THE SYNTHESIS OF DENDRITIC & LIQUID CRYSTAL CONDUCTING POLYMER HYBRIDS

By

Sarah Banfield

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ACKNOWLEDGMENT

I would like to thank all of my family and friends for their continual support, encouragement and cups of tea along the away. You have all contributed in your own special way and I love you dearly. Mum and dad, I offer this to you. You have been my inspiration and determination and I thank you for your patience and belief in me.

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The end of education is character.....

Sri Sathya Sai Baba

ABSTRACT

The aim of this project was to synthesise N-substituted pyrrole monomers with liquid crystal and dendritic side groups, followed by their subsequent polymerisation and measurement of the polymer properties. The second objective beyond the synthesis of these novel polymer materials was to investigate how potential liquid crystals and dendritic side groups affected the conjugation and planarity of the polypyrrole backbone, for the purpose of conductivity applications. Four different types of molecules were synthesised:

1. Polypyrroles with terminally and laterally attached mesogenic side groups (monomers/polymers 1 & 2)
2. Polypyrroles with first and second generation dendritic side groups, terminated by alkyl chains (monomers/polymers 3 & 4)
3. Polypyrroles functionalised by first and second generation dendritic moities with hydrophilically-terminated alkyl chains (monomers/polymers 5 & 6)
4. Polypyrrole hybrid materials: second generation dendrimer with terminal liquid crystal groups (monomers/polymers7)

Although seven polymers were intended to be synthesised, polymers (4) and (6) were unable to be characterised, due to very poor solubility. However polymers (1), (2), (5) and (7), successfully underwent hydrolysis of the terminal and lateral ester side groups to carboxylic acids, making a total of nine novel N-substituted polypyrroles synthesised, within this project. The synthesis began with the generation of the monomer compounds (monomers 1-7). This was done by nucleophilic substitution of the potential side chain liquid crystal or dendritic moieties on a benzyl ring using a Williamson ether synthesis. A flexible hexyl spacer group was substituted onto the intermediate compounds, followed by the attachment of pyrrole at the heteroatom site.

Thin layer chromatography was used to follow the progress of each reaction and the intermediate compounds were subjected to column chromatography and high vacuum distillation for purification. Characterisation techniques such as Fourier-transform infrared spectrophotometry, gas chromatography/mass spectrometry, ^{1}H NMR spectrometry and elemental analysis were used to determine the purity and structural identity of each monomer compound. Electrochemical (EC) polymerisation of monomers (1) and (3) on conductive indium-tin oxide (ITO) glass were attempted first. The cyclic voltammograms indicated that the polymerisation was successful, and the monomer oxidation and polymer doping and dedoping potentials were determined. However this method of polymer synthesis was abandoned, as the yield of the polymer film was too low and the polymer product was very difficult to remove from the ITO substrate for further analysis. Chemical polymerisation with $FeCl_3$ in chloroform was successful, as indicated by ^{1}H NMR, KBr IR, and

UV-visible spectrometry, and the yields of the polymer products were significantly higher than those of the EC method.

Physical properties measurements (electrical conductivity, scanning electron microscopy, hot-stage optical microscopy, solubility testing and differential scanning calorimetry) were carried out, in order to determine the general natures and to indicate any possible applications of the novel polypyrrole materials synthesised. From the spectroscopic data and physical measurements, it was concluded that polymers (1), (2), (3), (5) and (7) and their corresponding carboxylic acids (1a), (2a), (5a) and (7a) had been successfully synthesised, as proton NMR confirmed the disappearance of the 2,5-hydrogens of pyrrole, and in addition conductivity measurements using simple 2-probe and van der Pauw 4-probe methods on undoped polymers (1a), (2a), and (7a) gave reproducible conductivity values which classified them as being potential semi-conductors ($2.2x10^{-4}$, $6.7x10^{-5}$ and $7.8x10^{-5}$ Sm^{-1} respectively).

UV-visible spectrophotometry indicated that hydrolysis of the laterally attached liquid crystal ester groups to carboxylic acids significantly reduced the pp* energy gap of polymer (1). (from 3.9eV to 2.48eV). It was suggested that hydrogen bonding in the carboxylic acid might have improved the planarity and conjugation of the polymer backbone and transformed the insulating ester polymers to potential semi-conductors.

Differential scanning calorimetry (DSC) and hot-stage optical microscopy (HSM) were used to determine the phase transitions of polymers (1a) and (2a). The DSC traces showed small peaks, indicating liquid crystal phase transitions (nematic phases observed from 105-248 ^{o}C, 105-170 ^{o}C respectively). These were later confirmed by the use of HSM, as nematic textures were observed in the expected temperature region for nematic liquid crystals. In addition the enthalpy changes for the phase transitions were estimated, and polymers (1a) and (2a) were found to have nematic-isotropic phase transitions within the expected range of values.

Scanning electron microscopy was used to examine the morphology of the polymer materials. Generally the N-substituted polypyrroles with dendritic side groups were found to have more porous morphologies, while N-substituted polypyrroles with potentially mesogenic side groups appeared to have more continuous and smoother morphologies. However, polymer (7a) was found to have the most porous morphology and it also add an unexpectedly high conductivity value. Polymer (7a) was the only polypyrrole hybrid material synthesized in this project, and it appeared that combining all three polymeric units (dendrimers, LC and CP) into one polymer system improved the planarity of the polymer backbone, encouraged the formation of a porous structure which facilitated p-type doping of the polymer by iodine vapour.

ABBREVIATIONS

HOMO	Highest Occupied Molecular Orbital
LUMO	Lowest Unoccupied Molecular Orbital
TBAFB	tetrabutylammonium tetrafluroborate
TBAP	tetrabutylammonium perchlorate
ITO	indium tin oxide
Nphth	naphthalene
GOD	Glucose Oxidase
L-AAOD	L-Aminoacid Oxidase
PPY/ATP	Polypyrrole/adenosine triphosphate
py	pyrrole ring
CAGR	Compound Annual Growth Rate
ICPs	Inherently Conductive Polymers
MBBA	N-(4-Methoxybenzylidene)-4-butylaniline
LCDs	Liquid Crystal displays
IPS	In-Plane Switching
PAMAM	Poly(amidomine) dendrimers
PPV	Poly(phenylene vinylene)
PAA	Poly(amidoalcohol)s
PPI	Poly(propylene Imine)
POPAM	Poly (propylene Amine)
PAMAMOS	Poly(amidoamine-organosilicon)
SANS	Small-angle neutron scattering

SAXS	Small-angle X-ray scattering
MRI	Magnetic Resonance Imaging
hFR	high-affinity folate receptor
D.I.M.S	Direct Insertion Mass Spectrometry
DIP	Direct Insertion Probe
DEP	Direct Exposure Probe
CV	Cyclic Voltammetry
IR	Infra Red
SEM	Scanning Electron Microscopy
Eg	Energy gap
DSC	Differential Scanning Calorimetry
LC	Liquid Crystal
LCCP	Liquid crystal conducting polymers
TLC	Thin Layer Chromatography
GCMS	Gas Chromatography / Mass Spectrometry
^{1}H NMR	Proton Nuclear Magnetic Resonance
UV-Vis	Ultraviolet-Visible
DSC	Differential Scanning Calorimetry
RMM	Relative Molecular Mass
σ	sigma
π	pi electrons
DEE	Diethyl ether
EC	Electrochemical polymerisation
NaCl	Sodium chloride

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CHAPTER 1

INTRODUCTION TO CONDUCTING POLYMERS

CHAPTER 1: Introduction

1.1 The Discovery of Conducting Polymers

Until 40 years ago, all carbon-based polymers belonged to a class of materials known as "insulators" and their properties were generally the opposite of metals. Polymers were used to coat electric wires as a form of protection from short circuiting and the notion that they could actually conduct electricity would have been considered to be absurd [Freund], [Rose], [Hatano], [Menefee]. However in 1967 a postgraduate student of Hideki Shirakawa at the Tokyo Institute of Technology was attempting to synthesise polyacetylene, but instead of yielding a black powder as expected, a very thin silvery film was produced as a result of a mistake [Shirakawa], [Ito]. It was found that the Ziegler-Natta catalyst, $Ti(O\text{-}n\text{-}Bu^{t})_4$-EtAl, had been added in a 1000 times excess and when the film was investigated, it exhibited similar conductivity values to the best of the conducting black powders, but it was still categorised as a semi-conductor [Freund]. More in depth investigations were carried out to improve the conductivity of the polyacetylene film and in 1977 Shirakawa, MacDiarmid and Heeger discovered that upon exposure to halogens during a process known as "doping", chlorine, bromine or iodine vapour increased the conductivity of polyacetylene a billion fold [Shirakawa]. On a physical level the undoped polymer was silvery, insoluble, intractable and had a conductivity range similar to semi-conductors, but when weakly oxidised by iodine vapour the doped form of polyacetylene turned coppery in colour, was partially soluble and its conductivity increased to 10^4 Sm^{-1}. This was a remarkable discovery and marked a turning point in the history of polymer science. As an acknowledgement, Shirakawa, MacDiarmid and Heeger were awarded a Nobel Prize for Chemistry in 2000 for the discovery and development of electrically conducting polymers [Vetenskapsakademien], [Chiang], [Shirakawa], [MacDiarmid], [Heeger].

1.2 Polyacetylene

As previously mentioned, one of the first conducting polymers to be synthesized was polyacetylene. Polymers of acetylene date back to the 19th century when initial attempts at acetylene polymerization were carried out in the presence of copper-based catalysts to yield a highly cross-linked and extremely irregular product called "Cuprene". In its linear form, polyacetylene precipitates out of solution as a black, air-sensitive, infusible and intractable powder that cannot be processed, and although Natta *et al* were the first to polymerize acetylene in 1958 it remained of little interest [Natta], [Vetenskapsakademien]. In 1970 Shirakawa and co-workers embarked upon a new phase in the study of polyacetylene, as they had developed a simple method for preparing film samples, which upon doping with halogens or AsF_5, exhibited significant electrical conductivity. To date, Shirakawa's polymerisation method is the most widely used procedure for the polymerisation of acetylene. An alternative route for acetylene polymerisation was first described in 1960 by Luttinger, in which he described how powdered polyacetylene specimens prepared by traditional methods exhibited similar properties to material produced by Shirakawa's route (See Figure 1.1 below) [Luttinger]. Luttinger's method had an added advantage as the catalyst allowed the polymerisation process to take place even in the presence of water and oxygen.

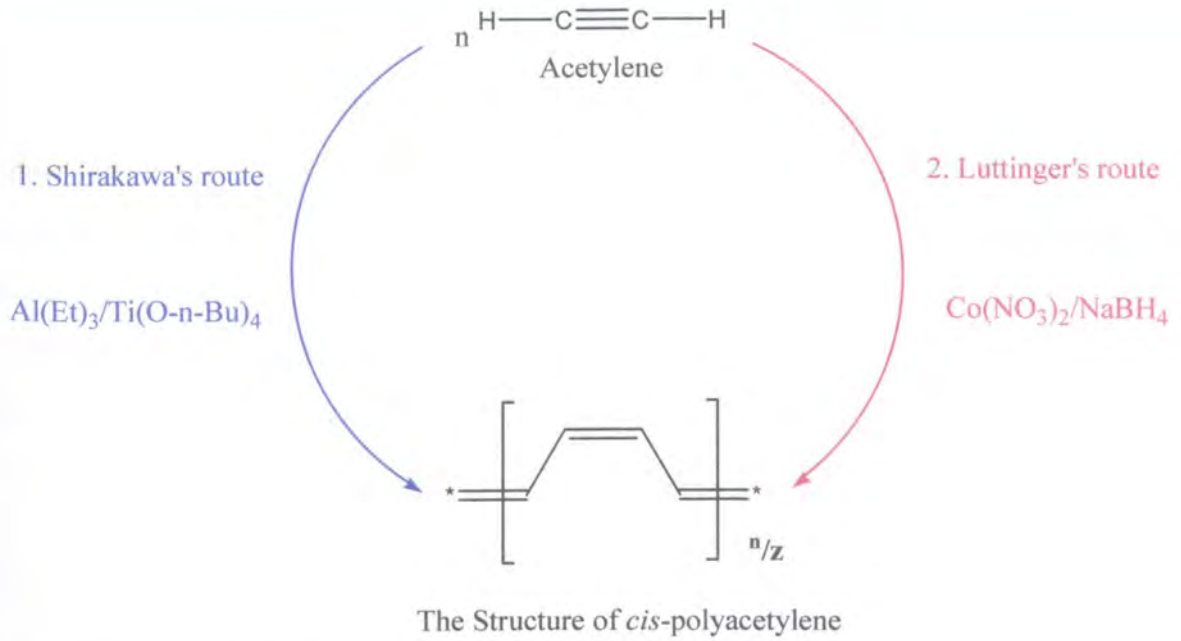


Figure 1.1 Shirakawa's and Luttinger's Routes to Polyacetylene .

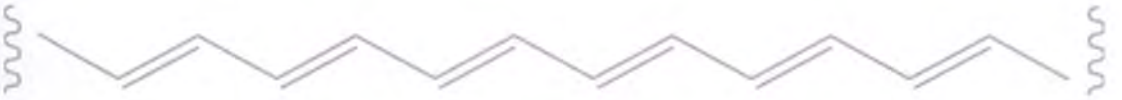
The uniqueness of Shirakawa's discovery meant that polymerisation could be effected at the surface of a highly concentrated solution of the catalyst system in an inert solvent. The general procedure involved adding $Ti(OBu)_4$ and then $Al(Et)_3$ to a small volume of toluene under inert atmosphere. [Ito], [Shirakawa], [Abadie]. The mixture was allowed to stand for 45 minutes at a temperature of 20^0C and then was cooled to -78^0C (Refer to Scheme 1). The reaction vessel was evacuated and acetylene gas introduced to the system to react with a film of catalyst which had already been formed around the walls of the vessel. Thereupon, a film of polyacetylene immediately formed. The reaction was controlled by removing un-reacted acetylene gas, to yield a product that was 95% *cis*-polyacetylene [Vetensakademien]. The film produced was copper-coloured and was composed of all *cis*-polyacetylene, but it was also found that if the reaction was run in n-hexadecane at 150^0C a silvery product of all-*trans*-polyacetylene was formed [Vetensakademien]. Conductivity measurements determined that *cis*-polyacetylene had a value of 10^{-8} -10^{-7} S m^{-1}, whereas *trans*-polyacetylene had a higher value of 10^{-3} -10^{-2} S m^{-1} [Vetensakademien].

Later exciting experiments followed in which Heeger, MacDiarmid and Shirakawa began to control the ratio of *cis/trans* polyacetylene and it was found that doping *cis*-polyacetylene with AsF_5 resulted in an increase of conductivity by a factor of 10^{11} (See Figure 1.2 below) [Chiang 77], [Chiang 78], [Vetenskapsakademien]. The high conductivity found by the three scientists clearly opened up the potential field of "plastic electronics". Polyacetylene remains the most crystalline conductive polymer, but due to its poor sensitivity to humidity and facile oxidation in air it was not the first polymer to be commercialised.

all-*cis*-polyacetylene

Copper coloured

Conductivity 10^{-8}-10^{-7} Sm^{-1}



all-*trans*-polyacetylene

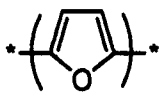
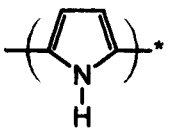
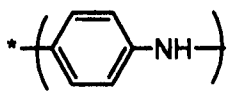
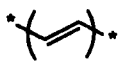
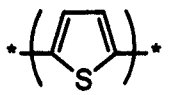
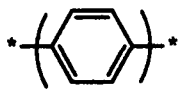
Silver coloured

Conductivity 10^{-3}-10^{-2} Sm^{-1}

Figure 1.2 All –Cis- and all-trans-polyacetylene

Other polymers such as polypyrrole, polythiophene, poly(phenylene vinylene) and polyaniline were also successfully synthesised during the early 1980's; however, although their conductivities were notably lower than polyacetylene (around 10^{-4} S m^{-1}), they were very stable in the atmosphere and could therefore be used for many practical applications. (See table 1.1).

Table 1.1 Conductivity Values of Common Polymers

NAME	STRUCTURE	DOPANT	CONDUCTIVITY (S cm^{-1})	Ref
Polyfuran		BF_3	1-100	[Edwin]
Polypyrrole		$FeCl_3$, BF_3	10^2-10^3	[Edwin]
Polyaniline		HCl, R-SO_3H	1-400	[Edwin]
Polyacetylene		I_2, Br_2, Li, Na, AsF_5	10^4-10^5	[Edwin]
Polythiophene		$FeCl_3$, $NOPF_6$, BF_3	10-10^3	
Poly(p-phenylene)		Li, K, AsF_5	10^2-10^3	[Edwin]

1.3 What Makes a Polymer Conductive?

Before discussing the synthesis, properties and useful applications of conducting polymers, it is important that the processes responsible for making a polymer conductive are understood. The key to making a polymer conductive is to provide electrons which are not fixed in their position. The electrons must be free to migrate from one end of the polymer backbone to the other, and in doing so, electricity can be conducted. Nearly all polymers which are considered conductive have a conjugated backbone structure.

