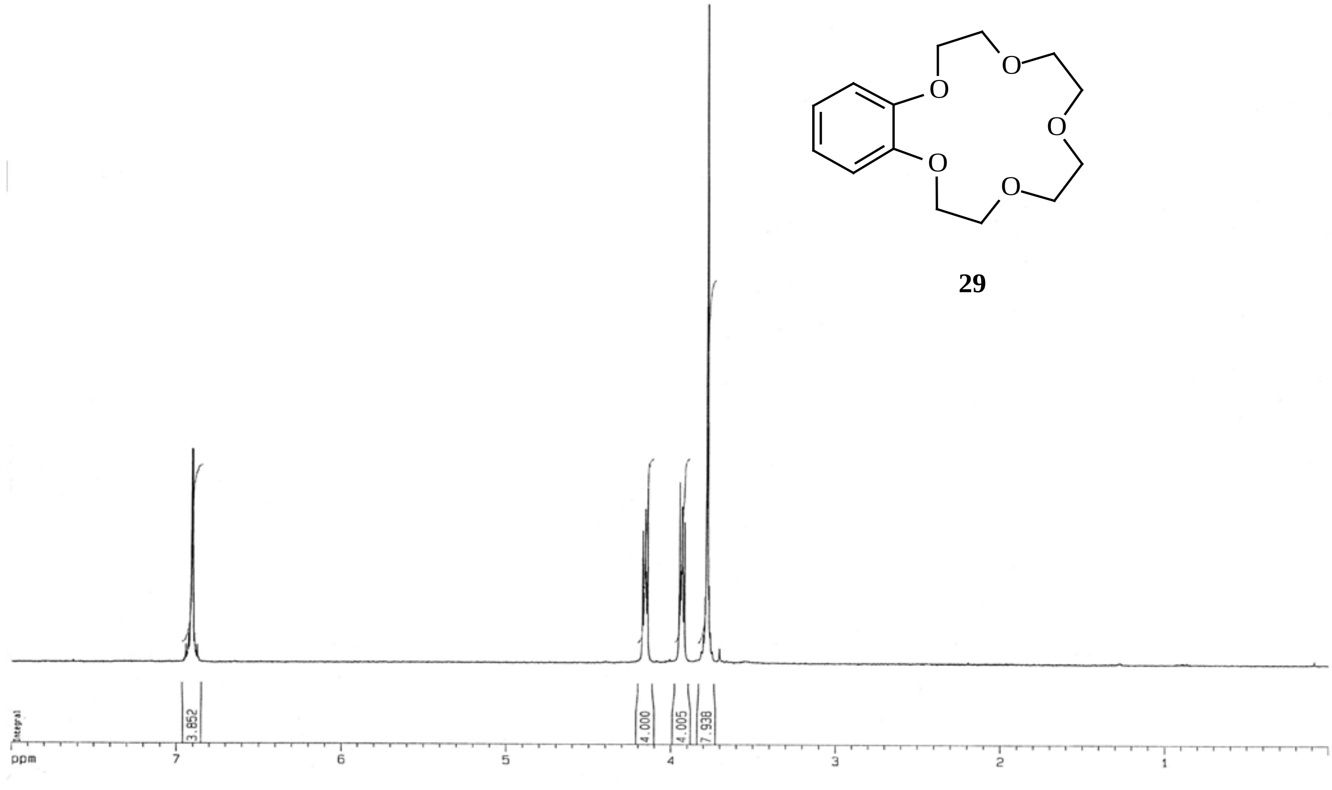
The successful preparation of highly reactive polyepichlorohydrin derivatives achieved in this study opens up a variety of research. Firstly, methods to anchor onto these polymers sodium metal ion-scavenging ligands, i.e. benzo-15-crown-5, and other crown ether ligands selective for specific metal ions can now be developed. The use and efficiency of these polyepichlorohydrin derivatives as polymeric spacer linking units between a solid support and a crown ether sodium cation scavenging ligand, as mentioned in Chapter 1, need to be investigated. Once all that has been successfully achieved a device such as that in Figure 1.1, p. 3, need to be assembled, and a study on the efficiency of such a device to remove metal ions from industrial wastewater and to release these metal cations from the contaminant scavenging device need to be conducted. Research also needs to be extended by developing metal ion-scavenging ligands capable of trapping more metal ions, other than sodium, especially precious metals such as gold and platinum.

Many polymer-bound ferrocene derivatives with bioactivity had previously been prepared, but according to the knowledge of the author none has ever been anchored onto polyepichlorhydrin derivatives. Polyepichlorohydrin-anchored ferrocene derivatives prepared in this study, calls for further research into their bioactivity, physical and chemical behaviour.

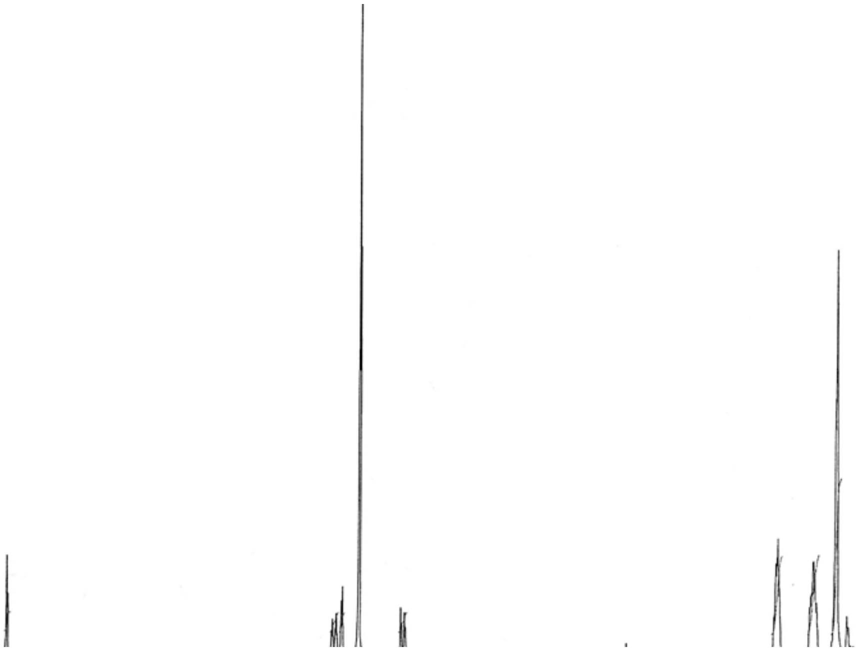
In recent years, energetic polymeric binders have proved to be essential in solid propellant industry, though only a small number of these binders have thus far been successfully prepared. The high reactivity of polymers developed in this study also opens up a new avenue for the use of these polymers as possible energetic binders needed in solid propellant industry.

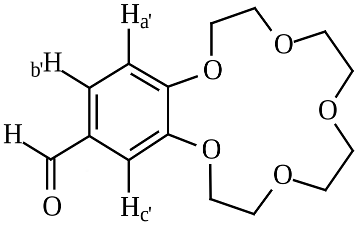

Cl
O
O
O
Cl
1.00
1.35

58

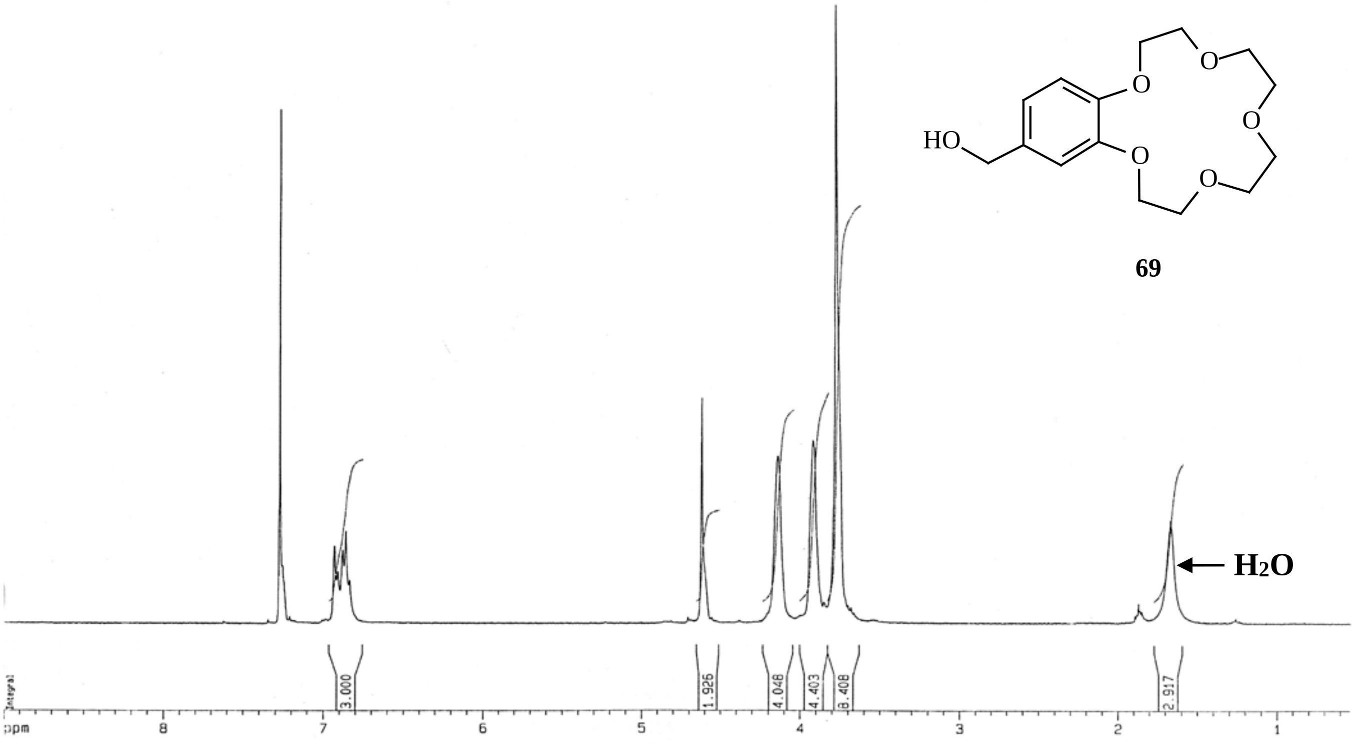

O
O
O
O
O
Integral
3.852
4.000
4.005
7.938
ppm
7
6
5
4
3
2
1

29

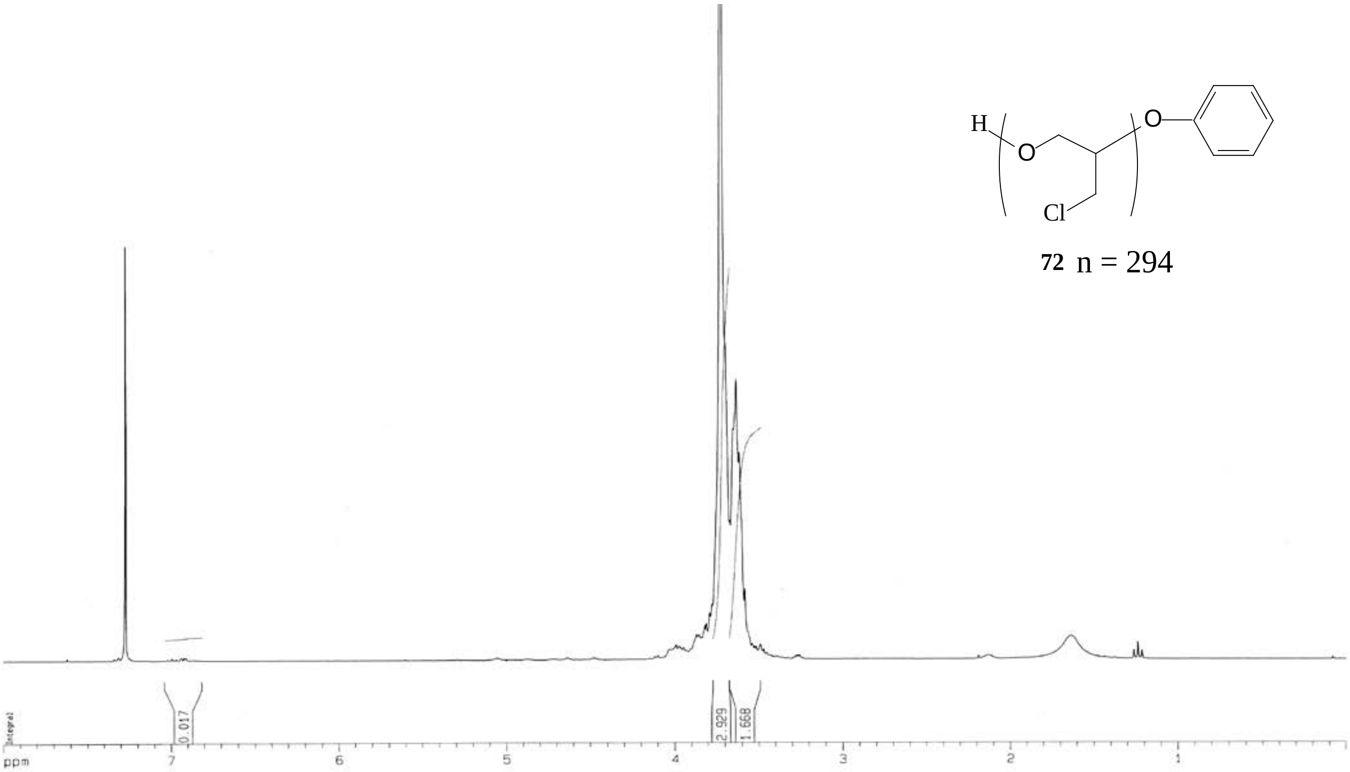



Ha'
b'H
H
O
Hc'
O
O
O
O
O

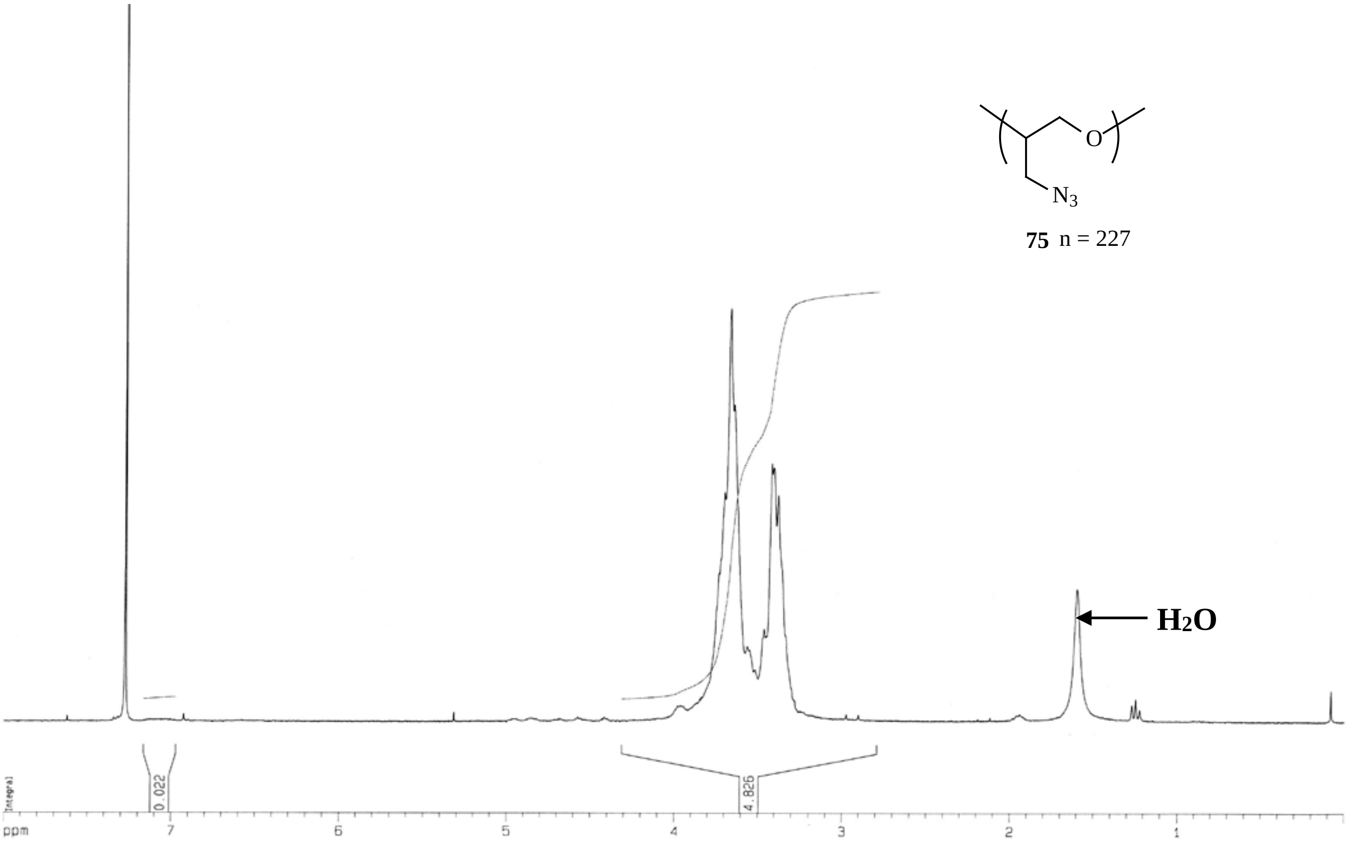
68


HO
O
O
O
O
O
H2O
Integral
3.000
1.926
4.048
4.403
8.408
2.917
ppm
8
7
6
5
4
3
2
1