Conjugation occurs when the bonds between the carbon atoms are in a sequence of alternating double and single bonds along the polymer backbone. Organic chemistry demonstrates that conjugated double bonds behave quite differently from isolated double bonds. As the word indicates, conjugated double bonds act collectively. Hückel's theory predicts that pi-electrons are delocalised over the entire chain and that the band gap becomes vanishingly small for a long enough chain [Vetenskapsakademien]. When looking at the distribution of electron density, the electrons are predicted to be spaced out evenly along the entire chain and all bonds are predicted to be equal (metallic state). However polyacetylene is a semiconductor and not a conductor, due to the bonds being unequal, with every second bond having some double bond character (See Figure 1.3). This results in sigma "σ" bonds between all the carbon atoms and pi "π" electrons forming double bonds. In conducting polymers the pi-orbitals overlap above and below the plane of the sigma orbitals and when a voltage is applied, the delocalised pi-electrons carry the charge along the polymer backbone. (See Figure 1.4)

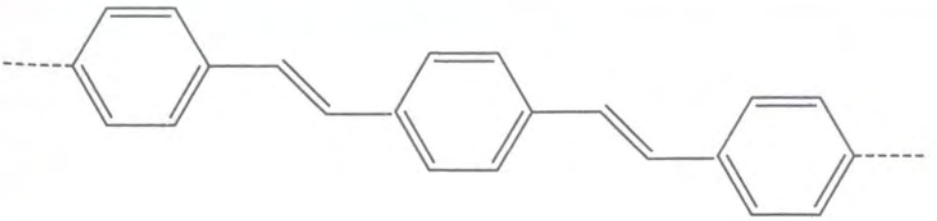
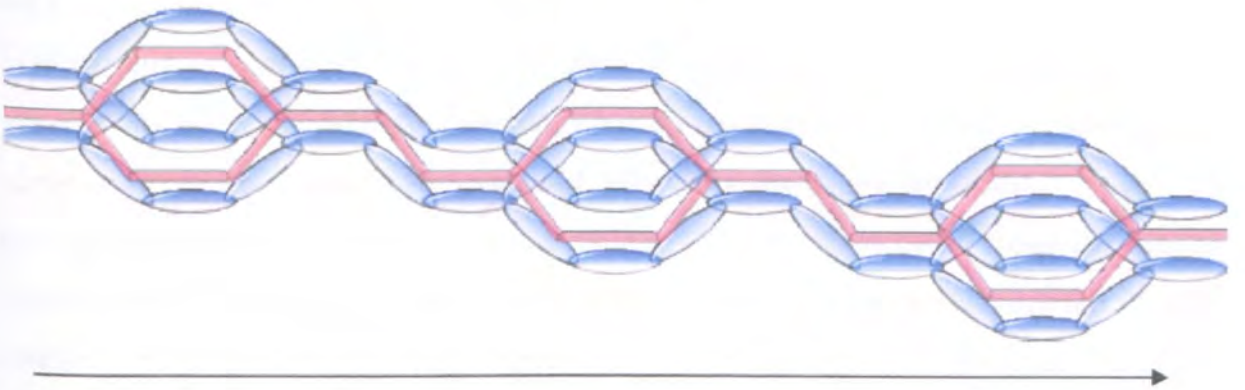


Figure 1.3 Molecular structure of Poly(phenylene vinylene) PPV

- π-orbitals overlap above and below plane-Blue region



- Delocalised electrons are free to move along polymer backbone, thus generating a charge as they do so.

Figure 1.4 Overlapping of pi-orbitals in PPV

1.4 Conduction Mechanism

The electronic properties of any material are determined by its electronic structure. The capability of electrons to move through a polymer network has been explained using the Band Theory. In metals, the orbitals of the atoms overlap with the equivalent orbitals of their neighbouring atoms in all directions, to form molecular orbitals similar to those of isolated molecules. Where there are N interacting atomic orbitals, there will be N molecular orbitals. However in metals, or any continuous solid state structure , N will be a very large number (approximately 10^{22} for a 1 cm^3 piece of metal) [Vetenskapsakademien]. As there are so many molecular orbitals spaced very closely together in a given range of energies, a continuous band of energy level is formed. When the atoms are very closely spaced, the energy levels appear to form continuous bands. The highest occupied molecular orbitals (HOMO) constitute the valence band and the lowest unoccupied molecular orbitals (LUMO), constitute the conduction band (see figure 1.5). The energy difference between the HOMO and LUMO is called the band gap.

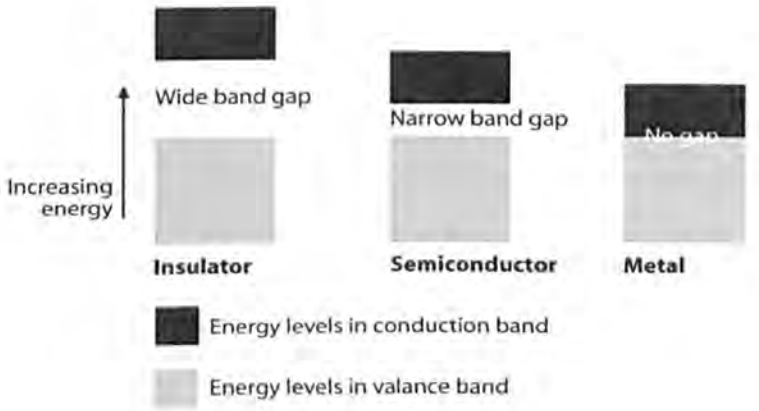


Figure 1.5 Simple band picture explaining the difference between an insulator, a semiconductor and a metal.

The way in which these bands are filled will dictate the properties of the material. In bands that are completely filled or empty no conduction is observed. If a band gap is narrow at room temperature, thermal excitation of electrons from the valence band to the conduction band gives rise to conductivity. Materials that behave in such a manner are known as semi-conductors. If the band gap is too wide, thermal energy at room temperature is insufficient to excite electrons across the gap and these materials are known as insulators. Where there is complete overlapping of the valence band and conduction band, no band gap arises. Materials that have this property have very high conductivity and are called conductors, [Freund]. Conducting polymers do not necessarily conduct electrons via the same mechanism used to describe classical semiconductors. The electronic conductivity of conducting polymers results from mobile charge carriers introduced into the conjugated pi-system through doping. An increase in conductivity resulting from doping in inorganic semiconductors involves the formation of unfilled electronic bands [Foot]. During oxidation, the electrons are removed from the top of the valence band (also known as *p*-type doping), or added to the bottom of the conduction band during reduction (termed *n*-type doping). The mechanism for the conductivity increase resulting from doping in conjugated polymers is explained in terms of local lattice distortion and localised electronic states. As the valence band remains full and the conduction band remains empty, there are no characteristics of a metallic state. During the redox doping process, a lattice distortion occurs and the equilibrium geometry for the doped state is different than the ground-state geometry. Most conjugated polymers behave similarly upon redox doping and have nondegenerate ground states [Foot]. When an electron is added to (or removed from) the polymer chain, a radical ion is formed. This results in a lattice distortion, that causes an upward shift of the highest occupied molecular orbital (HOMO) and a downward shift in the lowest unoccupied molecular orbital (LUMO) [Foot]. As the radical species is not delocalised over the entire polymer chain, a localised lattice distortion occurs, creating a localised electronic state.

Separation and delocalisation of the radical ion generates further energetically unfavourable lattice distortions, and the radical ion associated with this lattice distortion is termed a "polaron" [Gangopadhyay].

When electrons are removed, the process is known as oxidative (p-type) doping, whereas the addition of electrons results in a process is known as reductive (n-type) doping. The species responsible for the addition or removal of electrons is called the dopant. One example of a mild dopant is iodine (I_2). Iodine will remove an electron to form I_3^-. If an electron is removed from the top of the valence band of a semiconductive polymer such as polypyrrole or polyacetylene, the vacancy created does not delocalise completely as would be expected from classical band theory. If an electron is removed locally from one carbon atom, a radical cation (also called a "polaron") may be obtained. The polaron is localised due to attraction to its counterion (I_3^-) and has very low mobility due to a local change in the equilibrium geometry of the polaron relative to the neutral molecule [Vetenskapsakademien].

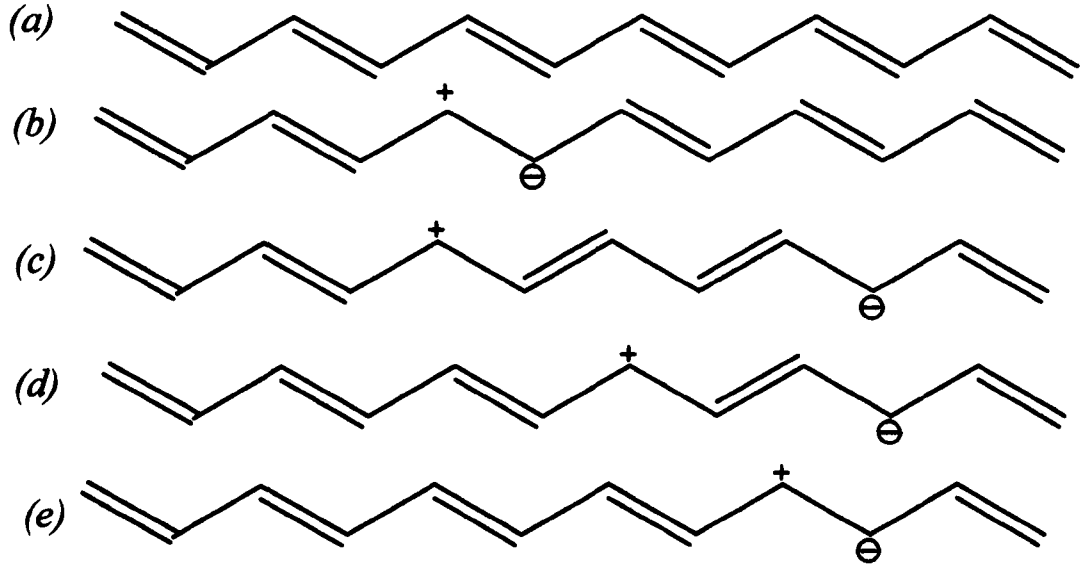


Figure 1.6 Radical cation ("polaron") formed by removal of one electron on the 5th carbon atom of a undecahexaene chain (a→b). The polaron migration shown in c→e.

A polaron is formed by the removal of one electron on the 5th carbon atom of an undecahexene chain (a --- b). Chains c ------ e illustrate the polaron migration. See Figure 1.6.

The mobility of a polaron along the polyacetylene chain can be high and the charge is carried along as shown above c-e. However since the counterion (I_3^-) near to the positive charge is not very mobile, a high concentration of counterions is required so that the polaron can move in the fairly uniform field of close counterions. This explains why excessive doping is required [Vetenskapsakademien].

1.5 Doping Process

As stated previously, conjugated polymers can exhibit properties of semiconductors or conductors once they undergo a process known as doping. The polymer has to be disturbed by either adding or removing electrons, via a redox process. Redox doping can be accomplished through either chemical or electrochemical means, and the polymers can be reduced and reoxidised in a reversible manner [Foot]. The charge on the polymer backbone must be compensated by ions from the reaction medium, which are then incorporated into the polymer lattice [Foot]. Conductivity can be controlled by the level of doping, and the rate of the doping process is dependent on the mobility of these charge-compensating ions into and out of the polymer matrix [Foot]. As previously mentioned, during redox doping, the number of electrons in the polymer backbone changes by removing or adding an electron to the polymer system. This is classified respectively as p-type or n-type doping.

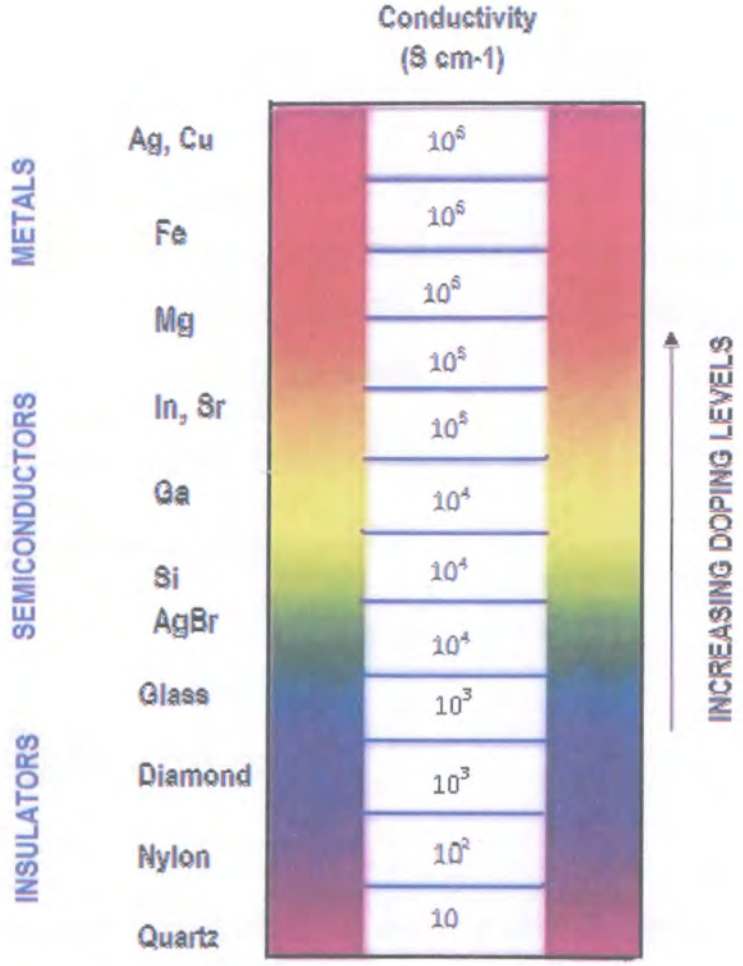


Figure 1.7 Material Conductivities [MacDiarmid]

1.5.1 p-Doping

This type of doping can be achieved by partially oxidising the π-system of the polymer backbone. For example in the case of polyacetylene, doping can be done using iodine. [MacDiarmid], [Vetenskapsakademien].

$$[CH]_n + 3x/2\ I_2 \longrightarrow [CH]_n^{x+} + xI_3^- \quad [3]$$

1.5.2 n-Doping

n-Doping is accomplished by partial reduction of the π system of the backbone, either chemically or electrochemically. For example in the case of trans-polyacetylene, n-doping has been achieved chemically using sodium naphthalide or n-butyl lithium in hexane [Eq. (1) (Nphth = naphthalene)] [Chiang], [Alan] [MacDiamid].

$$Trans\text{-}(CH)_x + (xy)Na^+(Nphth)^- \rightarrow [Na_y^+(CH)^{-y}]_x + Nphth \ (y \leq 0.1) \qquad (1)$$

There are a number of doping techniques.

1.5.3 Chemical Doping

This is accomplished in the vapour phase by exposing the polymer to the vapour of the dopant, usually under vacuum for a prolonged duration, or in the liquid phase, by immersing the polymer films in the dopant solution [Rebo].

1.5.4 Electrochemical Doping

In this process, conjugated polymers can be doped and undoped by immersing the material as an electrode in an organic electrolyte solution such as tetrafluoroborate dissolved in acetonitrile or other non-aqueous electrolytes. The nature of the doping produced (n- or p-type) depends on the polarity of the applied voltage [Rebo].

1.6 Ion Implantation

Ion implantation involves the insertion of bombarding ions into the polymer lattice and the subsequent possible formation of covalent bonds with the material. The doping level is then manipulated by the energy of the ion beam to which the material is exposed [Rebo].

1.7 Polypyrrole

The first modern reports on the synthesis of polypyrrole and its conducting properties were published in 1968 [Dall' Olio]. It was reported that the electrochemical oxidation of pyrrole in 0.1M sulphuric acid yielded a continuous black film [Dall' Olio]. Modifications to the initial approach, by using organic solvents and different electrolytes, have made the electrochemical method the most commonly employed polymerisation technique [Diaz, 79] [Kanazawa]. Polypyrroles tend to be "space filling" rather than fibrillar polymers, which makes them only moderate conductors in the neutral or reduced form [Pletcher]. However upon oxidation and doping with anions they become good electronic conductors [Pletcher].

The properties of polypyrrole tend to vary with the method of preparation and handling. The materials will differ with respect to their extent of oxidation, length of polymer chain, anionic doping, bonding within the chain and organisation of the chains within the film structure [Pletcher]. Heterocyclic monomers of pyrrole can be polymerised either by chemical or electrochemical methods to form fully conjugated polymers [Angeli], [Gardini], [Salmon]. It was first polymerised using H_2O_2 as an oxidant in 1916 by Angeli and Alessandri and it produced a powdery material known as "pyrrole black" [Angeli]. The amorphous powder was insoluble in organic solvents and from elemental analysis the formula was

estimated to be $C_{4.0\text{-}4.5}H_{3.0\text{-}4.5}N_{1.0}$ [Gardini]. This indicated that there was a presence of oxygen and linked pyrrole units. The molar mass was reported to be 800-1000 Da. Other oxidants such as H_2SO_4, $FeCl_3$, $Fe(ClO_4)_3$, $Cu(ClO_4)_2$, $Fe(BF_4)_3$, Fe(aryl-sulphonate)$_3$, I_2 and Br_2 have also been used to produce pyrrole blacks with low conductivity which has been a subject of interest to heterocyclic chemists [Gardini].