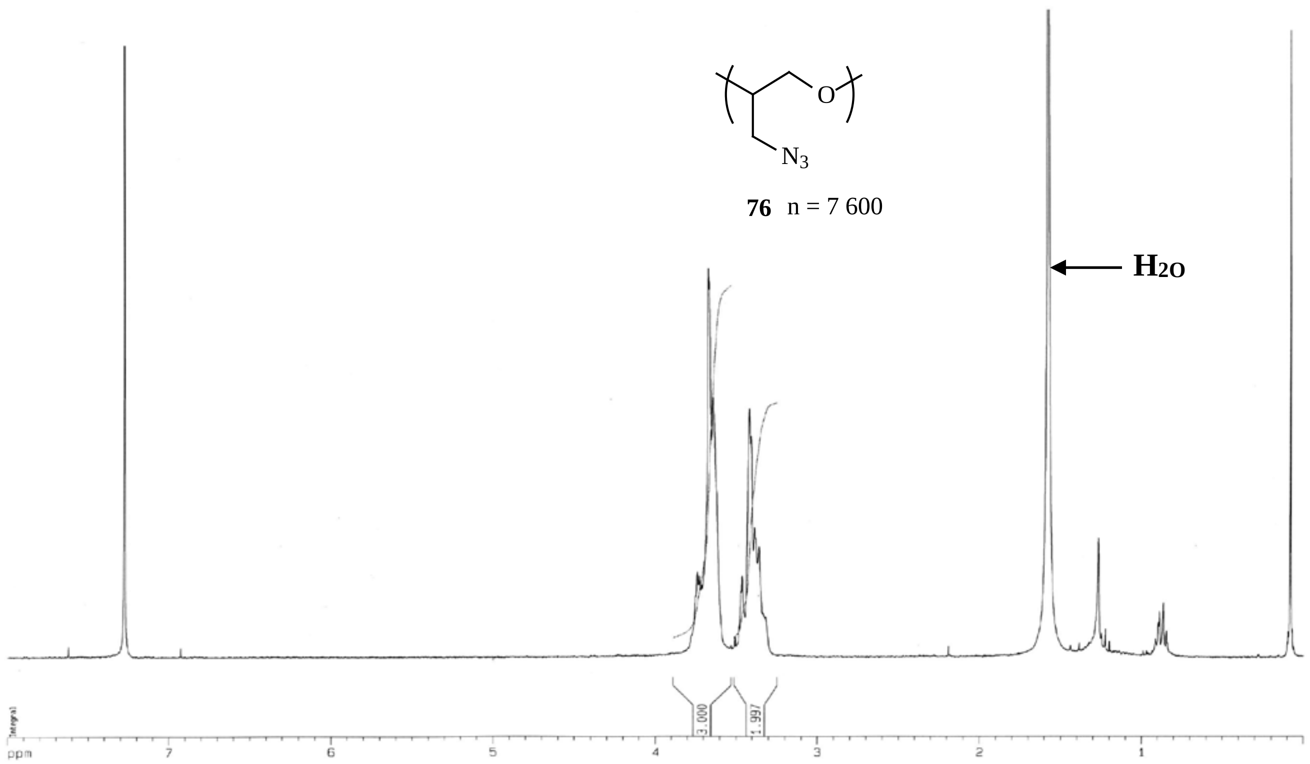
69



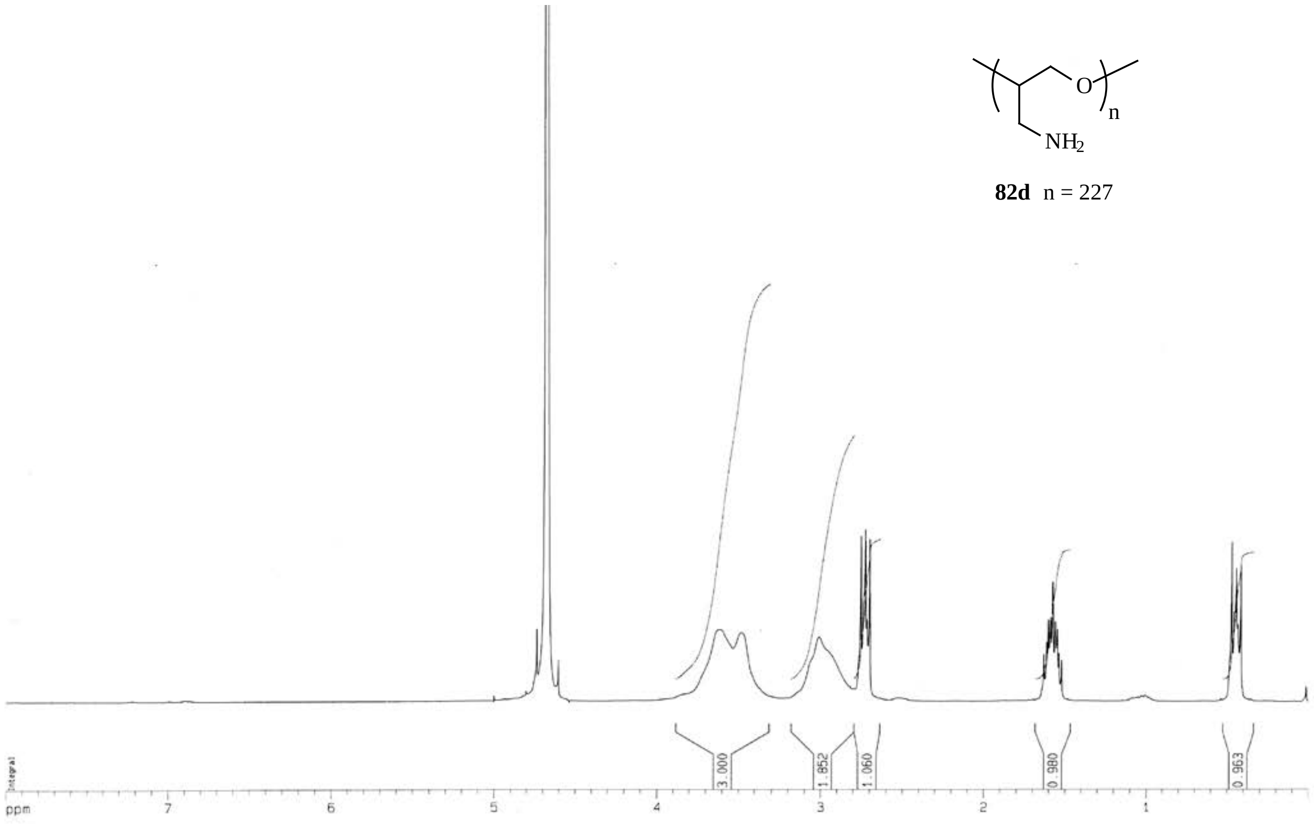
Spectrum A.5: ^{1}H NMR spectrum of polyepichlorohydrin (72) in $CDCl_3$.



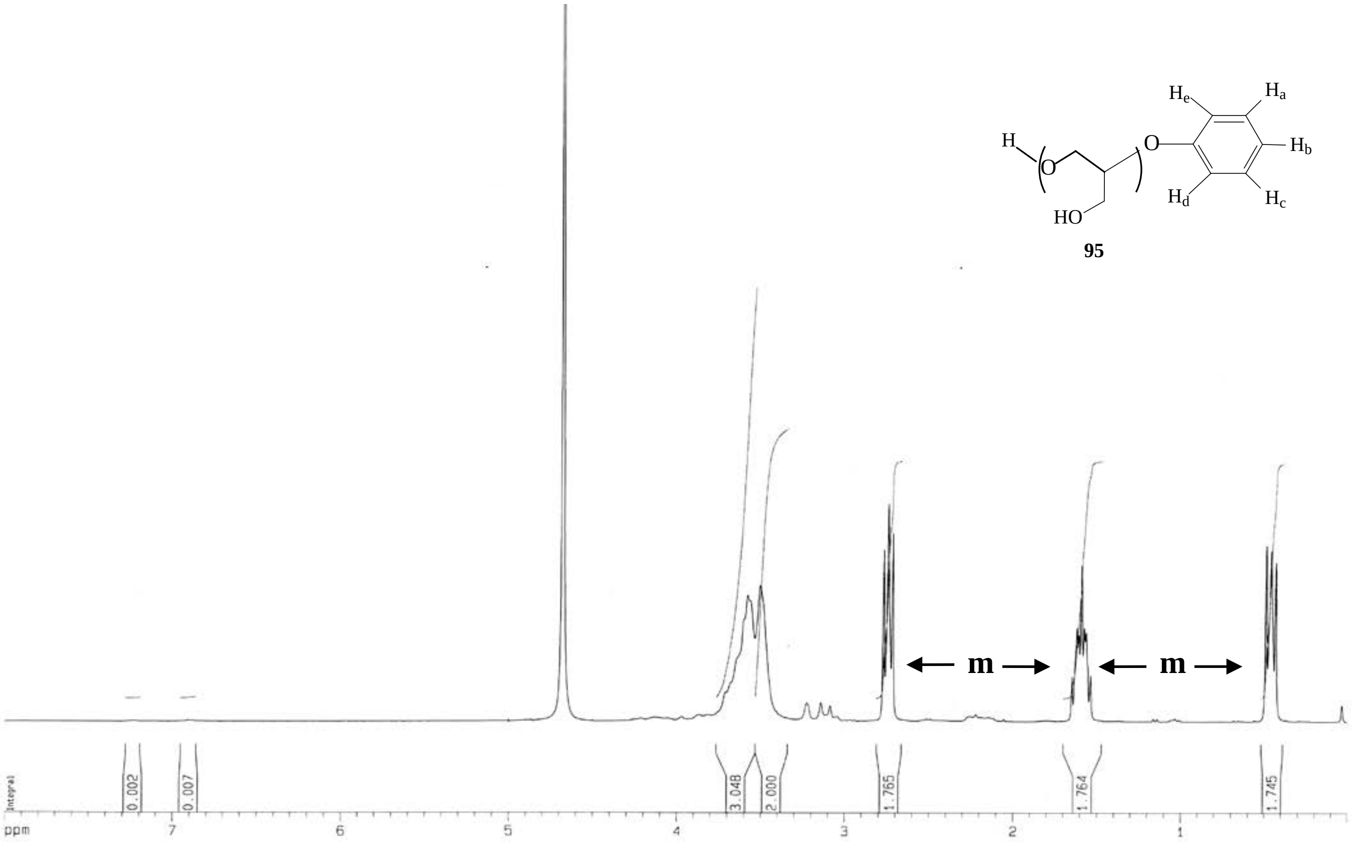
Spectrum A.6: ^{1}H NMR spectrum of poly(glycidyl azide) (75) in $CDCl_3$.



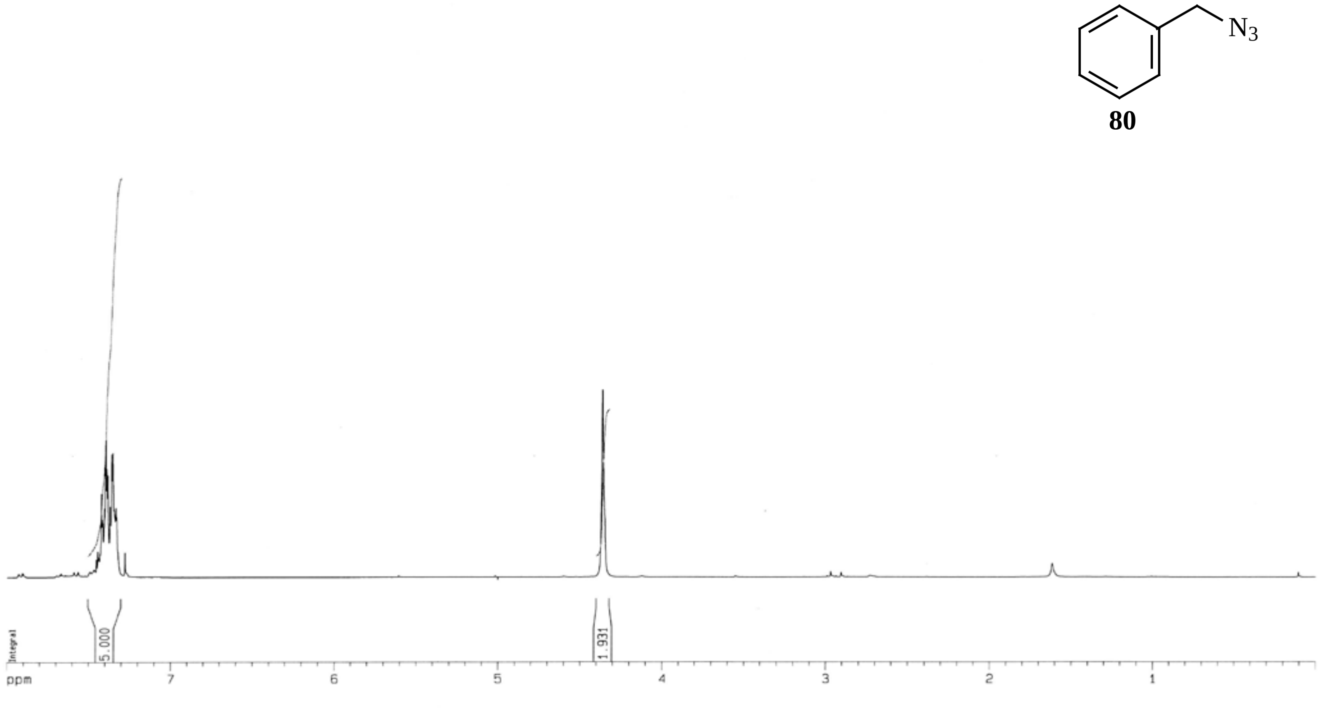
Spectrum A.7: ^{1}H NMR spectrum of poly glycidyl azide (76) in $CDCl_3$.



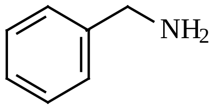
Spectrum A.8: ^{1}H NMR spectrum of amine-functionalised polymer (82d) in D_2O.



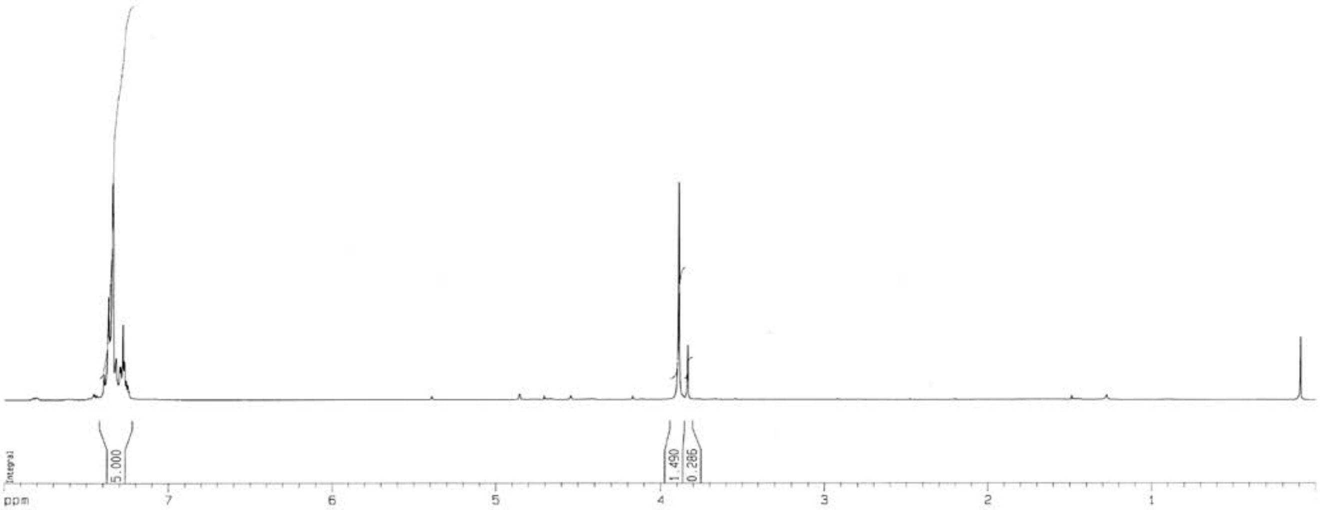
Spectrum A.9: **^{1}H NMR spectrum of hydroxyl-functionalised polymer (95) in D_2O.**



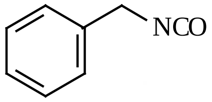
Spectrum A.10: **^{1}H NMR spectrum of benzyl azide (80) in $CDCl_3$.**



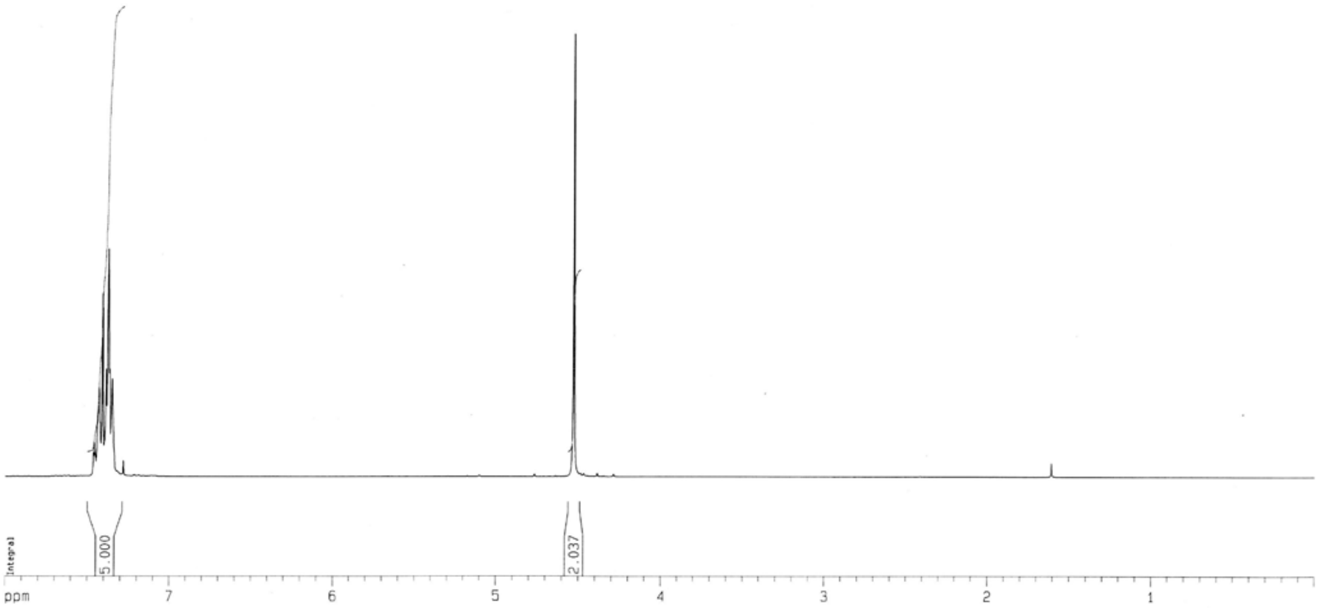
81



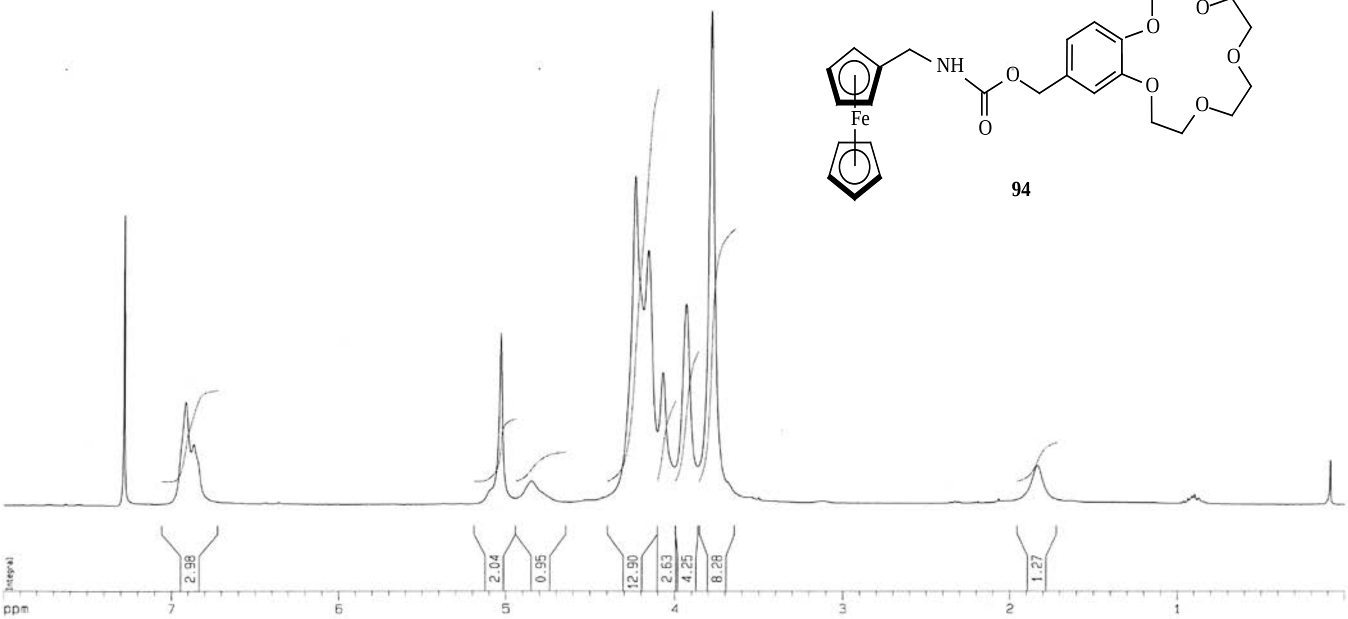
Spectrum A.11: ^{1}H NMR spectrum of benzylamine (81) in D_2O.