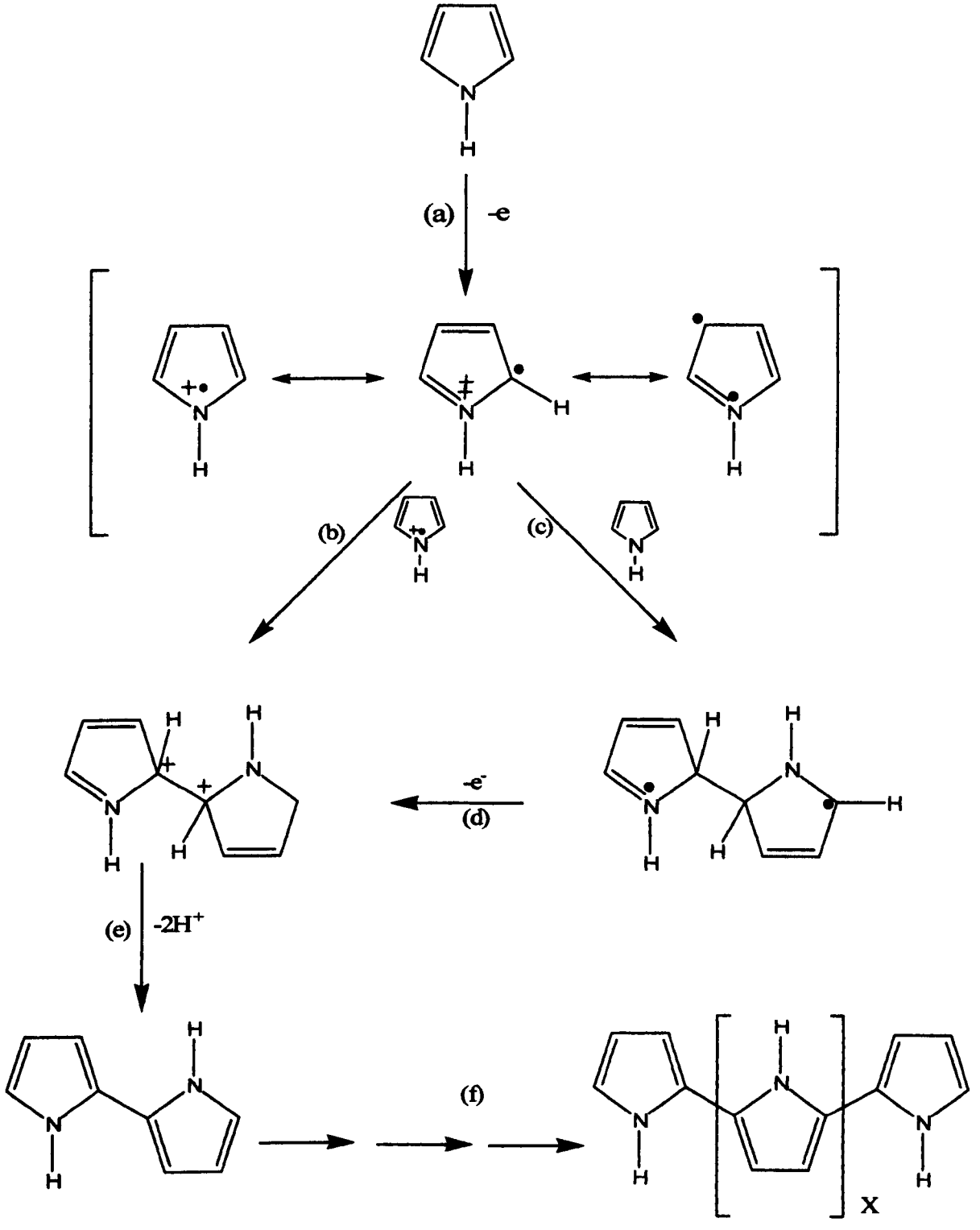
Polypyrrole can also be formed under acidic conditions; however the polymer chains contain alternating pyrrole and pyrrolidine monomer units and therefore do not have an extended π-system. Oxidised polypyrrole is stable under ambient conditions and can withstand temperatures in excess of 300^{0}C. The neutral form of polypyrrole, on the other hand has not been so well characterised due to its extreme sensitivity to oxidation (-0.02V vs SCE) [Feast].

Electrochemical oxidation of pyrrole provides good quality films and was first reported by Dall'Olio in 1968 [Dali'Olio]. The preparation was carried out in aqueous H_2SO_4 and the film was brittle with a conductivity value of 8 S cm $^{-1}$ at room temperature. Further interest developed in 1979 when Diaz *et al* reported that the anodic oxidation of pyrrole in acetonitrile containing 1% H_2O led to stable films which had metal-like conductivity and thermopower [Diaz, 79], [Kanazawa]. As a result of these findings, many papers were published, describing the electrochemical preparation of polypyrrole films, their chemical and physical properties and their behaviour as modified electrodes [Diaz, 81], [Burgmayer], [Street], [Pitchumani].

The properties of polypyrrole films are dependent upon the conditions used in their synthesis. Diaz *et al* reported that films grown in anhydrous acetonitrile had a rough surface with dendritic-like structure and SEM was used to study their morphology [Diaz, 81], [Kanazawa]. A much smoother and more adherent film was produced when as little as 1% H_2O or other hydroxylic solvents were used and the counterions were found to improve the conductivity of the films [Diaz, 79], [Kanazawa, 79], [Kanazawa, 80].

Another factor that affects the quality of the polypyrrole films produced is the substrate electrode material and in particular the adhesion of the film to the substrate. It was found

that polymerisation on inert anodes such as platinum or glassy carbon electrodes produced more adhering and continuous films than on tin oxide or single crystal n-type silicon [Frank]. It was also found that no polymerisation occurred on aluminium, indium, silver and iron [Frank]. As polypyrroles are known to be amorphous and insoluble in nature, the precise chemical composition and structure of the polypyrrole films is not fully understood despite intensive efforts [Street, 83a], [Street, 83b]. A mechanism was proposed for the electrochemical of polymerisation in acetonitrile (see figure 1.8 below).



(a) Oxidation of monomer. (b) radical-radical coupling. (c) radical monomer. (d) oxidation of dimer. (e) aromatization. (f) propagation to form polymer.

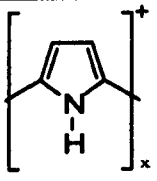
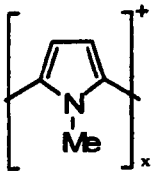
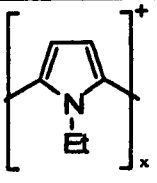
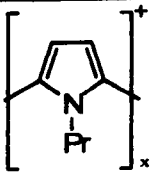
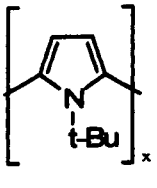
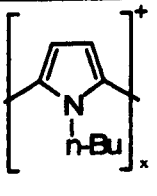
Figure 1.8 Mechanism for Polypyrrole Formation

Chemical polymerization of pyrrole is a good method of preparing polypyrrole particles of different and/or controlled size, ranging from several nanometres up to several micrometres. Although chemical polymerisation produces a large amount of polymer product, it is found that oligomers are mainly contained within the bulk solution and the high polymer is insoluble in most organic solvents so isolation of the product is quite difficult. To overcome this problem, doping can often be used to improve the polymer's solubility.

1.7.1 N-substituted Polypyrroles

Oxidation of N-substituted alkyl and aryl pyrroles can yield insoluble polymers on the electrode and as the size of the substituent increases it may become difficult to prepare thick continuous films [Diaz, 82]. In some situations, film deposition is accompanied by the formation of soluble products and cyclic voltammetric studies show that the oxidation of N-substituted pyrroles is irreversible [Diaz, 82]. The oxidation potential of pyrroles does not appear to be affected by the size of simple alkyl substituents, with the exception of N-aryl substituted pyrroles, which are more difficult to oxidise [Diaz, 82], [Salmon, 83]. As the size of the alkyl substituent increases, the conductivity and density of the N-substituted pyrrole film decrease. One exception to this rule is in the case of N-phenyl pyrrole, which shows a much higher density than expected, based on the size of the substituent alone [Diaz, 82].

Table 1.2 Summary of data for polypyrrole

N-Substituted Polypyrrole	Monomer E_{pa}/V vs.SCE	Polymer E^0 / V vs. SCE	Degree of partial oxidation	Density / g cm^{-3}	Conductivity S cm^{-1}	Ref.
	1.200	-0.200	0.25-0.30	1.48	29-100	[Diaz, 82]
	1.120 1.2	0.450 0.5	0.23-0.29 (<0.05	1.46 1.33	10^{-3} 10^{-6}) * 10^{-3}	[Diaz, 82] [Gardini]
	1.220	0.450	0.20	1.36	$2x10^{-3}$	[Diaz, 82]
	1.260	0.500	0.20	1.28	$1x10^{-3}$	[Diaz, 82]
	1.220	0.640	0.11	1.24	10^{-4}	[Diaz, 82]
	1.240	0.600	0.08	1.25	$2x10^{-5}$	[Diaz, 82]

*Poly-N-methylpyrrole in neutral form

1.8 Applications of Conducting Polymers (Polypyrrole)

The applications of conducting polymers have grown enormously over the past 30 years, and now large areas of science and technology rely upon conducting polymers to support, improve or functionalize their products. Due to their unique combination of electrical and mechanical properties, conducting polymers can be used as corrosion protection and antistatic coatings [Pron], [Gerord], [Nabid, 02], [Nabid, 03], [Hosseini, 03], biosensors for coupling of electron transfer, [Hosseini, 01], [Namazi], preparation of pH references or electrodes, immobilisation of biomolecules, fabrication of electrochemical windows and gas sensors, [Bar- Cohen], [Otero] and development of integrated devices. Conducting polymers have many advantages because of their low density, mechanical flexibility and optical properties. Polypyrrole has had many applications in the field of pharmaceutics and biological science, for example in biosensor design [Ramanavicius] . When creating any type of electrochemical biosensors some of the most important factors to be considered are:-

- The immobilisation of the bio-catalyst
- Application of the appropriate electrochemical technique
- Establishment of efficient electron transfer if amperometric detection is applied.
- Biological recognition properties and/or catalytic properties of the materials should remain after immobilisation
- Biomaterials should be well affixed on/within the substrate to maintain biological activity [Ramanavicius].

Among the conducting polymers, polyaniline is often used as an immobilizing substrate for biomolecules [Geise]; however as it is necessary to be able to detect bio-analytes at a neutral pH, this leads to electro-inactivity of the deposited films which makes the use of

polyaniline and polythiophene less desirable [Geise]. On the other hand, polypyrrole can be easily deposited from neutral pH aqueous solutions containing pyrrole monomer, and it has become one of the most extensively studied materials for the immobilisation of biomolecules and even living cells. Table 1.3 below shows various types of polymers used in enzyme biosensors.

Table 1.3 Types of Polymers used in enzyme biosensors

Analyte	**Polymer**	**Sensing element**	**Sensor properties**	**References**
Glucose	Polypyrrole Poly(N-methylpyrrole)	Glucose Oxidase (GOD)	Long term stability is 7 days Detect analyte within concentration range of 0.0-22 mol/dm^3	[Muhammad] [Florito]
L-Amino acids	Polytyramine	L-Aminoacid Oxidase (L-AAOD)	Lower limit of detection is 0.007 mM. Stability is more than 1 month	[Reddy]
Peroxides	Poly(anilinomethyl-ferrocene)	Horseradish		[Rahman]
Glucose, Urea, Triglycerides	Polyaniline	GOD, Urease, Lipase		[John]

1.9 Function of Conducting Polymers in Drug Delivery Systems

Recently there has been significant effort directed to finding new drug release systems in which bioactive molecules contained in a reservoir can be supplied to a host system, while controlling the rate and period of delivery [John]. Electrochemical switching of conducting polymers allows ion movement to maintain charge neutrality with the mobile species and the direction of ion flux is controlled by the polymer-ion interaction [Entezami]. Conducting polymers that have immobile high molar mass dopants exhibit cation-dominated transport [John], [Entezami]. They have also been proven to be useful materials for drug carriers as they can be easily processed and their physical and chemical properties can be modified by changes in their molecular architecture. The ideal mode of drug administration would be achieved if the drug was delivered to a precise region of the body where it was physiologically demanded, avoiding un-wanted biological interactions en-route to the site of action, to prevent harmful side effects.

Conducting polymers show great potential as electro-mechanical actuator materials and can be ideal for controlled drug delivery purposes [Entezami]. Their unique redox properties allow controlled ionic transport through the polymer membrane. In addition, the electrochemical switching properties of conducting polymers allow the movement of counter-ions (dopant ions) in and out of the membrane for charge balance. Polypyrrole actuators in particular can generate a strain of 1%-3% under electrochemical excitation, thereby generating a high stress (100-1000 times greater than a skeletal muscle). They require low voltage for actuation (1 V or less), are biocompatible, and operate ideally in liquid electrolytes (including biofluids). All these features make them very promising for biomedical applications.

One example of the useful electrochemical ability of polypyrrole as a drug encapsulating/release molecule is polypyrrole/adenosine triphosphate (PPy/ATP). It has

been reported that PPy/ATP has shown varied release properties depending on the synthesis conditions and cycling electrolyte [John], [Entezami]. A number of anions including salicylate, ferrocyanide and glutamate have been electrostatically entrapped in conducting polymer membranes and released during reduction. The entrapment of such large dopant anions inside the membrane also assisted cation release during oxidation of the polymer in the form of protonated dopamine. One of the major drawbacks of these systems, was the fact that they may exhibit spontaneous drug release, which has hampered their development as drug-release devices [John]. [Entezami].

Polymer-modified electrodes, consisting of a bilayer of two physically segregated electroactive materials with different redox potentials (a high redox potential inner film and a low redox potential outer film), can show interesting properties such as charge trapping for energy storage when subjected to electrochemical switching [Massoumi]. The construction of a bilayer such as PPy-ATP means that a single polymer-modified electrode can be used to absorb or release bioactive anions by manipulation of the redox state of the films.

CHAPTER 2

INTRODUCTION TO LIQUID CRYSTALS

CHAPTER 2: Introduction

2.1 History of Liquid Crystals

During 1850 and 1888, researchers in the field of organic solids observed strange behaviour of several materials at temperatures near their melting points. It was found that with an increase in temperature, the optical properties of these compounds changed discontinuously. One of the earliest examples of this unusual type of behaviour was first noted by W. Heintz in 1850. He found that stearin melted from a solid to a cloudy liquid at 52^0C, then changed to an opaque liquid at 58^0C, and lastly a transparent liquid at 62.5^0C [Collings, 90]. In addition to this, biologists were also observing anisotropic optical behaviour in what they termed "liquids", and up until this point this behaviour was only expected in the crystal phase.

Thirty-eight years later (1888), an Austrian botanist named Friedrich Reinitzer was carrying out research into the melting behaviour of organic substances related to cholesterol [Reinitzer]. He observed the same findings as Heintz did with stearin, that cholesteryl benzoate melted to a cloudy liquid at 145.5^0C and became a transparent liquid at 178.5^0C [Reinitzer]. However unlike Heintz, Reinitzer also observed distinct colour changes that occurred when cooling the substances, because he had at his disposal a new hot stage microscope invented by a German physicist and close friend, Otto Lehmann [Lehmann]. Reinitzer found that upon cooling the clear liquid a blue colour was observed at the transition temperature, and just before crystallisation a blue/violet colour appeared [Lehmann]. This was the emergence and initial identification of the fourth state of matter called the liquid crystal phase.

Later Otto Lehmann continued the research with a systematic study, first of cholesteryl benzoate, and then of related compounds which exhibited the double-melting phenomenon [Lehmann]. With the aid of his hot stage microscope, which enabled high temperature observations, he was able to make observations in polarized light. Although the intermediate cloudy phase clearly sustained flow, other features, especially the signature under a microscope, convinced Lehmann that he was dealing with a solid [Lehmann].

Other significant contributors were Daniel Vorlander, a German chemist who expanded Lehman's work by synthesizing most of the liquid crystals known; Georges Friedel who described the structure and properties of liquid crystals and classified them into 3 types (nematics, smectics and cholesterics) [Senyuk] and Vsevolod Frederiks who in 1927 devised the electrically switched light valve, called the Fréderiks transition, the essential effect of all LCD technology.

In 1962, Richard Williams discovered that liquid crystals had some interesting electro-optic characteristics. Through the application of a voltage, he realized an electro-optical effect by generating stripe-patterns in a thin layer of liquid crystal material. This effect is based on an electro-hydrodynamic instability and forms what is now known as "Williams domains" inside the liquid crystal [Williams].