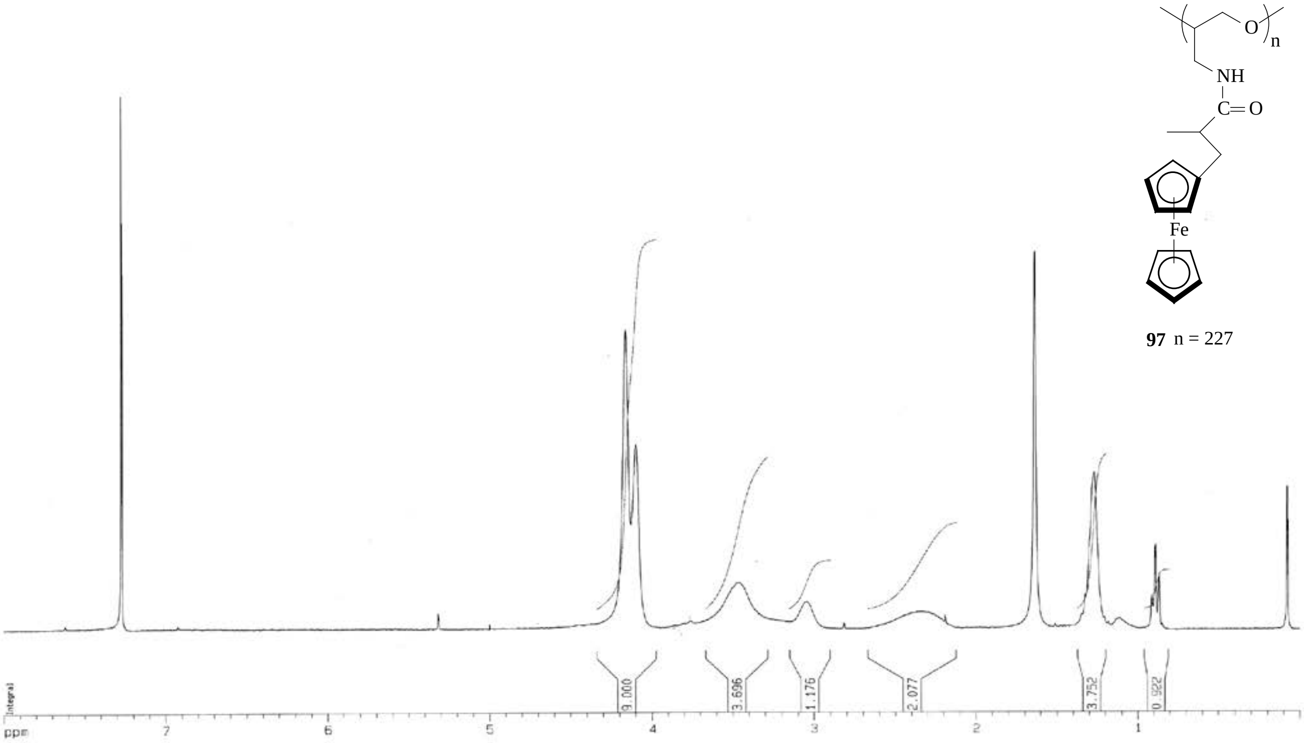
91



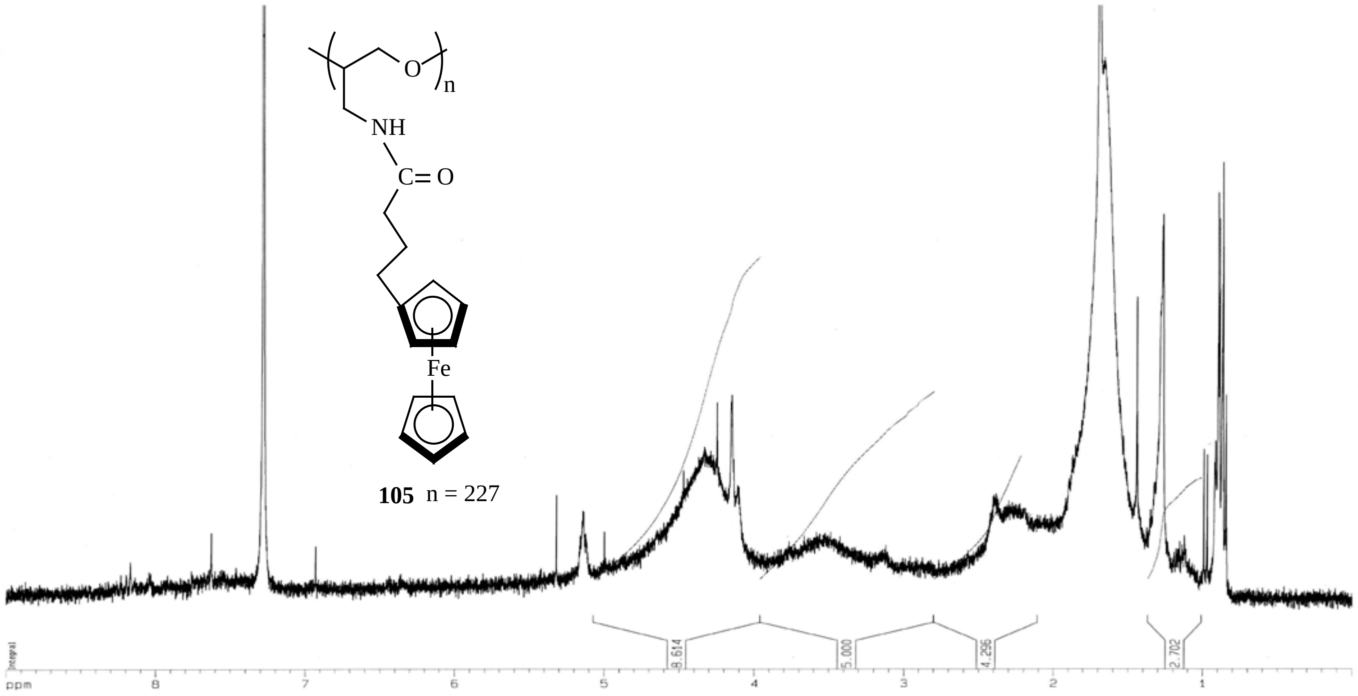
Spectrum A.12: ^{1}H NMR spectrum of benzyl isocyanate (91) in $CDCl_3$.



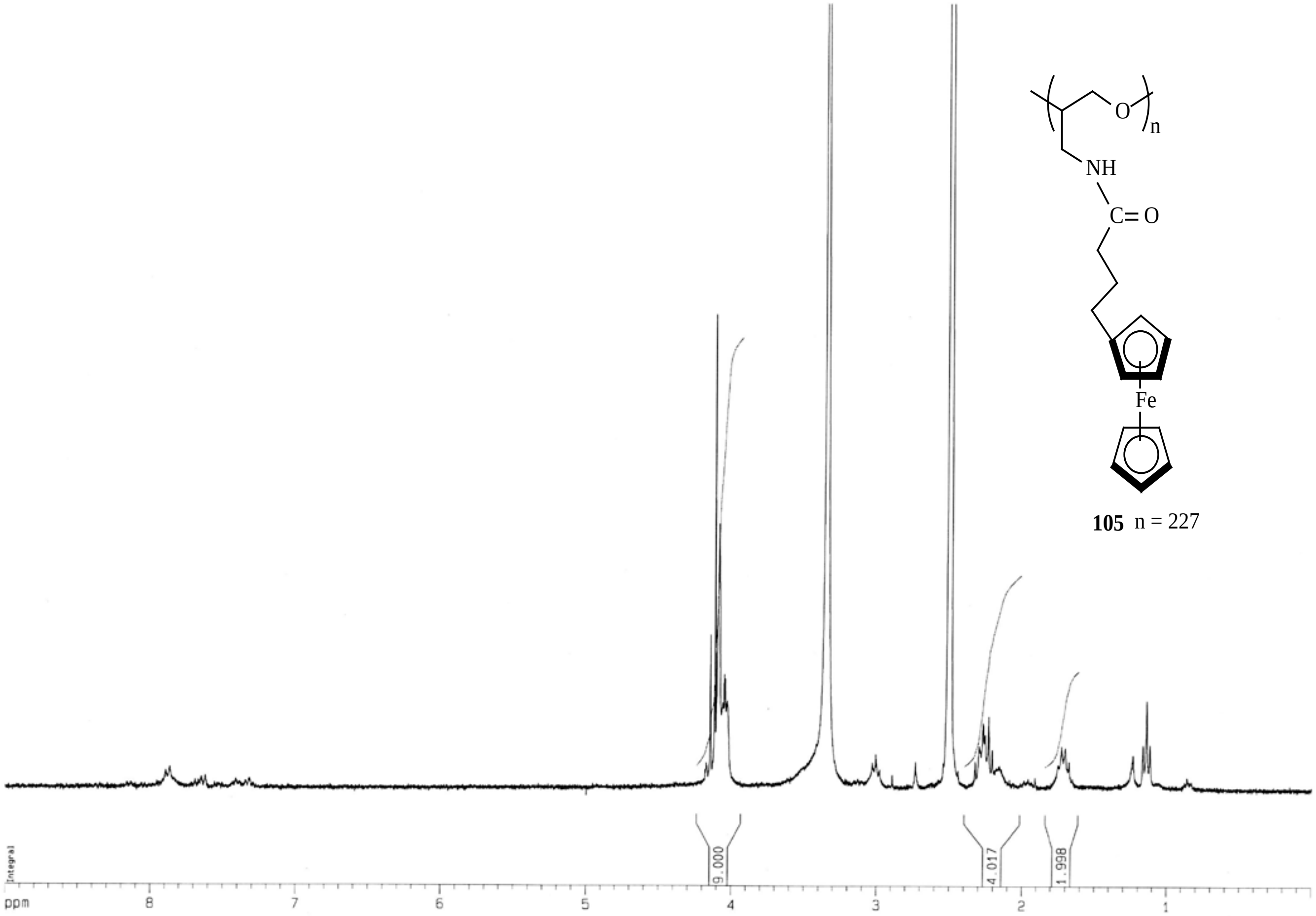
Spectrum A.13: ^{1}H NMR spectrum of crown ether bound ferrocene derivative (94) in $CDCl_3$.



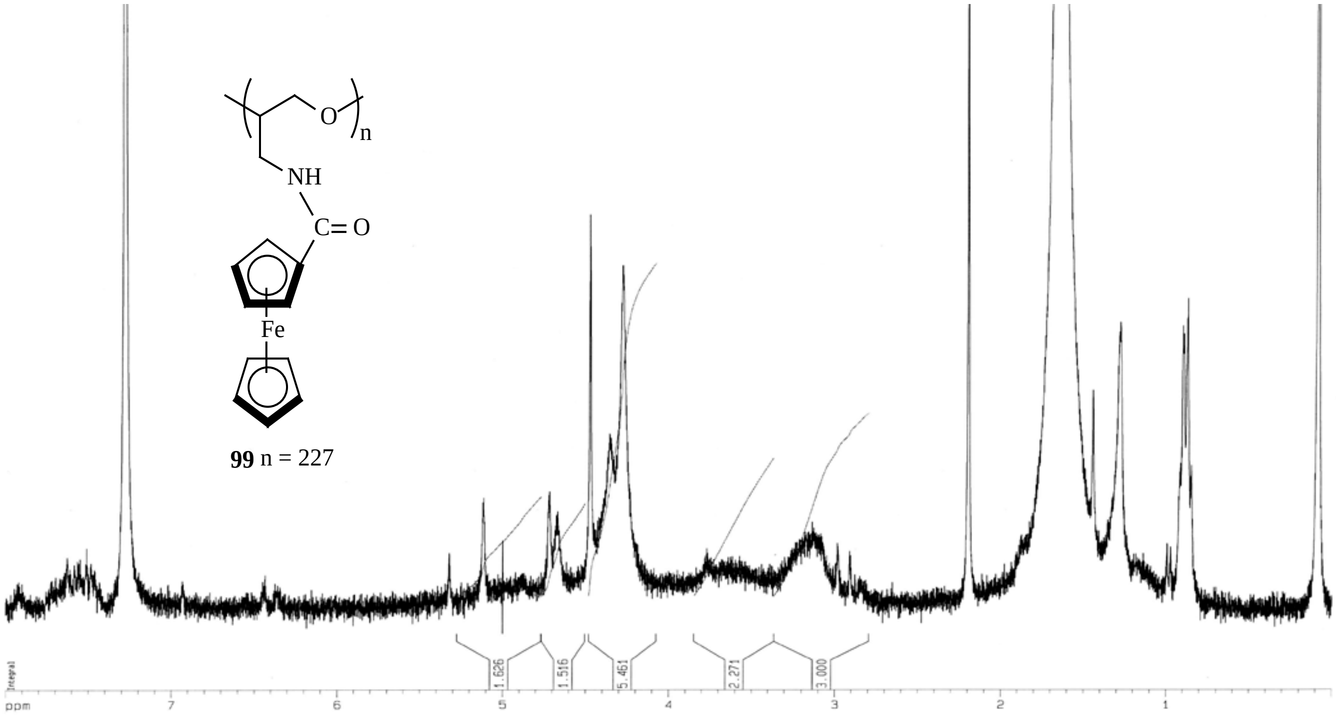
Spectrum A.14: ^{1}H NMR spectrum of polymer 97 in $CDCl_3$.



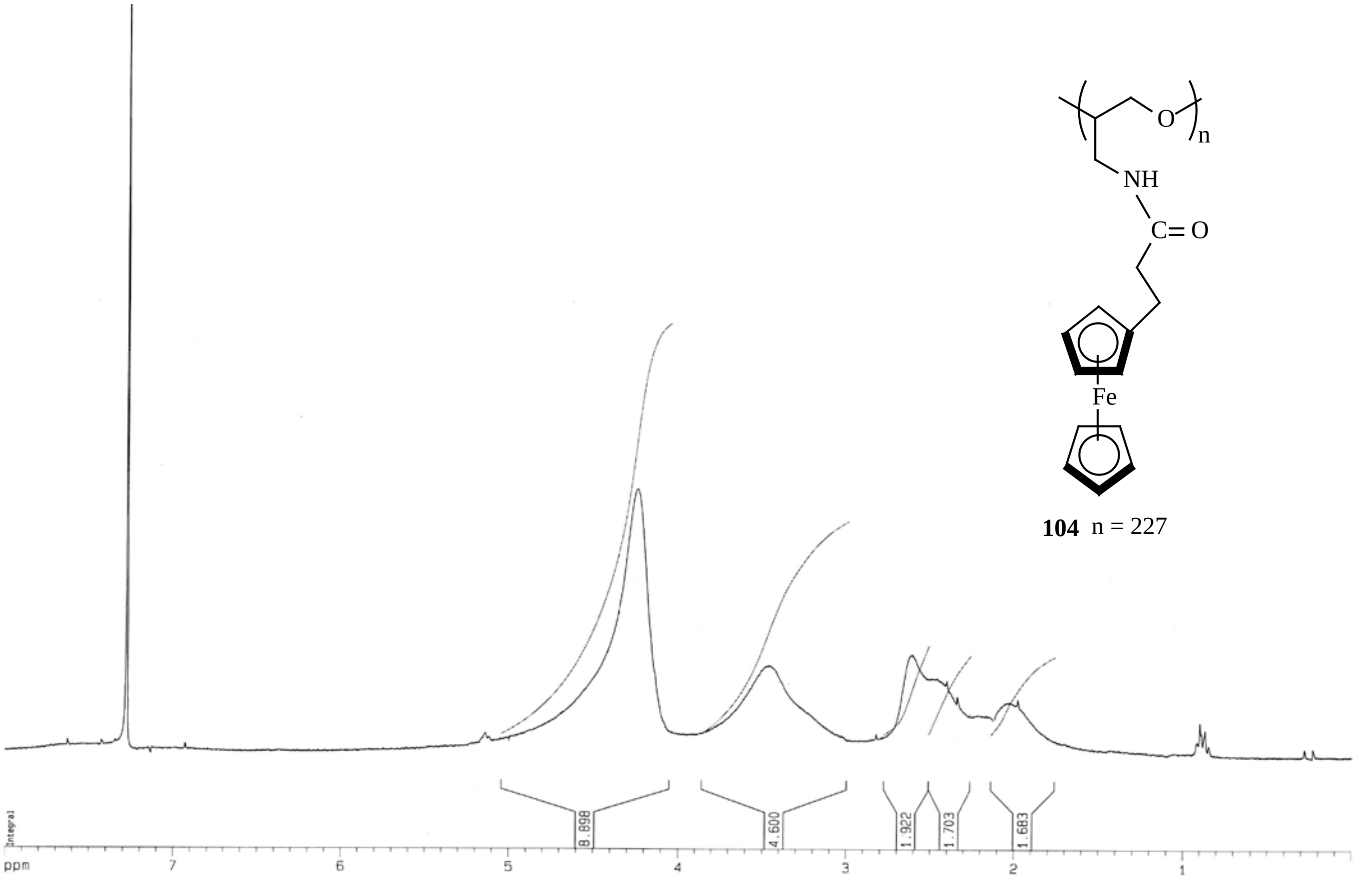
Spectrum A.15: ^{1}H NMR spectrum of polymer 105 in $CDCl_3$.



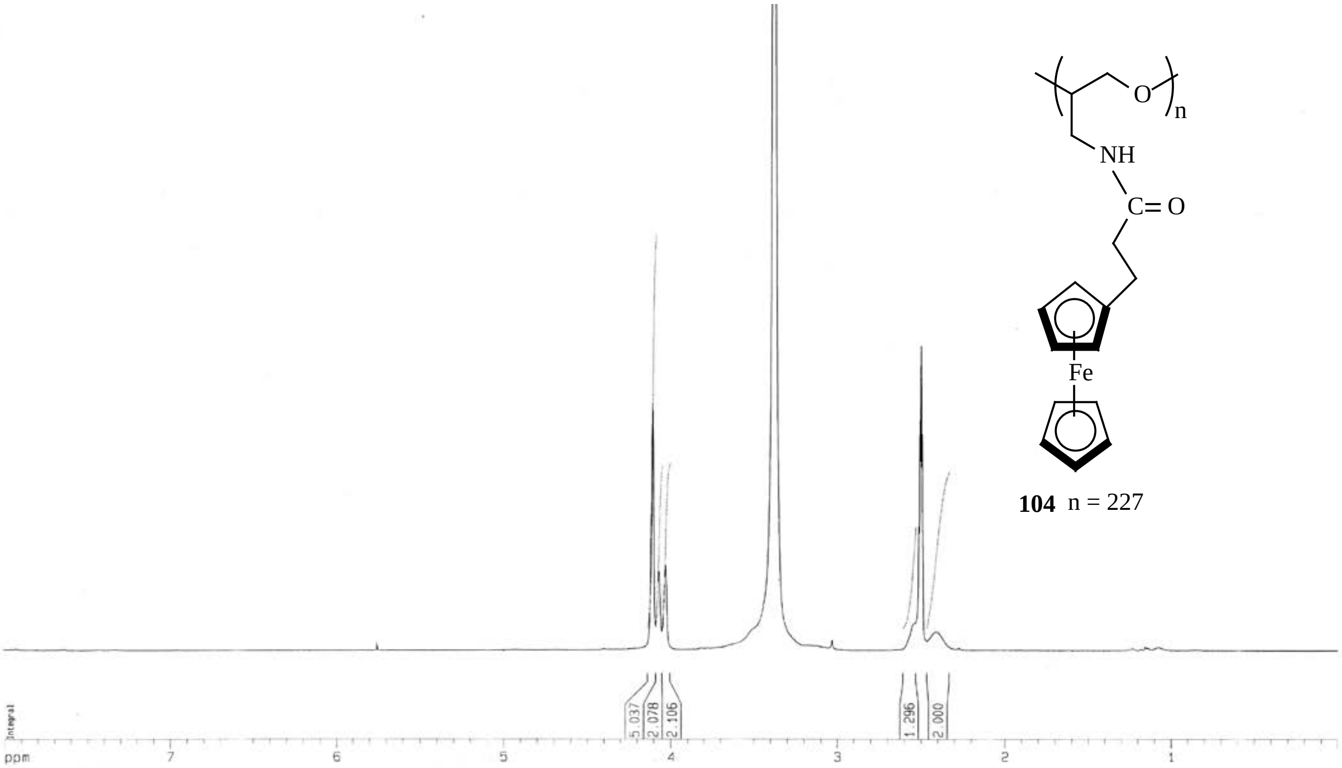
Spectrum A.16: ^{1}H NMR spectrum of polymer 105 in deuterated DMSO.



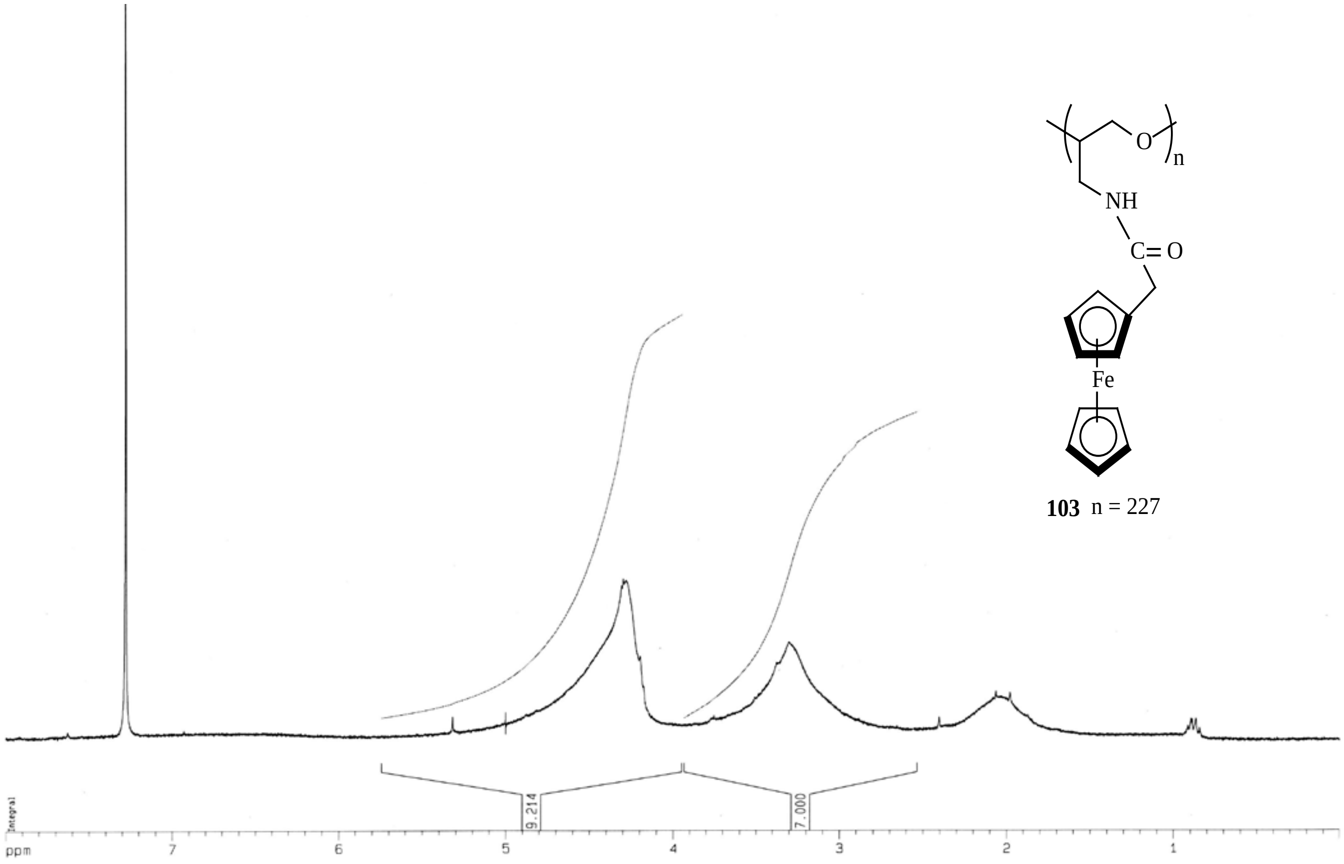
Spectrum A.17: ^{1}H NMR spectrum of polymer 102 in $CDCl_3$.