George H. Heilmeier (1964) worked on the effect discovered by Williams and achieved the first operational liquid crystal display based on what he called the dynamic scattering mode (DSM) [Heilmeier]. DSM displays could be operated in transmissive and in reflective mode but they required a considerable current to flow for their operation [Heilmeier]. Heilmeier was inducted in the National Inventors Hall of Fame as the inventor of LCD [http://www.invent.org/2009induction/1_3_09_induction_heilmeier.asp].

In 1969, Hans Kelker was able to synthesize a substance that had a nematic phase at room temperature, N-(4-Methoxybenzylidene)-4-butylaniline (MBBA), which is one of the most popular subjects of liquid crystal research [Kelker]. The synthesis of further chemically stable substances (cyanobiphenyls) with low melting temperatures by George Gray led to the next step in the commercialization of liquid crystal displays [Gray]. Gray was the author of the

first major English language publication on the subject *"Molecular Structure and Properties of Liquid Crystals"* [Gray].

Meanwhile, in the late 1960s, pioneering work on liquid crystals was carried out by the UK's Royal Radar Establishment at Malvern, England. The team at RRE supported the ongoing work by George Gray and his team at the University of Hull who ultimately discovered the cyanobiphenyl liquid crystals (which had correct stability and temperature properties for application in LCDs). This led to the rapid adoption of small area LCDs within electronic products.

In 1991, Pierre-Gilles de Gennes received the Nobel Prize in physics "for discovering that methods developed for studying order phenomena in simple systems can be generalized to more complex forms of matter, in particular to liquid crystals and polymers" [De Gennes].

The development of optical patterning techniques by Samsung in 1996 (which enables multi-domain LCD), and the resurrection of In-Plane Switching (IPS) technology by Hitachi in 1997 (which produces visual quality acceptable for TV application), subsequently remained the dominant LCD designs through 2010.

2.2 Liquid Crystals - A Unique State of Matter

Liquid crystals, often referred to as mesogens, are typically elongated organic molecules with an uneven distribution of electrical charges along their axes (dipole) [Wu]. They have been defined as the fourth state of matter with the ability to exhibit characteristics of both crystalline solids and liquids [Collings, 97]. This is the origin of a special physical characteristic to which liquid crystals owe their name: between the crystalline and liquid states they exhibit a further state of aggregation, namely the liquid crystalline or mesophase. In this phase, the liquid crystal molecules are aligned parallel to each other but are able to rotate about their long axes.

The difference between crystals and liquids, the two most common condensed phases of matter, is that the molecules in crystals possess both positional and orientational order and are forced to occupy specific sites in a crystal lattice in which their molecular axes point in a specific direction [Collings, 97]. Molecules in normal liquids on the other hand, diffuse randomly, possess no specific positional or orientational order, and their molecular axes tumble wildly [Collings, 97].

The molecules in liquid crystals diffuse about much like the molecules of a liquid, but they are able to maintain some degree of orientational and positional order [Collings, 97]. The amount of order in a liquid crystal is quite small relative to that of a crystal, and is indicated by the value of enthalpy change when it transforms to a liquid crystal [Collings, 97]. Values are approximately 250 Jg^{-1}, which is very typical of a crystal to liquid transition [Collings, 97]. When a liquid crystal transforms to a liquid, the enthalpy change is much smaller, typically around 5 Jg^{-1}, indicating that they do not possess very strong intermolecular forces for high positional order [Collings, 97].

The liquid crystal state (mesophase) exists within some temperature range, $T_m<T<T_c$, where T_m is temperature of melting from solid state into a mesophase, and T_c is clearing temperature, when the liquid crystal transforms into an isotropic liquid (See Figures 2.1 and 2.2) [Senyuk]. In the solid state, the centres of gravity of molecules posses long-range positional order, and also the molecules orientation in the same direction providing the long-range orientational order. When solid melts into a liquid crystal at T_m, the positional order is lost although some orientational order of the molecular long axes remains. At still higher temperature T_c, mesophase melts into an isotropic liquid with no positional or orientational order [Senyuk].

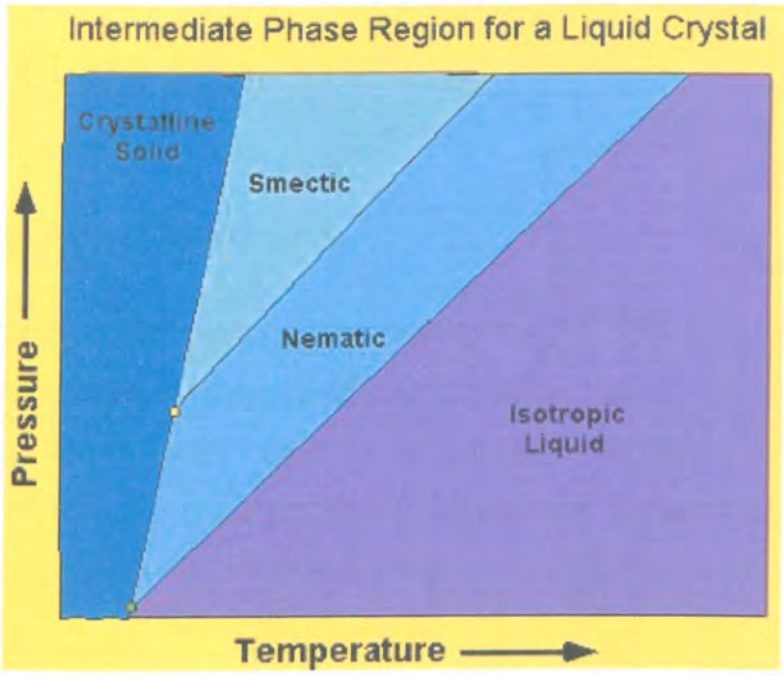


Figure 2.1 Intermediate Phase region for a Liquid Crystal [Senyuk]

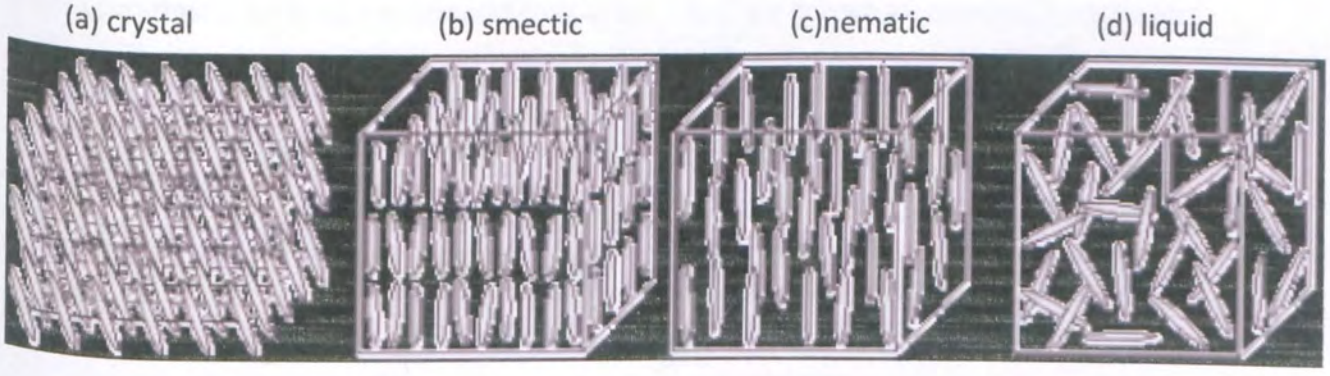


Fig 2.2 Thermotropic liquid crystals (with the increase of temperature): (a) crystal ; (b) smectic; (c) nematic; (d) liquid [Senyuk].

2.3 Types of Liquid Crystals

There are two main types of liquid crystals: -

1. **Lyotropic liquid crystals: -** Exist in mixtures consisting of compounds with relatively high polarity (amphiphilic compounds) and certain solvents.
2. **Thermotropic liquid crystals**: - exist as pure compounds but also as mixtures. The phase transitions of thermotropic liquid crystals depend on temperature, while those of lyotropic liquid crystals depend on both temperature and concentration.

Some compounds also have the ability to form thermotropic and lyotropic liquid crystals, and they are called **Amphotropic** [Collings, 90].

Thermotropic Liquid crystals can be further subdivided into three classes to distinguish between their positional and orientational order. They are known as: nematic, smectic and cholesteric (See Figure 2.3 below).

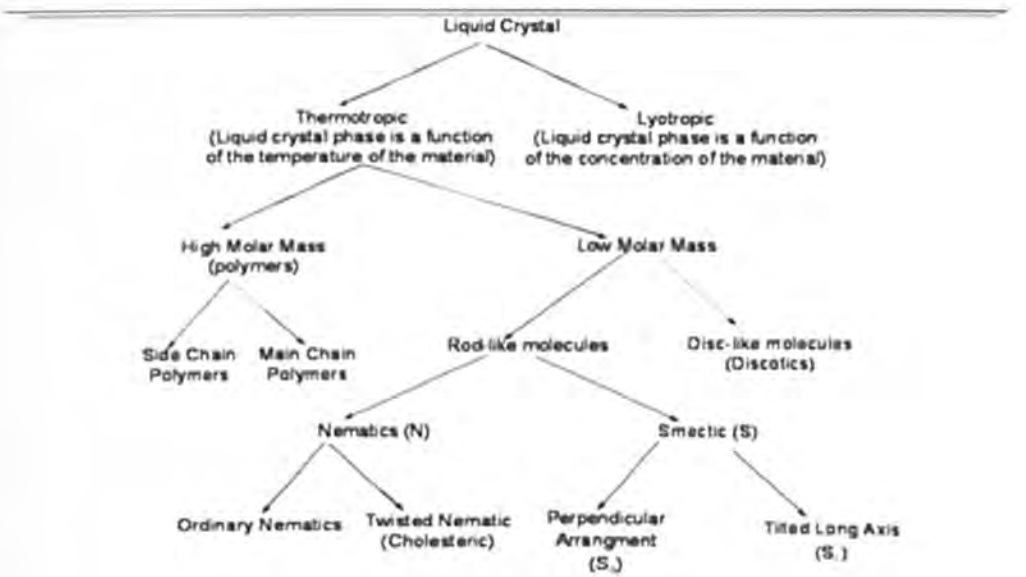


Figure 2.3 Classification of Liquid Crystals

[http://photonicswiki.org/index.php?title=Classification_and_Examples_of_Liquid_Crystals]

2.3.1 Thermotropic Liquid Crystals

Thermotropic liquid crystals exhibit liquid crystalline phases in certain temperature regions, and if transitions between phases are produced by temperature change, they are called thermotropic [Collings, 90]. The most common type of thermotropic liquid crystals have rod-shaped molecules (i.e one molecular axis is much longer than the other two) [Collings, 90]. Such compounds are called calamitic liquid crystals and many different phases are possible. It is important that the molecule remain rigid for at least some portion of its length, since it must maintain an elongated shape in order to produce interactions that favour alignment [Collings, 97].

In order for a molecule to display the characteristics of a liquid crystal, it must be rigid and rod-shaped. This is accomplished by the interconnection of two rigid cyclic units, which cause the resulting compound to have a linear planar conformation. Linking units containing multiple bonds such as -(CH=N)-, -N=N-, -(CH=CH)n-, -CH=N-N=CH-, etc. are used, since they restrict the freedom of rotation. These groups can conjugate with phenylene rings, enhancing the anisotropic polarizability. In addition, the molecular length increases and rigidity is maintained.

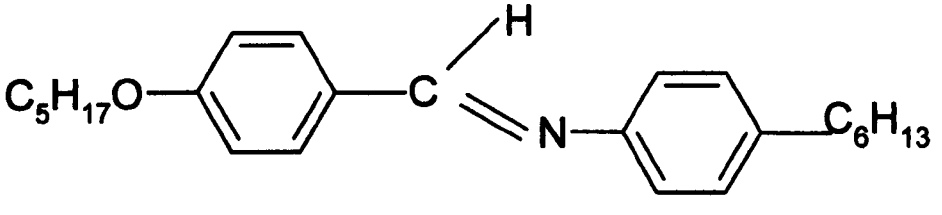


Figure 2.4 An example of a Calamitic Liquid Crystal [Collings 90]

Here it can be seen that a typical calamitic liquid crystal is composed of two or more ring structures linked together directly or via a rigid linking group with hydrocarbon chains at each end (See Figure 2.4 above).

2.3.2 Nematic Liquid Crystals

The term *nematic* comes from the Greek νημα (*nema*) meaning *thread*, a word used literally to describe the thread-like topological defects seen in the nematic structures under microscopic observation. Nematic liquid crystals are often polarizable rod-like (or *calamitic*) organic molecules of the order of 2 nm in length. They have no positional order, but they self-align to have long-range directional order with their long axes roughly parallel [Rego]. They exhibit interesting and useful optical properties; for example, digital watches and televisions use nematic liquid crystals for their display [Collings, 90].

The nematic phase is essentially a one-dimensionally ordered elastic fluid in which the molecules are orientationally ordered, but there is no positional ordering of the molecules. The average direction along which the molecules point is called the *director* of the phase, denoted by the symbol n (See Figure 2.5). The rod-like molecules in the *nematic* phase rotate freely about their short axes and to some extent about their long axes and tend to align parallel to each other with their long axes all pointing roughly in the same direction. In most liquid crystals both directions of the vector n, +n and -n are fully equivalent. However, this may not be the case for molecules with permanent dipole moments. In these cases, the sign of n becomes important [Senyuk].

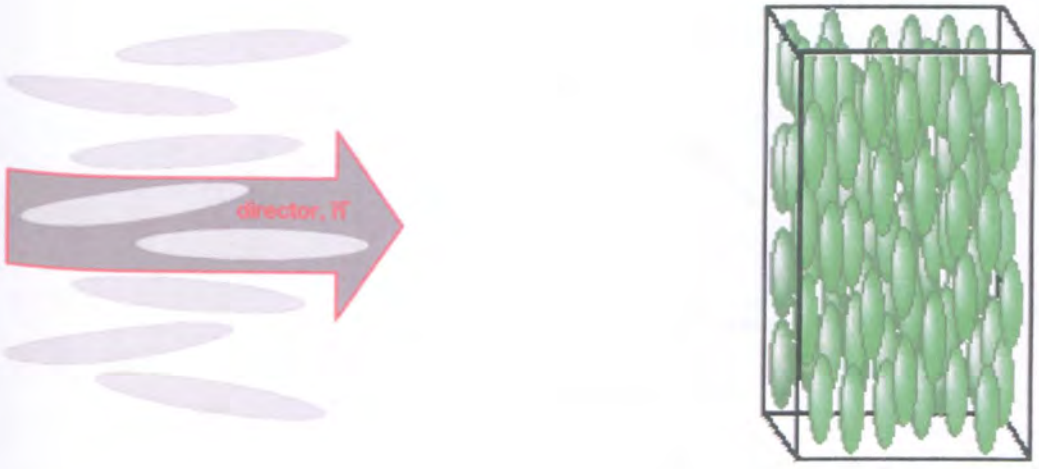
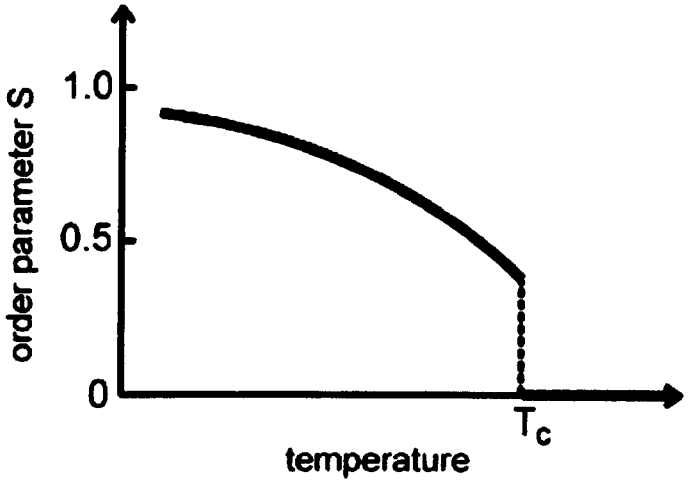


Figure 2.5 An illustration of a nematic liquid Nematic Liquid Crystals [Senyuk]

The *local nematic director*, which is also the *local optical axis*, is given by the spatial and temporal average of the long molecular axes. To determine quantitatively the amount of the orientational order in the liquid crystal phase, the scalar order parameter S is usually employed: $0 < S < 1$

$$S = \frac{1}{2}\langle 3\cos^2\theta - 1\rangle$$

where θ is an angle between the individual molecular long axis and the director n and the brackets indicate the average value [Gopal], [Senyuk]. In a perfectly oriented system $S = 1$, and in an isotropic liquid state, with no orientational order, $S = 0$ [Gopal], [Senyuk].



Scalar order parameter S vs temperature: T_c is clearing temperature

Figure 2.6 A graph of *Scalar order parameter S vs temperature [Senyuk]*

The order parameter (S) of the liquid crystals decreases as the temperature increases (see figure 2.6) and typical values are in the range 0.3-0.9 [Ghosh]. The order parameter can be measured experimentally in a number of ways. For instance, *diamagnetism*, *birefringence*, *Raman scattering*, and *NMR* can also be used to determine S [Collings, 97].