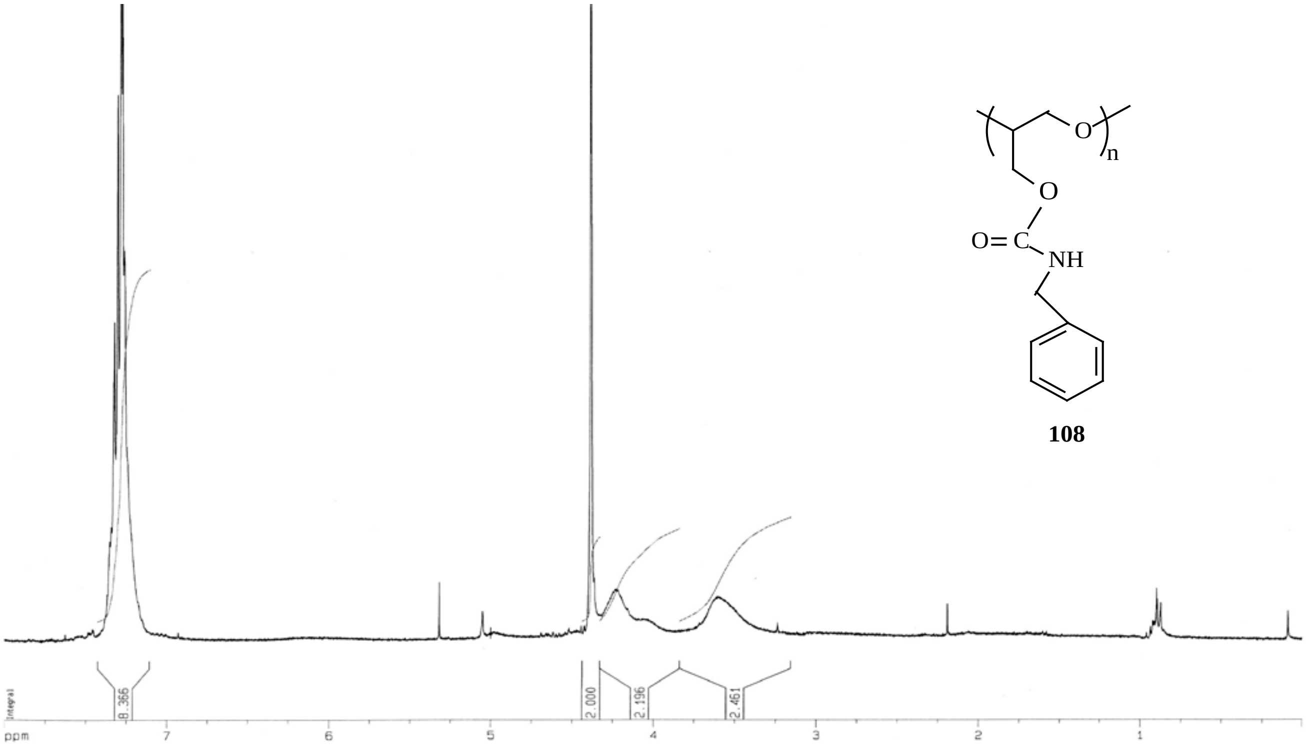
Spectrum A.18: ^{1}H NMR spectrum of polymer 104 in $CDCl_3$.



Spectrum A.19: ^{1}H NMR spectrum of polymer 104 in deuterated DMSO



Spectrum A.20: ^{1}H NMR spectrum of polymer 103 in $CDCl_3$.



Spectrum A.21: ^{1}H NMR spectrum of polymer (108) in $CDCl_3$.

[1] UNESCO web page: http://www.unesco.org.

[2] J. C. Swarts, *RSA Patent 2004/0076*, **2004**

[3] S. Inoue, T. Aida, *Cyclic Ethers. Int: Ring Opening Polymerization*, (editors, K. J. Ivin and T. Saegusa), Elsevier Applied Science Publishers Ltd, **vol. 1**, **1984**, p. 185 [Chapter 4]

[4] S. Penzeck, P. Kubisa, K. Matyjaszewski, *Oxirane. Int: Cationic ring opening polymerization Part II: Synthetic applications. Advance polymer Science*, Berlin: Springer Verlag, **vol. 68/69**, **1985**, p. 52 [Chapter 4]

[5] J. M. Hammond, J. F. Hooper, W. G. P. Reobertson, *J. Polym. Sci., Part A I*, **9 (1971)**, 265

[6] B. Tadeusz, K. Przemyslaw, P. Stanislaw, *J. Polym. Sci., Part A: Polym Chem*, **29 (1991)**, 619

[7] E. J. Goethals (editor), *Telechelic polymers: Synthesis and application*, CRC press, **1989**, p. 121

[8] A. U. Francis, S. Venkatachalam, *Macromolecules Int: Current Trends* (editors. S. Venkatachalam, V. C. Joseph, R. Ramaswamy and V. N. Krishnamuurthy), New Delhi: Allied Publishers; **1995**, p. 1

[9] A. U. Francis, S. Venkatachalam, *Int: Propellants explosives rockets and guns (Proceedings of the Second International High Energy Materials Conference and Exhibit December 8-10,1998, IIT Madras, Chennai, India)*, (editors, S. Krishnan and S. K. Athitan), Chennai: Allied Publishers; **1998**, p. 253

[10] R. B. Merrifield, *J. Am. Chem. Sci.*, **85 (1963)**, 2149

[11] A.U. Francis, S. Venkatachalam, M. Kanakavel, P. V. Ravindran, K. N. Ninan, *European Polym. J.*, **39 (2003)**, 831

[12] M. B. Frankel and J. E. Flanagan, *US Patent 4 268 450*, **1981**

[13] G. E. Manser, *US Patent 4 393 199*, **1983**

[14] J. P. Kennedy, E. G. M. Törnquist, *Polymer Chemistry of Synthetic Elastomers*, Wiley: New York, **vol. 23**, **1973**, p. 382

[15] K. J. Saunders, *Organic Polymer Chemistry*, Chapman and Hall Int. Ed., **1973**, p. 162

[16] E. M. Fettes (editor), *Chemical Reaction of Polymers*, Wiley Interscience: New York, **1964**

[17] J. M. J. Frechet, M. J. Farrall, *Chemistry and Properties of Crosslinked Polymers* (editor. S. S. Labana), Academic press: New York, **1977**, p. 59

[18] J. A. Moore (editor), *Reaction of Polymers*, D. Reidel: Boston, MA., **1973**

[19] R. W. Lenz, *Organic Chemistry of Synthetic High Polymers*, Wiley Interscience: New York, **1967**, [Chapter 17]

[20] L. D. Loan, F. H. Winslow, *Reactions of Macromolecules*, in *Macromolecules: An Introduction to Polymer Science* (editors. F. A. Bovey and F. H. Winslow), Academic Press: New York, **1979**, [Chapter 7]

[21] R. J. Ceresa, *The chemical modification of polymers*, in *Science and Technology of Rubber* (editor. F. R. Eirich), Academic Press: New York, **1978**, [Chapter 11]

[22] E. F. V. Scriven, K. Turnbull, *Chem. Rev.*, **88 (1988)**, 351

[23] Y. Nakajima, J. Oda, Y. Inouye, *Tetrahedron Lett.*, **34 (1978)**, 3107

[24] J. March, *Advanced Organic Chemistry*, 4th Ed., Wiley: New York, **1992**, p. 428

[25] J. A. Miller, *Tetrahedron Lett.*, **(1975)**, 2959

[26] A. Hassner, R. Fibiger, D. Andisik, *J. Org. Chem.*, **49 (1984)**, 4237

[27] G. Adam, J. Andrieux, M. Plat, *Tetrahedron*, **41(1985)**, 399

[28] J. March, *Advance Organic Chemistry*, 4th Ed., Wiley: New York, **1992**, p. 429

[29] J. March, *Advance Organic Chemistry*, 4th Ed., Wiley: New York, **1992**, p. 1091

[30] S. Ozaki, *Chem. Rev.*, **72 (1972)**, 457; H. J. Twitchett, *Chem. Soc. Rev.*, **3 (1974)**, 209

[31] *Organic Syntheses*, **III**, pp. 846, **IV**, p. 819

[32] J. March, *Advance Organic Chemistry*, 4th Ed., Wiley: New York, **1992**, p. 1219

[33] E. J. Corey, K. C. Nicolaou, R. D. Balanson, Y. Machida, *Synthesis*, **(1975)**, 590

[34] J. March, *Advance Organic Chemistry*, 4th Ed., Wiley: New York, **1992**, p. 1212

[35] G. W. Kabalka, P. P. Wadgoankar, N. Chatla, *Synth. Commun.*, **20 (1990)**, 293

[36] T. Satoh, S. Suzuki, Y. Suzuki, Y. Miyaji, Z. Imai, *Tetrahedron Lett.*, **(1969)**, 4555; A. Rahman, A. Basha, N. Waheed, S. Ahmed, *Tetrahedron Lett.*, **(1976)**, 219; M. E. Kuehne, P. J. Shannon, *J. Org. Chem.*, **42 (1977)**, 2082; S. R. Wann, P. T. Thorsen, M. M. Kreevoy, *J. Org. Chem.*, **46 (1981)**, 2579; S. B. Mandal, V. S. Giri, S. C. Prakashi, *Synthesis*, **(1987)**, 1128

[37] H. C. Brown, P. Heim, *J. Org. Chem.*, **38 (1973)**, 912; S. Krishnamurthy, *Tetrahedron Lett.*, **23 (1982)**, 3315

[38] P. Strazzolini, A. G. Giumanini, S. Cauci, *Tetrahedron*, **46 (1990)**, 1081

[39] A. R. Katritzky, H. X. Chang, B. Yang, *Synthesis*, **(1995)**, 503

[40] J. Barluenga, P. J. Campos, E. Gonzalez-Nuňenz, G. Asensio, *Synthesis*, **(1985)**, 426

[41] G. A. Olah, L. Ohannesian, M. Arvanaghi, *Chem. Rev.*, **87 (1987)**, 671

[42] J. March, *Advance Organic Chemistry,* 4th Ed., Wiley: New York, **1992**, p. 542

[43] *Organic Syntheses,* **II**, p. 98, **IV**, p. 331; p. 539; p. 915

[44] *Organic Syntheses,* **III**, p. 549

[45] *Organic Syntheses,* **III**, p. 463

[46] *Organic Syntheses,* **IV**, p. 866

[47] G. Casiraghi, G. Casnati, G. Puglia, G. Sartofi, G. Terenghi, *J. Chem. Soc.*, *Perkin Trans.*, **(1980),** 1862

[48] S. Jo, S. Taimoto, T. Sugimoto, M. Okano, *Bull. Chem. Soc. Jpn,* **54 (1981)**, 2120

[49] J. March, *Advance Organic Chemistry,* 4th Ed., Wiley: New York, **1992**, p. 910

[50] J. March, *Advance Organic Chemistry,* 4th Ed., Wiley: New York, **1992**, p. 1209

[51] *Organic Syntheses,* **II**, p. 499, **III,** p. 444, p. 786; **IV**, p. 203

[52] *Organic Syntheses,* **IV**, p. 510

[53] Huang-Minlon, *J. Am. Chem. Soc.*, **68 (1946)**, 2487; Huang-Minlon, *ibid***, 71 (1949),** 3301

[54] E. J. Vandenburg, *US Patent 3 645 917,* **1972**

[55] M. B. Frankel, E. R. Wilson, D. O. Woolery, *European Patent 0 296 310*, **1988**

[56] I. B. Mishra, D. E. Rickenbaugh, C. L. Ashmore, A. K. Mehrotra-Dev, *GAP-TAGN-PEG Propellant-Part 1 – Study of Ingredients Vol. II; JANNAF Propulsion meeting,* New Orleans: LA, John Hopkins University Chemical Propulsion Information Agency, **1984**, pp. 153

[57] N. Kubota, *Prop. Explos. Pyro.,* **13 (1988)**, 172

[58] N. Kubota, T. Sonobe, A. Yamamoto, H. Shimuzu, *J. Prop. Power,* **6 (1990)**, 686