The order parameter has the same symmetry properties as the nematic phase, in that the order parameter is unchanged by rotating any molecule through an angle of 180°.

A special group of nematic liquid crystals is called *chiral* nematic. *Chiral* denotes the exceptional ability to reflect selectively one component of circularly polarized light [De Gennes]. This phase was first observed for *cholesterol* derivatives. Hence, it is often called the *cholesteric* phase and only molecules that lack inversion symmetry (*chiral molecules*) can give rise to it. Within this phase, there is a twisting of the molecules perpendicular to the director, with the molecular axis parallel to the director. The asymmetric packing in chiral molecules is the cause of the finite twist angle between adjacent molecules, which leads to longer-range chiral order [Collings, 97].

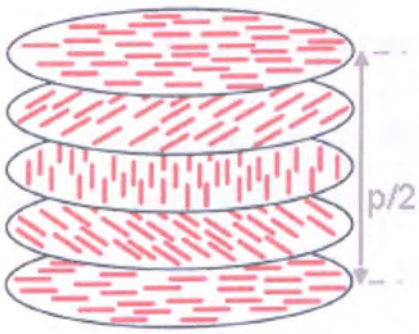


Figure 2.7 Chiral nematic phase; p refers to the chiral pitch [Gopal].

The *chiral pitch*, p, refers to the distance over which the liquid crystal molecules undergo a full 360° twist (See Figure 2.7). The pitch of the helix can vary from about 0.1 x 10^{-6}m to almost infinity [Gopal]. When the pitch of the phase is comparable to the wave length of light, the mesophase will selectively reflect light of a relatively narrow wavelength band. This causes these systems to exhibit unique optical properties, such as *Bragg* reflection and low-threshold laser emission [Kopp]. The pitch of the phase is temperature dependent, and so are the selective refection properties. This makes it possible to build a liquid crystal thermometer that displays the temperature of its environment by the reflected colour. Mixtures of various types of these liquid crystals are often used to create sensors with a wide variety of responses to temperature change [Kopp].

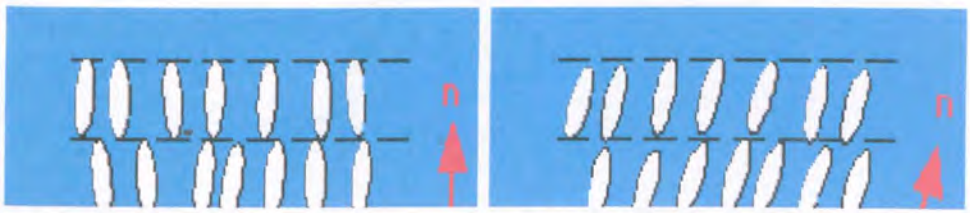
2.1.1 Smectic Liquid Crystals

The smectic state is another distinct mesophase of liquid crystal substances which show a degree of translational order not present in the nematic. In the smectic state, the molecules maintain the general orientational order of nematics, but also tend to align themselves in layers or planes within which there is loss of positional order. Motion is restricted to within

these planes, and separate planes are observed to flow past each other. The increased order means that the smectic state is more "solid-like" than the nematic.

Smectic liquid crystals can be classified into types such as **Smectic A** – where molecules align perpendicular to the layer planes, or **Smectic C** -where molecules align themselves at an arbitrary angle to normal [Collings, 90].

On the average, the molecules in smectic A phase are parallel to one another and are arranged in layers, with the long axes perpendicular to the layer plane (Figure 2.8). The centre of gravity of the molecules are ordered randomly within the layers, with the layer thickness equivalent to the molecule length. Thus, smectics A have the one-dimensional quasi long-range positional order showing a relatively high mobility [Senyuk].



The smectic A (left): director is perpendicular to the smectic plane, and there is no particular positional order in the layer. Smectic C (right): director is at a constant tilt angle measured normally to the smectic plane. http://www.mc2.chalmers.se/pl/lc/engelska/tutorial/lctypes.html

Figure 2.8 Alignment of smectic A and smectic C liquid crystals

The structures of the smectic A and the smectic C liquid crystals are closely related. Both molecules are arranged in layers, but the long axes of the molecules of the Smectic C are tilted to the layer planes (Figure 2.8). The tilt angle is constant in some materials and in others it is dependent on the temperature. The molecules' centre of gravity are ordered randomly and they rotate freely around their long axes. Smectic C phases are optically biaxial [Senyuk].

The Smectic C* phase is different from the Smectic C phase because it is made up of the chiral molecules (Figure 2.9), which rotate the direction of the director projection on the layer plane. The twist axis of the Smectic C* is at right angles to the layers. Therefore, these phases show characteristics similar to the cholesterics, such as optical activity, positive uniaxial, and selective reflection [Senyuk].

Figure 2.9 Helical structure of Smectic C* liquid crystals: n is director; z is twist axis; μ is dipole moment [Senyuk]

If the molecules in Smectic C* have the permanent dipole moments at right angles to their long axes, they have the ability to exhibit ferroelectric properties.

2.3.4 Cholesteric Liquid Crystals

These consist of layers of nematic crystals arranged in different directions, which upon rotation form a helical structure, due to the presence of a chiral centre in the molecule

[Collings, 90]. The *cholesteric* (or chiral nematic) liquid crystal phase is typically composed of nematic mesogenic molecules containing a chiral centre which produces intermolecular forces that favour alignment between molecules at a slight angle to one another [Palana], [Gopal]. This leads to the formation of a structure which can be seen as a stack of very thin 2-D nematic-like layers with the director in each layer twisted with respect to those above and below. In this structure, the directors actually form in a continuous helical pattern about the layer normal as illustrated by the black arrow in Figure 2.10. The black arrow in the figure represents director orientation in the succession of layers along the stack [Gopal].

Figure 2.10 Director Orientation of Chiral Nematic Mesogens [Gopal]

The molecules shown are merely representations of the many chiral nematic mesogens lying in the slabs of infinitesimal thickness with a distribution of orientation around the director. This is not to be confused with the planar arrangement found in smectic mesophases.

The *pitch,* p, is an important characteristic of the cholesteric mesophase and is defined as the distance it takes for the director to rotate one full turn in the helix as illustrated in figure 2.10 [Gopal].

2.3.5 Lyotropic Liquid Crystals

Lyotropic liquid crystals have a structure which combines a hydrophobic group at one end with a hydrophilic group at the other end. They have ordered structures in both polar and non-polar solvents, and good examples of such compounds are soaps and phospholipids [Collings, 97].

When dissolved in a polar solvent such as water, the hydrophobic hydrocarbon tails join together and present the hydrophilic phosphate heads to the solvent. The resulting structure for soap is termed micelle and for phospholipids, vesicle. Both soap and phospholipid molecules form bilayer structures, with the hydrocarbon chains separated from the water by the polar head group [Collings 97]. These lamellar phases are of extreme importance especially in the case of phospholipids as they constitute about 40% of cell membranes, and allow the influx and efflux of substances into and out of the cell. In addition the possibility for the anisotropic LC phase to be formed in a solution of long rigid rods (lyotropic LC systems) was demonstrated for the first time in the 1950's by Onsager and Flory [Flory].

2.4 Building Blocks

There are many ways to generate a liquid crystal phase. Usually, the thermotropic liquid crystals are produced by molecules with anisotropic shape, either elongated or disk-like [Senyuk]. The components of these molecules are often made up of a central rigid core (usually aromatic) and a flexible tail (typically aliphatic groups). The elongated or rod-like molecules (Figure 2.11) form calamitic liquid crystals, and disk-like molecules (Figure 2.12) form discotic liquid crystals. The banana-shape molecule (Figure 2.13) is an example of building blocks with more complicated shape, which form thermotropic liquid crystal phases. In most practical applications, the calamitic liquid crystals are employed [Senyuk].

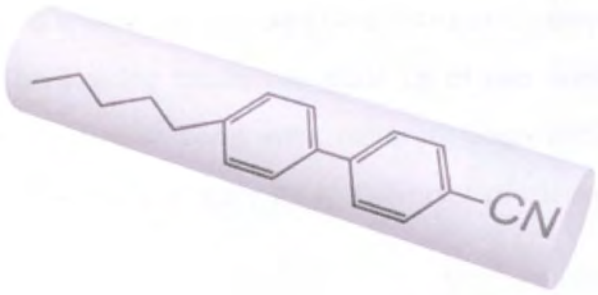


Figure 2.11 Molecular Structure of 5CB

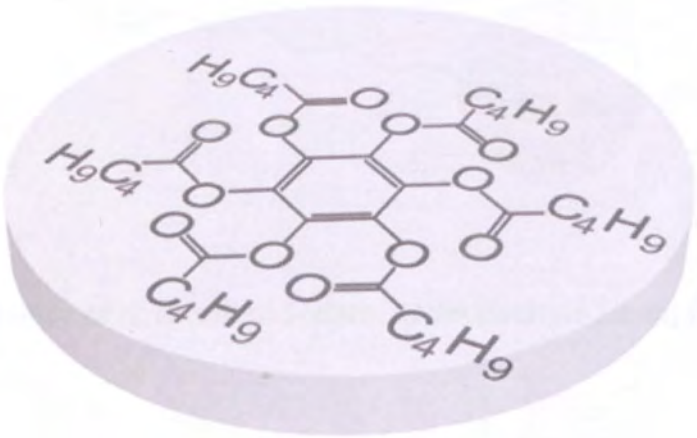


Figure 2.12 Benzene-Hexa-n-alkanoate Derivatives

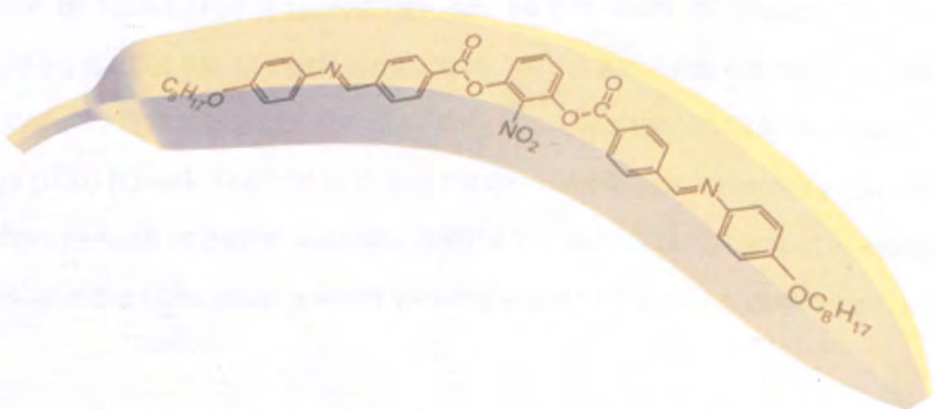


Figure 2.13 Banana Shaped Liquid Crystals [Senyuk]

The lyotropic liquid crystals are usually two-part systems in which amphiphilic compounds are dissolved in a solvent. The building blocks are made up of two distinct parts, a hydrophilic polar head (which can transiently bond with water through hydrogen bonding) and a hydrophobic nonpolar tail [Senyuk]. (Figure 2.14). Examples of these kinds of molecules are soaps.

Furthermore, the liquid crystal phases can be formed by molecules with high molecular weight such as main-chain or side chain polymers made of rigid mesogenic parts, attached to flexible links. [Senyuk].

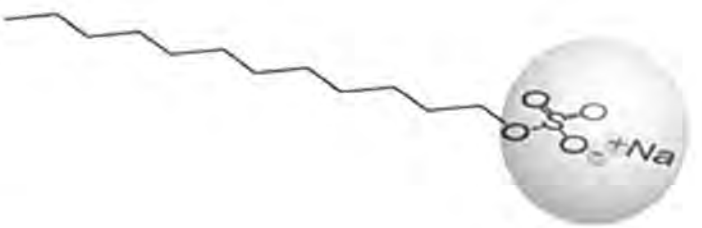


Figure 2.14 Molecular structure of Sodium Dodecylsulfate (soap) [Senyuk]

2.5 Applications of Liquid Crystals

The importance of liquid crystal technology can be observed all around us. Technically speaking, liquid crystals of the nematic type are by far the most important. They are used in electro-optic systems and one of the most widely used applications can be found in liquid crystal displays (LCD) [Chen]. The first LCD was made in 1968, and today they can be found in electronic devices such as digital watches, televisions, calculators, computer monitors and mobile phones, and the LCDs allow a wider viewing angle and displays can remain in use for

years with minimal power supply [Chen]. As well as having applications in the domain of physics and chemistry, liquid crystals can also be applied in biological systems to gain more insight into understanding the characteristics of a bio-membrane of a cell.

Smectic and nematic liquid crystals are used in heat-sensing devices such as thermometers and egg timers largely because of their light transmission properties and their ability to change their form when subjected to temperature changes. They can split a beam of ordinary light into two polarized components to produce the phenomenon of double refraction [Wu].
The use of cholesteric liquid crystals in clinical thermometry has been shown by several studies. In medical application, liquid crystals implanted in a self-adhesive polymer film have been marketed in the form of a tape to obtain the thermal mapping of skin. Temperature sensors use this technique to detect illness in human beings by reflecting the skin temperature patterns from the liquid crystal thermography [Wu].
In addition, super-strength, lightweight materials used in bullet-proof vests, high-performance cables and tyres, and stealth aeroplanes are built from liquid crystalline polymer (LCP) fibres.

2.6 Application of Liquid Crystal Formulations in Drug Delivery

As delivery systems, liquid crystals can potentially enhance the dissolution of poorly water-soluble drugs. Lyotropic liquid crystals can incorporate relatively high drug loadings. However, the high surfanctant concentrations and the occurrence of colloidal dispersions of liquid crystals are major disadvantages [Wu]. Examples of applications of liquid crystal formulations in drug delivery are shown in Table 2.1 below [Wu].

Table 2.1 Examples of applications of liquid crystal formulations in drug delivery

Formulation	Phase	Drug	Delivery route	Release kinetics	Reference
Brij 96 (poly-oxyethylene-10-oleyl ether)/ water/ liquid petrolatum (LP)/glycerol	Lamellar	Ephedrine hydrochloride; Tenoxicam	*In vitro*	First-order Zero-order	Makai
Synperonic A7 (PEG7-C13-15) (non-ionic)	Lamellar, Hexagonal	Chlorhexidine base and salts	*In vitro*	NT*	Farkas
Glyceryl monooleate	Lamellar, Cubic	[D-Ala^2, D-Leu^5]enkephalin (DADLE)	*In vitro*	NT	Lee, 00
Oleyl glycerate, phytanyl glycerate	Reverse hexagonal (H_n)	Paclitaxel, irinotecan, glucose, histidine, octreotide	*In vitro*	All obeyed Higuchi kinetics	Boyd
Glyceryl monooleate; Phytantriol	Reversed hexagonal	Glucose, Allura Red, FITC-dextrans	Oral	Diffusion-controlled	Lee, 09
Poloxamer; Monoglyceride	Cubic	Tetracycline	Periodontal intrapocket administration	Fickian diffusion	Esposito

*NT = Not tested

CHAPTER 3

INTRODUCTION TO DENDRIMERS

CHAPTER 3: Introduction

3.1 What are Dendrimers?

Dendrimers are well-defined globular macromolecules constructed around a core unit [Marcos]. They have a symmetrical structure that resembles trees with branched sub-units called dendrons which radiate from a central core, and the distance between subsequent branching points is fixed and a regular branching pattern unfolds [Tomalia]. At the end of each dendron are surface groups, which can be modified to meet various functionalities. Dendrimers have high concentrations of functional groups which in turn increases the density of surface atoms [Tomalia]. This allows the dendrimer more structural features and optimises its applications and use. However as the dendrimer grows larger, the end groups on the surface globule become more densely packed, and because of steric hindrance arising from interactions between neighbouring functional groups of the surface molecules, the dendrimer reaches its upper generation limit, which is termed "starburst effect" or "de Gennes dense packing" [Tomalia]. This effect was named after a French physicist called Pierre-Gilles de Gennes, as he was the first person to report this effect and was awarded a Nobel Prize in Physics for this contribution [Tomalia].

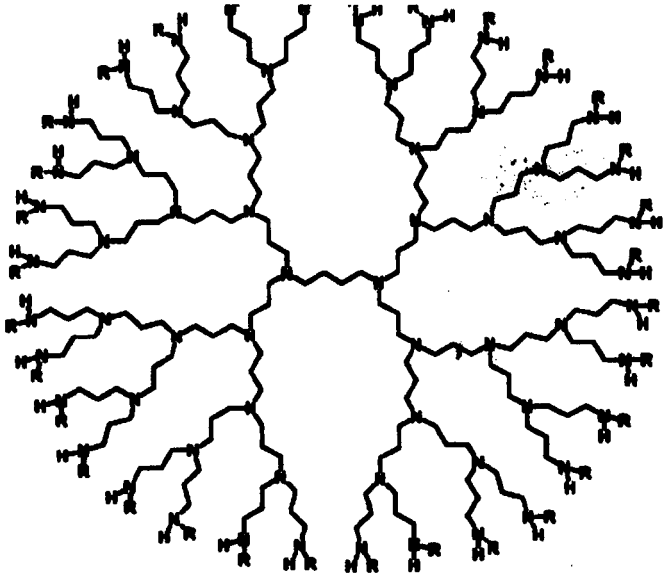


Figure 3.1 An illustration of an Amine core Dendrimer [Newkome]

The core of a dendrimer usually consists of an amine molecule, (Figure 3.1) although sugars and other molecules can be used. Core molecules have multiple reaction sites that are identical to one another. For example ammonia (NH_3) has three possible reaction sites [Newkome].

Dendrimers consist of a series of chemical shells, often termed generations, which are built on a central core molecule [Guillon]. During synthesis, each successive step leads to an additional generation of branching. Each generation consists of two chemicals always in the same order, and like many other organic molecules, the first three generations are very small, floppy, and without much consistency or specific three dimensional shape [Tomalia]. It is not until the fourth generation that we begin to see some structural characteristics of dendrimers as they begin to become spherical and three-dimensional in structure. By the fifth generation they have consistency, and a specific three-dimensional shape, and as the generations increase thereafter, it is observed that the dendrimers become highly structured spheres [Tomalia]. As

the size of the dendrimer increases the density of the terminal groups also increases, and the central cavity has the ability to accommodate a guest molecule whilst the terminal groups protect the contents [Tomalia]. It is this consistency and spherical structure that makes dendrimers ideal molecules for drug delivery, nanotechnology and several other applications [Marcos].

3.2 History of Dendrimers

The word dendrimer derives from the ancient greek word **dendron** meaning tree, and from the Greek suffix- **"mer"** meaning segment [Newkome]. Progress towards the construction of macromolecules possessing branched architecture can be considered to have occurred in three periods. The first period occurred from the late 1860's to the early 1940's, when branched structures were considered responsible for the insoluble and intractable materials formed in polymerisation reactions. Isolation and proof of structure was not attainable during that period, as physical characterisations, synthetic control and mechanical separation techniques were primitive. The second period took place during the early 1940's to the late 1970's. Branched structures were considered primarily from a theoretical perspective and initial attempts of their preparation involved classical or single-pot polymerisation of functionally differentiated monomers. The early 1980s marked the third period of development. Denkewalter, Tomalia and Vögtle were the pioneers of dendrimer chemistry, and the first dendrimer was synthesised in 1984 by Vögtle who was the scientific director of the Center for Biological Nanotechnology at the University of Michigan [Newkome]. However dendrimers did not draw much attention until 1985 when two groups published different papers detailing the synthesis of branched macromolecules. This encouraged chemists to carry out work on the dendrimers, in which they came to realise that these globular macromolecules behave differently from conventional linear polymers [Tomalia].

In 1985 Tomalia used a divergent synthesis method to synthesize poly(amidamine) dendrimers known as PAMAM dendrimers, in which the growth of sucessive generations of the dendrimer radiated outward from a central ammonia core [Tomalia]. The PAMAM dendrimers synthesised from this divergent method were commercially used as immunodiagnostic and gene transfection vectors, as it was found that the PAMAM dendrimers have a very close match to the size and contours of fundamental proteins and bioassemblies, and the 5^{th} and 6^{th} generations of the PAMAM dendrimers had the same diameter as those of cell membranes encasing all biological cells [Tomalia], [Astruc]. Also in 1985 another pioneer of dendrimer chemistry, George R. Newkome published a report on the use of the divergent synthesis to prepare poly(amidoalcohol)s (PAA) with micellar structures called "arborols" which means trees, as the overall structure is based on the architectural model of trees, in which the outer surface groups at the end of each dendrimer is covered with polar hydroxyl functional groups [Newkome].

It was during 1990 that Tomalia and Newkome introduced a new method of synthesising dendrimers, and it involved the construction of dendrimer segments called dendrons which were assembled around a central core. This method was called "Convergent Synthesis" [Tomalia].

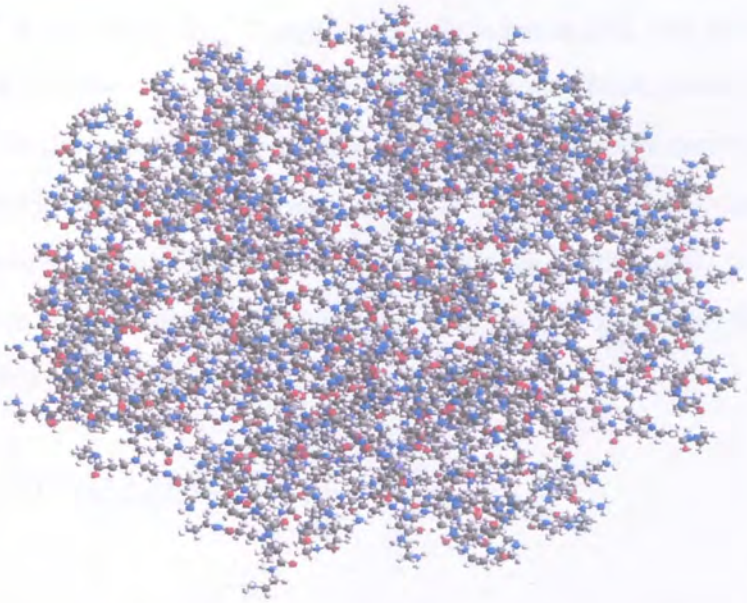


Figure 3.2 An Illustration of a PAA Dendrimer Built using the Convergent Synthesis Produced using Molecular Modelling [Newkome]

3.3 Synthesis of Dendrimers

A dendrimer can be synthesized to have different functionality in the three major parts (core, inner shell and outer shell) so as to control properties such as solubility, thermal stability, and attachment of compounds for particular applications. Synthetic processes can also precisely control the size and number of branches on the dendrimer.

In other to obtain dendrimers without structural defects, the synthesis must be clean and occur in high yield with no significant side reactions. In general, this synthesis involves the repeating of a two-step reaction sequence which comprise of a generation growth step and an activation growth step.

There are two different defined synthetic strategies employed to construct dendritic frameworks. These are the divergent growth approach developed by Tomalia *et al* and

Newkome *et al* [Tomalia, 85], [Tomalia, 86], [Newkome 85], and the convergent approach developed by Hawker and Frechet, [Hawker]. In both step-by-step synthetic approaches, quantitative coupling are needed to construct high generation dendrimers. Some examples of these dendrimers include, polyamidoamine (PAMAM), poly(propyl imine)(DAB-*dendr*-NH_2), polyethers, polyesters, poly(ester amides), poly(ether amides), polyalkanes, polyphenylenes, poly(phenylacetylenes), polysilanes, phosphorous dendrimers and others [Newkome], [Matthews], [Roovers]

3.3.1 Divergent Methods

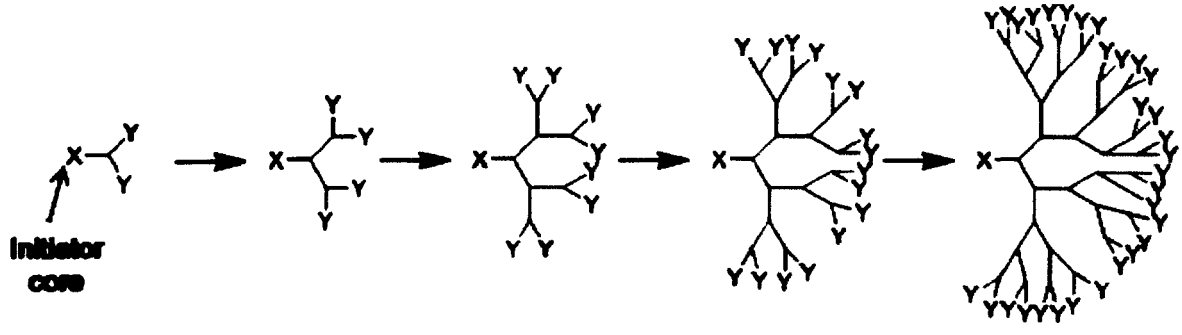


Figure 3.3 Schematic of Divergent Synthesis of Dendrimers

[http://en.wikipedia.org/wiki/Dendrimer]

The divergent approach was employed in the early dendrimer synthesis. The term "divergent" comes from the way in which the dendrimer grows outwards from a multifunctional core to the periphery through a series of reactions. The core consist of multiple reaction sites (typically 2 or 3 sites) and it is treated with an excess of the first monomer reacting with all the core reaction sites. The monomer also has reactive groups that are ready to react. An excess of a second monomer is reacted with the half generation (core and monomer), giving rise to the first generation. Repetition of this iterative reaction leads to second and third generation. However, it is only in the fourth generation that the dendrimer becomes a highly branched sphere. Above the fifth generation, steric

overcrowding can occur, and may prevent complete reaction of the molecules, and this may also damage the shape of the uniform structure of dendrimers [Nagasaki], [Hobson], [Tomalia].

A most important quality of the divergent approach is the exponentially increasing number of reactions that are required for the attachment of each subsequent layer or generation. Branching is dependent on monomer valency and proceeds in a 1→2 manner. With three monomers, the resulting product is an ammonium salt, in which branching proceeds in a 1→3 fashion. Perhaps one of the most well known divergent approach is the synthesis of PAMAM.

3.3.2 Convergent Methods

The convergent method was developed in order to overcome some of the disadvantages of the divergent approach [Tomalia]. In the convergent synthesis, dendrimer growth starts at the chain end and proceeds inwards through successive addition of the growing dendritic molecules to a single monomer unit. When the growing wedges are large enough, several can be attached to a suitable core to give a complete dendrimers.

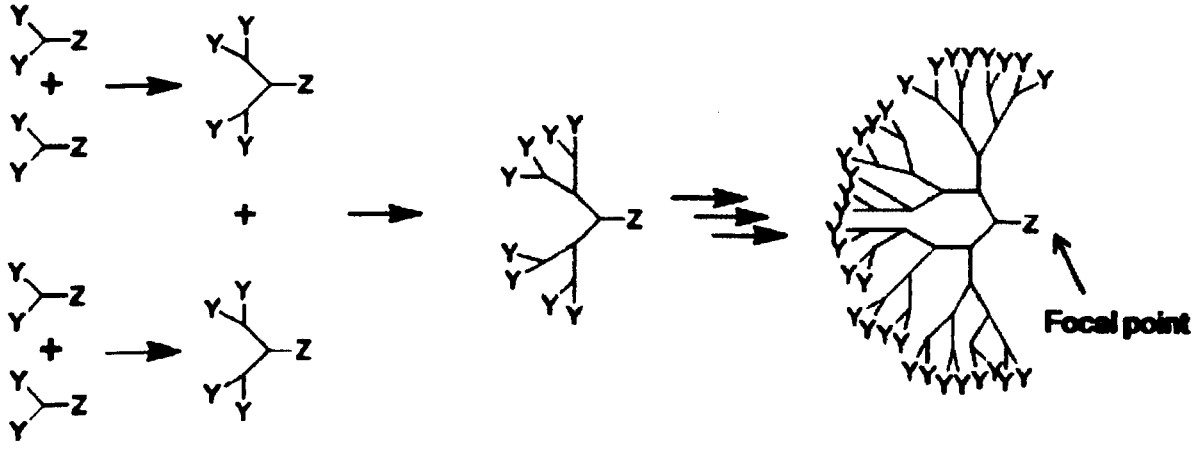


Figure 3.4 Schematic of Convergent Synthesis of Dendrimers

[http://en.wikipedia.org/wiki/Dendrimer]

The advantage of the convergent over divergent approach is that for the convergent, only two simultaneous reactions are required for any generation- adding step. This makes purification less problematic and the occurrence of defects in the final structure is minimised. Again, the convergent approach allows complete control over all molecular design parameters thereby making it easier to yield the desired dendrimers. On the other hand, the divergent approach has been shown to be suitable for larger-scale production of dendrimers. One of the disadvantages of the convergent synthesis is that it requires a great deal of starting material and thus the number of steps to build up a large structure is not reduced compared with the divergent method. It also suffers from low yields in the synthesis of large structures.

3.3.3 Recent Approaches

Due to the rapid growth of exploration of dendrimers, there was need for the development of more efficient synthetic processes which can circumvent the laborious and time-consuming steps of activation or protection of monomers, condensation reactions and purification by chromatography separations involved in the convergent and divergent approaches [Inoue]. Subsequently, several methods to reduce the number of synthetic steps and to obtain the desired dendrimer in high yield have been demonstrated. These include, a double-stage convergent growth approach [Ihre], a hypercore or branched monomer approach [Wooley, 94] [Wooley, 91], double-exponential dendrimer growth [Kawaguchi] and orthogonal coupling strategies [Zeng].

The **double-stage convergent growth approach** was reported by Hult and Frechet [Ihre]. In this synthesis, the focal points of dendrons are coupled in a divergent manner to the periphery of a monodendron or dendrimer prepared by convergent or divergent growth. Both core (hypercore) and wedges are of lower generations. In this way, for example, the

fourth generation dendritic aliphatic polyester starting with 2,2-bis(hydroxymethyl)propionic acid could be synthesized in six steps only involving two purifications by column chromatography separations [Inoue]. The number of purifications would have been higher if prepared by the conventional divergent approach. Hence, the newer method can reduce the number of growth steps and facilitate the purification of the final dendrimer product.

Frechet *et al* also showed alternate methods utilizing hypercores and hypermonomers which are pre-branched analogs of the cores and monomers [Wooley, 94], [Wooley, 91]. The pre-branched oligomers can then be linked together to give dendrimers in fewer steps and higher yields.

The **double-exponential dendrimer growth** was developed by Moore *et al* [Kawaguchi]. Here, both functional groups of AB_2 monomer are masked so as to be deprotected selectively, and then two growth monomers, one with protected B functional group is prepared by deprotection of A functional group (divergent-type monomer) and the other B functional group with protected A functional group (convergent-type monomer) in separate reactions. In order to provide a protected dendritic molecule, the divergent-type monomer was condensed with convergent-type monomer. The dendrimers of higher generations were synthesized by the repetition of selective deprotection and coupling processes [Inoue]. The generations can be grown in one pot without intermediate purification steps.

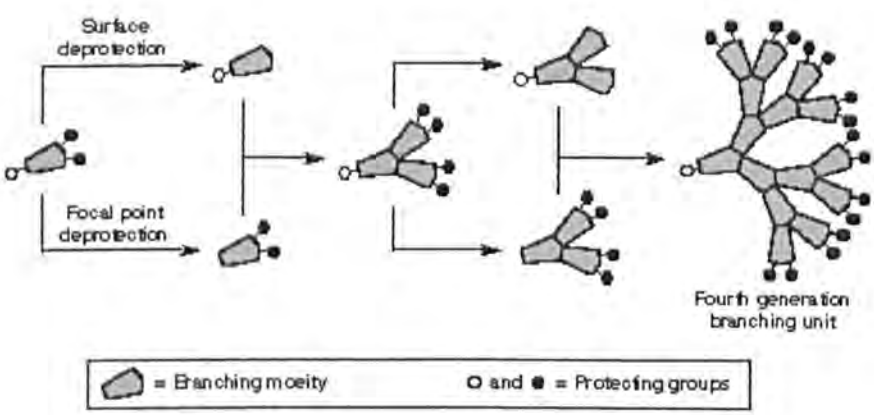


Figure 3.5 Double Exponential and Mixed Growth

[http://www.pharmainfo.net/reviews/dendrimer-overview]

Recently, Zeng and Zimmerman developed the **orthogonal coupling strategy** in the synthesis of dendrimers which is less-time consuming [Zeng]. Employing the Mitsunobu esterfication reaction [Mitsunobu] or the Sonogashira reaction, they were able to synthesize, in three steps and two chromatographic separations, the sixth generation dendrimer consisting of polyphenylacetylene linked with polyesters. The synthesis of dendrimers through the orthogonal coupling reactions eliminates (de)protection or activation steps and reduces the number of synthetic and purification steps required.

3.4 Types of Dendrimers

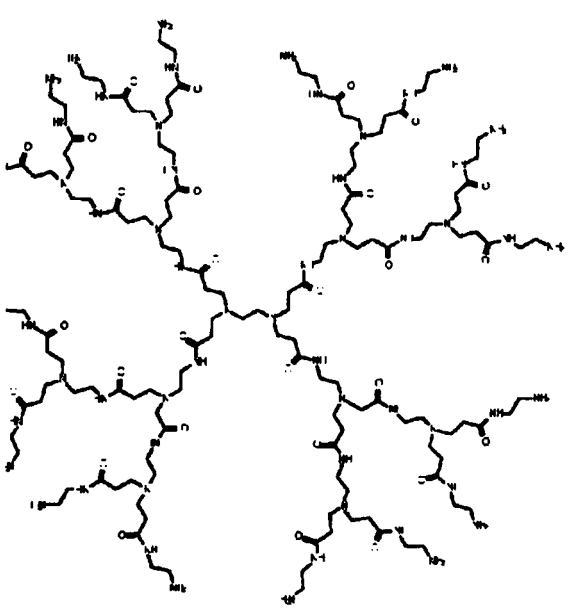
3.4.1 PAMAM Dendrimers

Poly(amidoamine), or PAMAM dendrimers are synthesized by the divergent method with a diamine (commonly ammonia or ethylenediamine) as the core reagent, which is reacted with methyl acrylate, and then another ethylenediamine to make the generation-0 (G-0) PAMAM. Successive reactions create higher generations, which tend to have different properties. Products up to generation $10^{(7)}$ (a molecular weight of over 9,30,000 g/mol) have been obtained. The functional group on the surface of PAMAM dendrimers is ideal for click chemistry, which gives rise to many potential applications [Hermanson]. Commercially, PAMAM dendrimers are available as methanol solutions. "Starburst" dendrimers is applied as a trademark name for a sub-class of PAMAM dendrimers based on a tris-aminoethylene-imine core.