[59] H. Tokui, T. Saitoh, K. Hori, K. Notono, A. Iwama, *Synthesis and Physico-Chemical Properties of GAP and the Application of GAP/AN Based Propellants to a small Motor, 21st Int. Conf. ICT,* Karlsruhe: Gemany, Fraunhofer Insitut für Chemische Technologie, **1990**, Section: 7-1

[60] A. Leu, S. Shen, B. Wu, *Thermal Characteristics of GAP/BDNPA/BDNPF and the Energetic Composites, 21st Int. Ann. Conf. ICT,* Karlsruhe: Germany, Fraunhofer Insitut für Chemische Technologie, **1990,** Section: 6-1

[61] R. L. Millar, A. G. Stern, R. S. Day, *US Patent 5 017 356,* **1992**

[62] H. J. Desai, A. V. Cunliffe, R. W. Millar, N. C. Paul, M. J. Stewart, A. J. Amass, *Polymer,* **37 (1996)**, 3471

[63] J. G. Koortzen, *A new method to remove and recover contaminating sodium salts from industrial wastewater utilising polymer-bound crown ethers,* PhD thesis (University of the Free State), **2001**

[64] C. J. Pedersen, *J. Am. Chem. Soc.,* **89 (1967)**, 7017

[65] C. J. Pedersen, *J. Am. Chem. Soc.,* **89 (1967)**, 2495

[66] J. S. Bradshaw, R. M. Izatt, A. V. Bordunov, C. Y. Zhu, J. K. Hathaway, *Crown Ethers* (editors. J. S. Bradshaw, R. M. Izatt, A. V. Bordunov, C. Y. Zhu, J. K) Hathaway Ed.; Pergamon, **vol. 1, 1997**, p. 35

[67] G. W. Gokel, *Crown ethers and Cryptands;* The Royal Society of Chemistry: Cambridge, **1991**

[68] N. N. Greenwood, A. Earnshaw, in: *Chemistry of the Elements,* Pergamon Press Inc: Tarrytown, **1984**, p.105

[69] B. Fabre, J. Simonet, *Coordin. Chem. Rev.,* **178-180 (1998)**, 1211

[70] R. W. Saalfrank, N. Low, S. Kareth, V. Seitz, F. Hampel, D. Stalke, M. Teichert, *Angew. Chem., Int. Ed. Engl.,* **37 (1998)**, 172

[71] R. G. Pearson, *J. Am. Chem. Soc.,* **85 (1963)**, 3533

[72] R. G. Pearson, *Science,* **151 (1966)**, 172

[73] S. D. Alexandratos, *Sep. Purif. Meth.,* **21 (1992)**, 1

[74] Z. Zong, S. Dong, Y. Hu, Y. Xu, W. Liu, *Eur. Polym. J.,* **34 (1998)**, 761

[75] E. Weber, *Phase Transfer Catalyst,* Merck, **1995**, p. 34

[76] R. M. Izatt, J. S. Bradshaw, S. A. Nielsen, J. D. Lamb, J. J. Christensen, D. Sen, *Chem. Rev.,* **85 (1985)**, 271

[77] U. Tunca, Y. Yagci, *Prog. Polym. Sci.,* **19 (1994)**, 233

[78] J. M. J. Frechet, *Tetrahdron,* **37 (1981)**, 663

[79] T. F. Baumann, J. G. Reymolds, G. A. Fox, *React. Funct. Polym.,* **44 (2000)**, 111

[80] T. F. Baumann, J. G. Reymolds, G. A. Fox, *Chem. Commun.,* **(1998)**, 1637

[81] S. D. Alexandratos, D. W. Crick, *Ind. Eng. Chem. Res.,* **35 (1996)**, 635

[82] J. C. Salamone (editor), *Polymeric Materials Encyclopedia,* CRC Press, Boca Raton, **vol. 2**, **1996**

[83] J. S. Bradshaw, R. L. Bruening, K. E. Krakowiak, B. J. Tarbet, B. J. Bruening, R. M. Izatt, J. J. Christensen, *J. Chem. Soc., Chem. Commun.,* **(1988)**, 812

[84] E. Ph. Horwitz, M. L. Dietz, R. Chiarizia, *J. Radioanal. Nucl. Chem., Articles,* **161**, **(1992)**, 575

[85] M. Cinouini, S. Colonna, H. Molinari, F. Montanari, *J. Chem. Soc., Chem. Commun.,* **(1976)**, 394

[86] F. Montanari, P. Tundo, *J. Org. Chem.,* **46 (1981)**, 2125

[87] P. L. Anelli, B. Czech, F. Montanari, S. Quici, *J. Chem. Soc.*, **106 (1984)**, 861

[88] M. Tomoi, N. Yanai, S. Shiki, H. Kakiuchi, *J. Polym. Sci., Polym. Chem. Ed.,* **22 (1984)**, 911

[89] M. J. Pugia, A. Czech, B. P. Czech, R. A. Bartsch, *J. Org. Chem.*, **51 (1986)**, 2945

[90] M. Tomoi, in J. C. Salamone edition, *Polymeric Materials Encyclopedia,* CRC Press, Boca Raton: FL, **vol. 2**, **1996,** p. 1580

[91] L. Collie, J. E. Denness, D. Parker, F. O'Carroll, C. Tachon, J. Chem. Soc., *Perkin Trans. 2,* **(1993)**, 1747

[92] G. Zimhlet, M. J. F. Leroy, J .P. Brunette, Y. Frere, Ph. Gramain, *Sep. Sci. Technol,* **28 (1993)**, 2419

[93] P. M. van Berkel, W. L. Driessen, A. A. Kodhaas, J. Reedjik, D. C. Sherrington, *J. Chem. Soc., Chem. Commun.,* **(1995)**, 147

[94] Y. Gotoh, Y. Kohno, W. Fukuda, M. Tomoi, *J. Polym. Sci., Part A: Polym. Chem.*, **32 (1994)**, 1543

[95] A. Favre-Régullion, N. Dumont, B. Dunjic, M. Lemaire, *Tetrahedron,* **53 (1997)**, 1343

[96] G. R. Newkome, C. N. Moorefield, F. Vögtle, *Dendrimers and dendrons, Concepts, Applications,* VCH: Weiheim, **2001**

[97] D. L. Jiang, T. Aida, *J. Chem. Soc., Chem. Commun.,* **(1996)**, 1523; J. P. Collman, L. Fu, A. Zingg, F. Diederich, *J. Chem. Soc., Chem. Commun.,* **(1997)**, 193; A. Zingg, B. Felber, V. Gramlich, L. Fu, J. P. Collman, F. Diederich, *Chim. Acta,* **85 (2002)**, 333

[98] D. K. Smith, F. Diederich, *J. Chem. Soc., Chem. Commun.,* **(1998)**, 2501; D. Smith, A. Zingg, F. Diederich, *Helv. Chim. Acta,* **82 (1995)**, 1225; A. Bähr, B. Felber, K. Schnieder, F. Diederich, *Helv. Chim. Acta,* **83 (2000)**, 1346

[99] S. Mattei, P. Seiler, F. Diederich, V. Gramlich, *Helv. Chim. Acta,* **78 (1995)**, 1904; S. Mattei, P. Wallimann, B. Kenda, W. Amrein, F. Diederich, *Helv. Chim. Acta,* **80 (1997)**, 2391; T. Habicher, F. Diederich, V. Gramlich, *Helv. Chim. Acta,* **82 (1999)**, 1066

[100] M. Rosenblum, *Chemistry of the Iron Group Metallocenes, Part I,* Wiley-Interscience: New York, **1965**, p. 201

[101] E. W. Neuse, H. Rosenberg, *Reviews In Macromolecular Chemistry,* (editors. K. F. O'Driscoll and M. Shen) Marcel Dekker: New York, **vol. 5**, **1970**

[102] D. E. Bublitz, K. L. Rinehart Jr., *Organic Reactions,* **17 (1969)**, 1

[103] G. Wilkinson, *Comprehensive Organometallic Chemistry,* Pergamon Press: Oxford, **1988, vol. 4,** [Chapter 31] and **vol. 8**, [Chapter 59]

[104] D. W. Mango, P. D. Shaw, M. D. Rausch, *Chem. Ind. (London),* **(1957)**, 1388

[105] R. W. Fish, M. Rosenblum, *J. Org. Chem.,* **30 (1965),** 1253

[106] M. T. Johnson, E. Kreft, D. D. N'Da, E. W. Neuse, C. E. J. van Rensburg, *J. Inorg. Org. Polym.,* **13 (2003)**, 255

[107] J. C. Swarts, E. W. Neuse, G. J. Lamprecht, *J. Inorg. Org. Polym.,* **4 (1994),** 143

[108] V. Dortoglou, B. Gross, V. Lambropolou, C. Zioudrou, *Synthesis,* **(1984)**, 572

[109] R. Deschenaux, J. W. Goodby, *Ferrocenes,* (editors. A. Togni and T. Hayashi) VCH: Weiheim, **1995,** [Chapter 9]

[110] L. Oriol, J. L. Serrano, *Adv. Mater.,* **7 (1995),** 348

[111] M. Altmann, U. H. F. Bunz, *Angew. Chem., Int. Ed. Engl.,* **34 (1995)**, 569; R. Deschenaux, I. Kosztics, J. L. Marenda, H. Stoecklei-Evans, *Chemia,* **47 (1993)**, 206; M. Altmann, V. Enkelmann, G. Leiser and U. H. F. Bunz, *Adv. Mater.,* **7 (1995)**, 726; A. A. Dembek, R. R. Burch, A. E. Feiring, *J. Am. Chem. Soc.,* **115 (1993)**, 2087

[112] J. March, *Advanced Organic Chemistr,* 4th Ed., Wiley: New York, **1992,** p. 326

[113] C. C. Lee, J. W. Clayton, D. G. Lee, A. J. Finlayson, *Tetrahedron,* **18 (1962),** 1395

[114] J. McMurry, *Organic Chemistry,* 5th Ed., p. 991

[115] R. J. Lewis, Sr., *Hazardous Chemicals, Desk reference,* 3rd Ed., Van Nostrand Reinhold: New york, **1993,** p. 1148

[116] S. E. Maree, Unpublished Results

[117] S. T. Sigurdsson, B. Seeger, U. Kutzke, F. Eckstein, *J. Org. Chem,* **61 (1996)**, 3883

[118] C. V Wilson, *Org. Chem. Bull.,* **35 (1963)**, 1

[119] S. Ozaki, *Chem. Rev.,* **72 (1972)**, 457

[120] J. H. Saunders, R. Slocombe, *J. Chem. Rev.,* **43 (1948)**, 203

[121] R. O. Hutchins, I. M. Taffer, *J. Org. Chem.,* **48 (1983)**, 1360

[122] *Inorganic Syntheses,* **vol. 2**, **1946**, p. 88

[123] N. M. Yoon, J. Choi, Y. S. Sohn, *Synth. Commun.,* **23 (1993)**, 3047