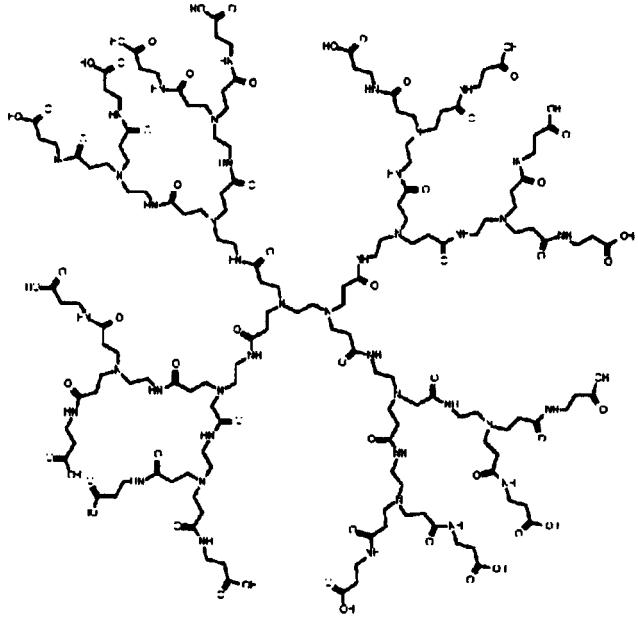
3.4.2 PPI Dendrimers

Poly(propylene imine) PPI-dendrimers are the oldest known dendrimer type developed initially by Vögtle describing the propylamine spacer moieties [Hawker]. In 1978, the first cascade structure of oligo(propylene imine) was synthesized by Vögtle *et al*, based on a repetitive reaction sequence of double Michael additions of an amine to acrylonitrile, followed by the reduction of the nitriles to primary amines [Buhleier]. Fifteen years later, a large scale synthesis of PPI poly(propylene imine) dendrimers was developed, using a modified Vögtle route by Wörner and Mülhaupt and de Brabander-van den Berg and Meijer respectively [Wörner], [de Brabander-van den Berg].

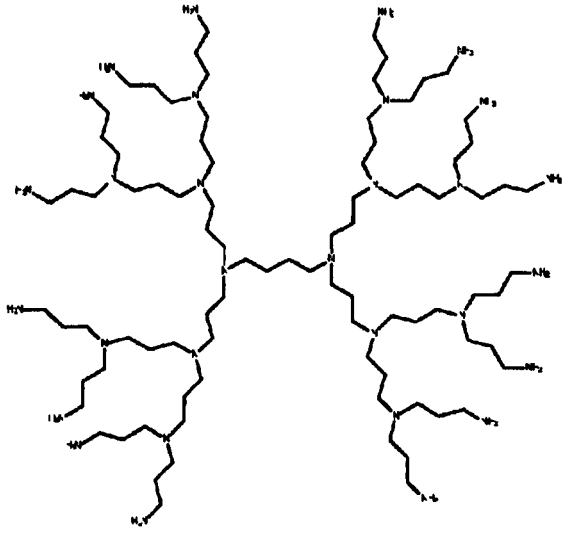
PPI dendrimers are generally poly-alkyl amines having primary amines as end groups, the dendrimer interior consists of numerous of tertiary tris-propylene amines. PPI dendrimers are commercially available up to G5, and have found widespread applications in material science as well as in biology. Sometimes, POPAM or "DAB-dendrimers" are used to describe PPI dendrimers. POPAM stands for Poly (propylene amine) which closely resembles the PPI abbreviation and DAB refers to the core structure, which is usually based on diamino butane.



Amine terminated PAMAM



Carboxylic acid terminated PAMAM



Amine terminated PPI

Figure 3.6 The structures of PAMAM and PPI dendrimers

[http://www.pharmainfo.net/reviews/dendrimer-overview]

3.4.3 PAMAMOS Dendrimers

Poly(amidoamine-organosilicon) (PAMAMOS) dendrimers are radially layered inverted unimolecular micelles that consist of hydrophilic, nucleophilic polyamidoamine (PAMAM) interiors and hydrophobic organosilicon (OS) exteriors [Dvornic 00], [Dvornic, 98].

PAMAMOS dendrimers which includes many compositional and functional variants, (among which are those with alkoxysilyl end-groups) was discovered by Dr. Petar Dvornic and his colleagues at Michigan Molecular Institute in the 1990s [Dvornic, 00]. These dendrimers are exceptionally useful precursors for the preparation of honeycomb-like networks with nanoscopic PAMAM and OS domains.

The domain sizes of these dendrimer networks can be controlled with the precision of about 1 nm with actual domain sizes ranging from about 2 to about 9 nm, depending on the precursor generation used. Scanning electron microscopy (SEM), small-angle neutron scattering (SANS) and small-angle X-ray scattering (SAXS) studies revealed uniform three-dimensional distribution of these domains throughout the bulk of the networks.

PAMAMOS dendrimer networks may be conveniently processed into self-supporting elastomeric or plastomeric films, sheets or coatings. Nucleophilicity of PAMAM domains of these unique nanostructured dendrimer networks enables topologically controlled complexation of a wide variety of different electrophilic species [Balogh], [Dvornic,02]. Among others, these may include organic dyes, organometallic molecules and/or inorganic cations, such as: methylene blue, methyl red, various salts of Ag^{+}, Cu^{+}, Cu^{2+}, Ni^{2+}, Cd^{2+}, Fe^{2+}, Co^{2+}, Pd^{2+}, Pt^{2+}, Fe^{3+}, Au^{3+}, Rh^{3+}, Pt^{4+}, or lanthanides, such as Eu^{3+}, Tb^{3+}, etc., [Balogh], [Dvornic,02].

The complexed species can be further chemically transformed (as if in confined nano-reactors) to yield nanoscopic particles of zero-valent metals, sulfides, selenides, etc., as shown in Figure 3.7 [Balogh].

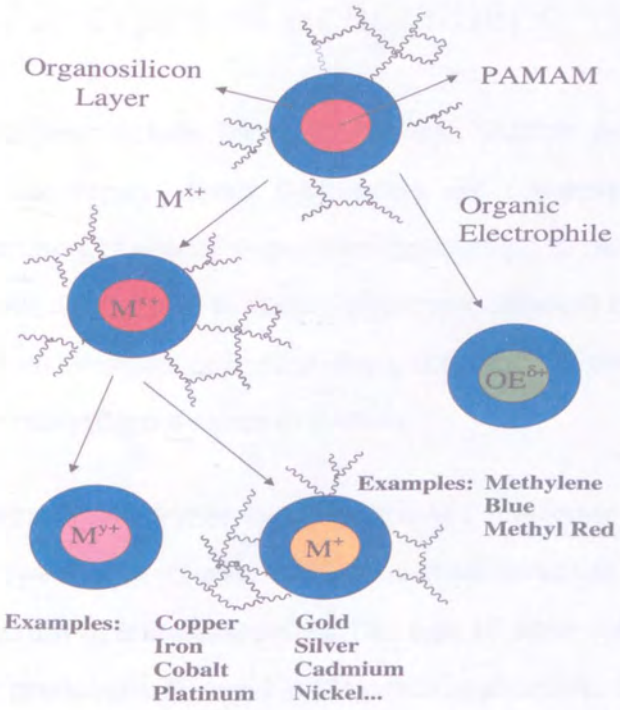


Figure 3.7 Schematic Representation of Complexation and Encapsulation of Guest Species in Nano-scaled PAMAM Domains of PAMAMOS Honeycomb-like Networks [Balogh].

The regularity of structure of PAMAMOS dendrimer networks and their ability to complex and encapsulate various guest species with nanoscopic topological precision provide unparalleled potentials for new applications in nano-lithography, electronics, photonics, chemical catalysis, etc [Dvornic,02].

3.4.4 Other types of Dendrimers

Other types of dendrimers include Tecto Dendrimers, Multiple Antigen Peptide Dendrimers and Fréchet-Type Dendrimers. Tecto Dendrimers are composed of a core dendrimer, surrounded by dendrimers of several steps (each type design) to perform a function necessary for a smart therapeutic nanodevice. In Tecto Dendrimers, different compounds perform varied functions ranging from diseased cell recognition, diagnosis of disease state drug delivery, reporting location to reporting outcomes of therapy.

Multiple Antigen Peptide Dendrimer is a dendron-like molecular construct based upon a polylysine skeleton. Lysine with its alkyl amino side-chain serves as a good monomer for the introduction of numerous of branching points. This type of dendrimer was introduced by J. P. Tam in 1988, and is predominantly used in biological applications, for example, vaccine and diagnostic research. Hawker and Fréchet developed the Fréchet-Type Dendrimer based on poly-benzyl ether hyper branched skeleton [Yiyun], [Hawker]. Usually, these dendrimers have carboxylic acid groups as surface groups, serving as a good anchoring point for further surface functionalisation, and as polar surface groups to increase the solubility of this hydrophobic dendrimer type in polar solvents or aqueous media.

3.5 Applications of Dendrimers

During November 1999, the journal *"Science and Technology"* released a report detailing some of the work that two universities in America were carrying out on the *use of dendrimers for targeted delivery of toxic drugs used in chemotherapy.*

They reported that:

"The drug is attached to the dendrimer via a cleavable linkage, solubilizing groups are added, and a chemical moiety capable of targeting the dendrimer to the target organ is attached" [Freemantel].

The results obtained from their studies confirmed that the straight chain dendrimers were non-toxic to the body, but branched chain dendrimers showed signs of toxicity. Also bio distribution studies were carried out in order to determine how well the drug could be eliminated by the body and in which regions it predominated. This was done using a dendrimer with radioactive iodine-125 attached to a phenolic core, and the results obtained showed that the dendrimer could be completely removed by the body [Freemantel].

Dendrimers are synthetic, highly branched, spherical, mono-disperse macromolecules of nanometre dimensions, prepared by the iterative synthetic methodology [Patri]. Many potential applications for dendrimers are based on their molecular uniformity, controllable 'surface' functionalities, the presence of internal cavities (or dendritic voids), their low polydispersity and their ability to mimic. These specific properties make dendrimers suitable for a variety of biomedical and industrial applications [Jansen] These include light harvesting and energy transfer, nanoscale catalysts, chemical sensors, the use of unimolecular micelles, enzyme mimics, the encapsulation of guest molecules, processes of biological recognition, gene and drug delivery and diagnostic agents [Liu].

3.5.1 Drug Delivery

A macromolecular drug-delivery system is a complex material in which a drug is attached to a carrier molecule. The absorption and distribution of the drug in such a system depend on the properties of the macromolecular carrier. Parameters such as site specificity, protection from degradation and minimization of side effects can be altered by modifying the properties of the carrier [Patri]. An ideal drug carrier must be biochemically inert and non-

toxic, while protecting the drug until it reaches the desired site of action, with the carrier then releasing the drug. Along with water solubility, dendrimers possess many of the above mentioned properties that make them attractive for biological and drug-delivery applications [Newkome], [Hawker].

3.5.2 Mechanisms of Drug Delivery

Dendrimers are particularly attractive as they offer a high drug-loading capacity. There are three major ways in which dendrimers can be used as potential drug delivery agents: (1) drug molecules can be physically entrapped inside the dendritic structure (encapsulation of drugs); (2) drug molecules can be covalently attached onto the surface, forming dendrimer-drug conjugates [Liu]; and (3) the dendrimer acts as a unimolecular micelle by encapsulation through the formation of a dendrimer-drug supramolecular assembly [Morgan], [Tekade].

3.5.3 Noncovalent Encapsulation of Drugs / Host –Guest Relation

The concept of encapsulating guest molecules into special, egg-shell-like structures was introduced by Maciejewski [Patel]. Encapsulation of drugs uses the bulk of the exterior of the dendrimer or interactions between the dendrimer and drug to trap the drug inside the dendrimer. Early studies of dendrimers as potential delivery systems focused on their use as unimolecular micelles and 'dendritic boxes' for the noncovalent encapsulation of drug molecules [Patel]. In these studies, DNA was complexed with PAMAM dendrimers for gene delivery applications, and hydrophobic drugs and dye molecules were incorporated into various dendrimer cores.

The use of dendritic unimolecular micelles rather than conventional polymeric micelles has the advantage of maintaining the micellar structure at all concentrations because the hydrophobic segments are covalently connected. In addition, the introduction of stabilizing PEO chains on the dendrimer periphery has broadened the scope of dendritic unimolecular micelles to incorporate anticancer drugs such as 5-fluorouracil methotrexate and doxorubicin. In this way, the drug release rates in these systems can be slowed down to some extent [Patel]. The use of hybrids of PEO and dendrimers with pH-sensitive hydrophobic acetyl groups on the dendrimer periphery presents a new approach to controlling the release of drugs from the encapsulating micellar compartment [Patel].

3.5.4 Covalent Dendrimer–Drug Conjugates

In dendrimer–drug conjugates, the drug is attached through a covalent bond either directly or via a linker/spacer to the surface groups of a dendrimer [Gillies]. Dendrimers have been conjugated to various biologically active molecules such as drugs, antibodies, sugar moieties and lipids. By altering the generation number of the dendrimer, the drug loading can be tuned. Also, the release of the drug can be controlled by incorporating degradable linkages between the drug and dendrimer. For example, aliphatic polyester dendrimers based on 2,2-bis(hydroxymethyl)propionic acid are promising dendrimer backbones for the development of anticancer drug conjugates [Gillies].

3.5.5 Dendrimers Drug Delivery: Targeted and Controlled Release Drug Delivery

Dendrimer drug molecules can be loaded both in the interior of the dendrimers as well as attached to the surface groups. Dendrimers can function as drug carriers either by encapsulating drugs within the dendritic structure, or by inter-acting with drugs at their terminal functional groups via electrostatic or covalent bonds (prodrug) (Figure 3.8). Perhaps polyamidoamine (PAMAM) dendrimers is the family of dendrimers most investigated for drug delivery [Patri]. PAMAM dendrimers are biocompatible, nonimmunogenic, water-soluble and possess terminal-modifiable amine functional groups for binding various targeting or guest molecules. The internal voids of PAMAM dendrimers can host metals or guest molecules as a result of its special functional architecture which contains tertiary amines and amide linkages [Patri].

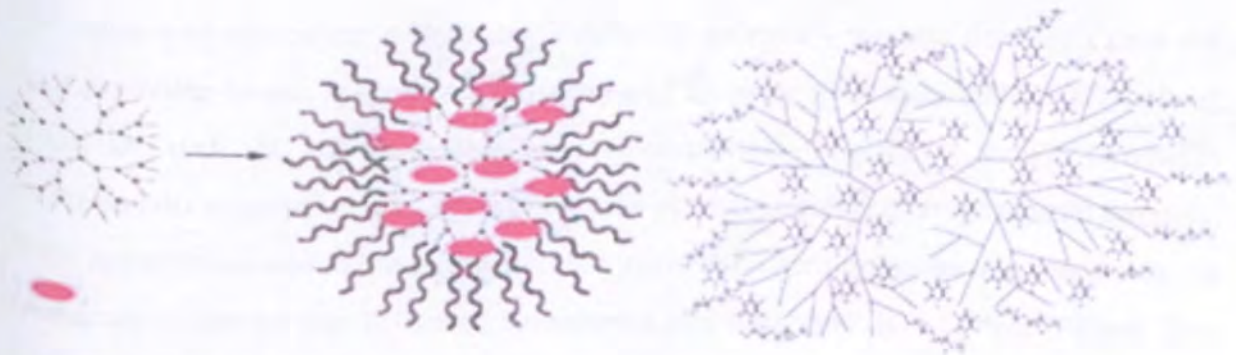


Figure 3.8 The Encapsulation of Anticancer Drugs Methotraxate (left) and 5-Fluorouracil (right) into PEGylated Generation 3 and 4 PAMAM Dendrimers [http://www.pharmainfo.net/reviews/dendrimer-overview]

Dendrimers have been tested in preclinical studies as contrast agents for magnetic resonance imaging (MRI), which is a diagnostic method producing images of organs and blood vessels. An early attempt to use dendrimers *in vivo* was efforts in the development of target-specific MRI contrast agents by Wiener *et al* [Wiener] These investigators produced gadolinium complexes of folate-conjugated PAMAM dendrimers for targeting tumour cells expressing high-affinity folate receptor (hFR). They demonstrated the specific targeting ability of folate-PAMAM dendrimers MRI contrast agents to ovarian tumour xenografts [Konda]. Due to the increased amount of gadolinium-ion delivery per receptor using the dendrimer complex, the investigators have shown a 33% increase in contrast enhancement compared with that of non-specific agent [Patri].

3.5.6 Delivery of Anticancer Drugs by Dendrimers and Dendritic Polymers

The delivery of anti-cancer drugs using a dendritic polymer - the star polymer - gave the most promising results regarding cytotoxicity and systemic circulatory half-life (72h). Drug properties such as solubility and plasma circulation time have shown significant improvements as polymeric carriers facilitate the passive targeting of drugs to solid tumours. These factors have lead to the selective accumulation of macromolecules in tumor tissue – a phenomenon termed the 'Enhanced Permeation and Retention' (EPR) effect [Gillies]. One example reported that the anticancer drug doxorubicin was covalently bound to this carrier via an acid-labile hydrazone linkage. Doxorubicin showed significant reductions in cytotoxicity (80–98%), and the drug was successfully taken up by several cancer cell lines.

3.5.7 Dendrimer as Solubility Enhancers

Some substances with high therapeutic activity have not been used for therapeutic purposes because they are not soluble in pharmaceutically accepted solvents. The use of dendrimers as drug carriers is a potential method for delivering these highly active pharmaceutical compounds that may not be in clinical use due to their limited water solubility. Hence, water soluble dendrimers are capable of binding and solubilizing small acidic hydrophobic molecules with antifungal or antibacterial properties. Dendrimers having a hydrophobic core and a hydrophilic surface layer, have been termed unimolecular micelles. Unlike traditional micelles, dendrimers do not have a critical micelle concentration. As a result, poorly soluble drugs are made soluble by encapsulating them within the dendritic structure. For example, a hydrophilic–hydrophobic core-shell dendrimer with PAMAM interior and long alkane chain exterior was shown to bind 5-flurouracil, a water-soluble anti-tumor drug [Gillies]. Again, the solubility of propranolol increased by over two orders of magnitude, when conjugated to surface-modified G3 PAMAM dendrimer. Thus, dendrimer nanocarriers offer the potential to enhance the bioavailability of drugs that are poorly soluble and/or substrates for efflux transporters [Mohammad].

3.5.8 Dendrimers as Nano-Drugs Delivery Systems

Dendrimers have been widely explored for controlled delivery of antiretroviral bioactives [Tathagata, 07]. The inherent antiretroviral activity of dendrimers enhances their efficacy as carriers for antiretroviral drugs [Tathagata, 08a], [Tathagata, 08b]. When poly (amidoamine) dendrimers (PAMAM dendrimers) are covalently modified with naphthyl sulfonate residues

on their surface, they exhibit antiviral activity against HIV by inhibiting early stage virus/cell adsorption and later stage viral replication. PAMAM dendrimers do this by interfering with reverse transcriptase and/or integrase enzyme activities.

Poly(lysine) dendrimers, modified with sulfonated naphthyl groups, seem to be useful as antiviral drugs against herpes simplex virus, and can reduce the transmission of HIV and other sexually transmitted diseases [Sonke]. Poly (propylene imine) dendrimers (PPI dendrimers) with tertiary alkyl ammonium groups attached to their surface have potent antibacterial effect against Gram positive and Gram negative bacteria.

Poly (lysine) dendrimers with mannosyl surface groups are promising antibacterial agents, as they inhibit the adhesion of E. coli to horse blood cells in haemagglutination assays. Chitosan–dendrimer hybrids seem to be useful as antibacterial agents, and as carriers in drug delivery systems.

3.5.9 Dendrimers in Gene Transfection

Dendrimers can act as vectors, in gene therapy. PAMAM dendrimers have been tested as genetic material carriers. In 1993, Haensler and Szoka published the first report of the use of PAMAM dendrimers for gene transfection [Haensler]. They discovered that PAMAM dendrimers mediated the high efficiency transfection of DNA into a variety of cultured mammalian cells and that the transfection was a function of both of the dendrimer-DNA ratio and the diameter of the dendrimers. Since then, numerous reports have been published describing the use of amino-terminated PAMAM or PPI dendrimers as non-viral gene transfer agents, enhancing the transfection of DNA by endocytosis and, ultimately, into the cell nucleus [Sonke]. A transfection reagent called SuperFectTM consisting of activated dendrimers is commercially available. Activated dendrimers can carry a larger amount of

genetic material than viruses. SuperFect–DNA complexes are characterized by high stability and provide more efficient transport of DNA into the nucleus than liposomes.

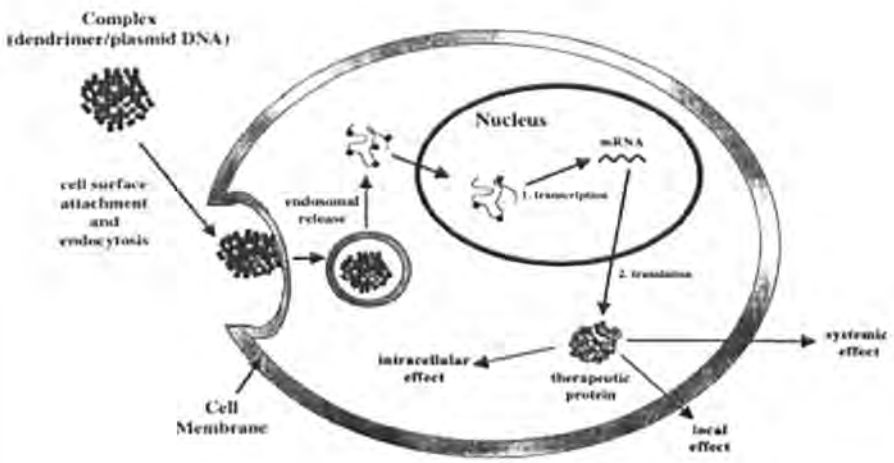


Figure 3.9 Dendrimer Involved in Gene Transfection [http://www.pharmainfo.net/reviews/dendrimer-overview]

It is clear that dendrimers have great potential for use as drug deliver agents. They provide a uniform platform for drug attachment that has the ability to bind and release drugs through several mechanisms. Furthermore, dendrimers can work as a useful tool for optimizing drug delivery for drugs with the problem of poor solubility, bioavailability and permeability. Although biocompatibility and toxicity problems may exist, this can be resolved by modification of the structure. Hence, in order for this technology to succeed in drug delivery, further work is needed to define the structure of the polymer and the relationship between the polymer and drug molecules. Again, recent breakthroughs in simplifying and optimizing the synthesis of dendrimers have been able to reduce cost of their production. In general, the future will witness newer applications of dendrimers as research progresses.

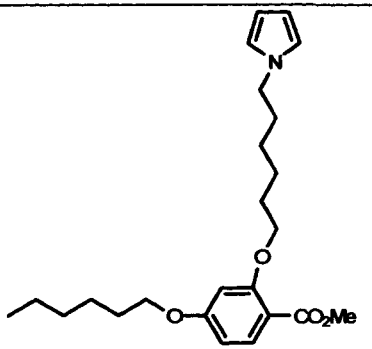
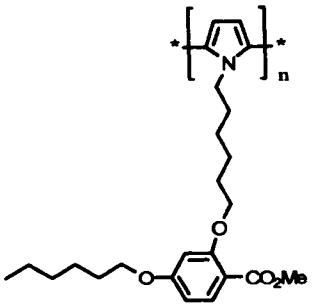
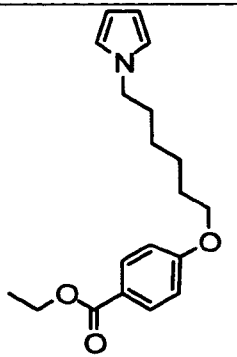
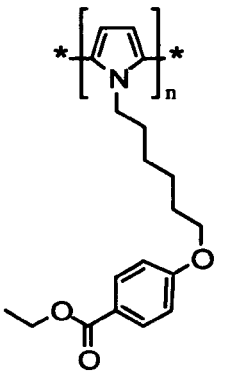
CHAPTER 4

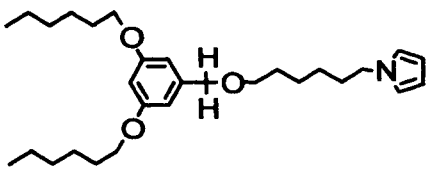
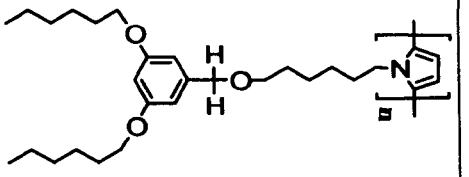
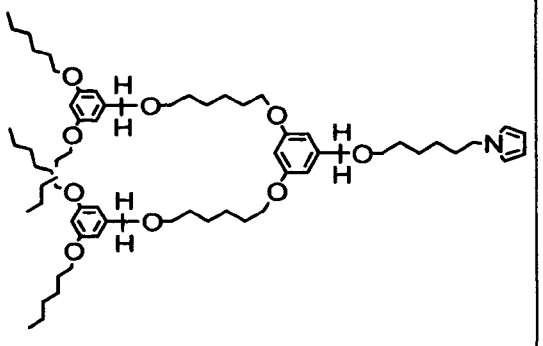
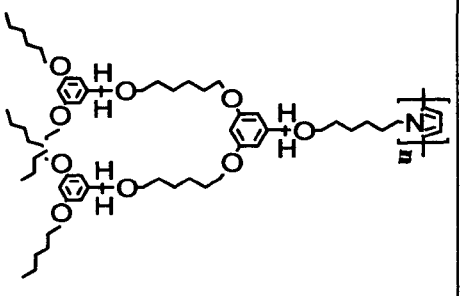
AIMS OF THE PROJECT

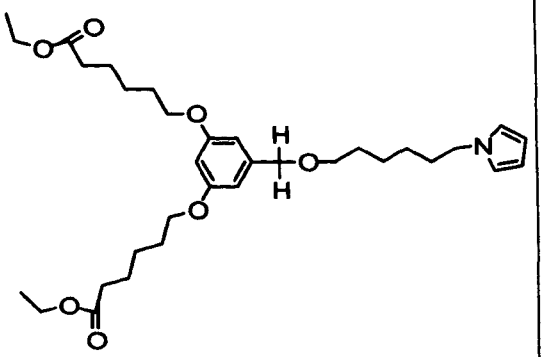
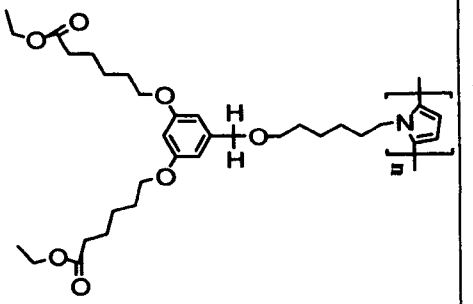
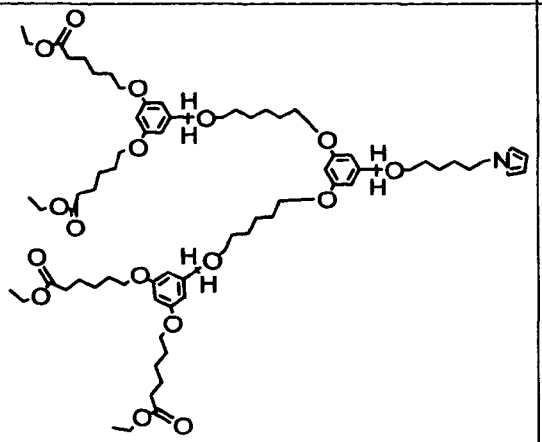
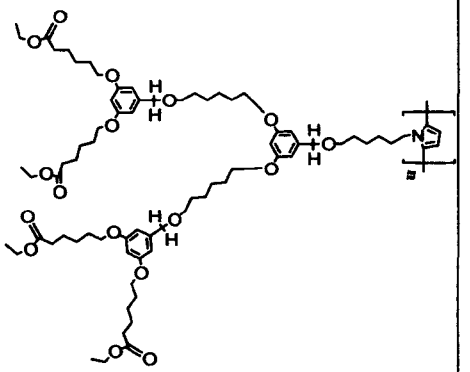
means of improving polymer properties, and providing novel applications. The synthesis of all three polymer sub-units into one system has never been embarked upon, and this project aims to investigate the potential of these novel hybrid polymers.

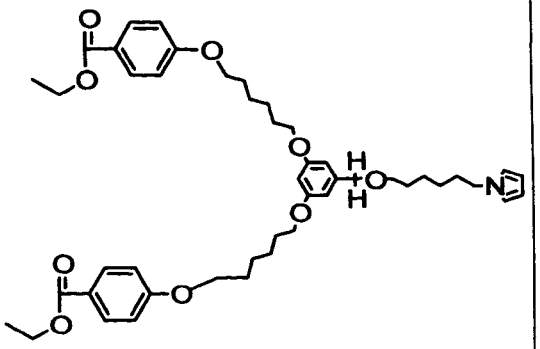
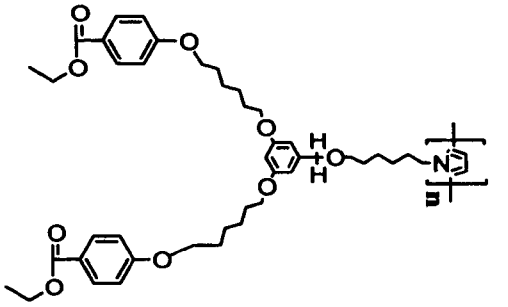
There were a total of 12 N-substituted pyrrole monomers synthesised, of which 9 were subsequently polymerised to yield N-substituted polypyrroles, with either liquid crystal or dendritic side groups.

Table 4.1 Final compounds synthesised in this project

Name of Monomer	*Structure of Monomer*	*Name of Polymer*	*Structure of Polymer*	*Additional Info*
Monomer (1) **IUPAC Name:** Methy2-(6-(1H-pyrrol-1-yl)hexyloxy)-4-(hexyloxy)benzoate	 **RMM = 401**	Polymer (1)		**Laterally attached** liquid crystal precursor ester group to be hydrolysed t o COOH after polymerisation (1a)
Monomer (2) **IUPAC Name:** Ethyl4-(6-(1H-pyrrol-1-yl)hexyloxy)benzoate	 **RMM = 315**	Polymer (2)		Same as no1**terminally Attached** ester Group to be hydrolysed to COOH after polymerisation(2a)

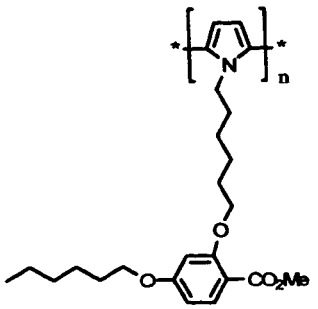
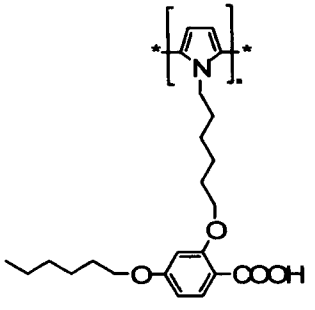
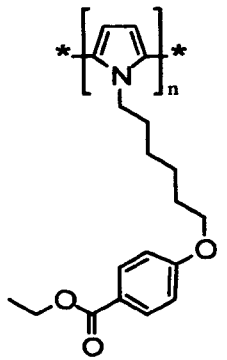
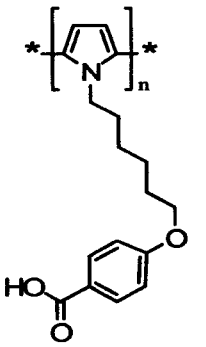
Monomer (3) **IUPAC Name:** 1-(6-(2-(3,5-bis(hexyloxy)phenyl) propan-2-yloxy)hexyl)-1H-pyrrole	 **RMM = 457**	Polymer (3)		First generation Dendron polymer
Monomer (4) **IUPAC Name:** 1-(6-(2-(3,5-bis(6-(2-(3,5-bis(hexyloxy)phenyl) propan-2-yloxy)hexyloxy)phenyl) propan-2-yloxy)hexyl)-1H-pyrrole	 **RMM = 1069**	Polymer (4)		2nd generation Dendron polymer

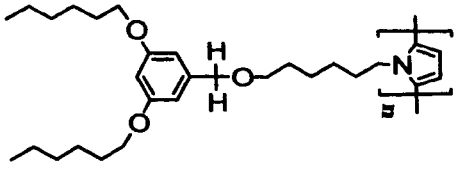
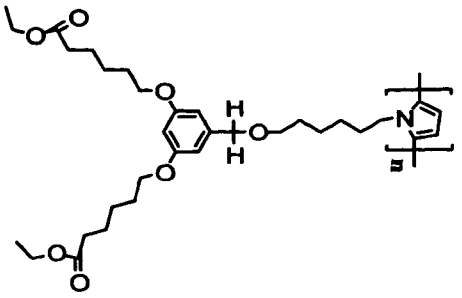
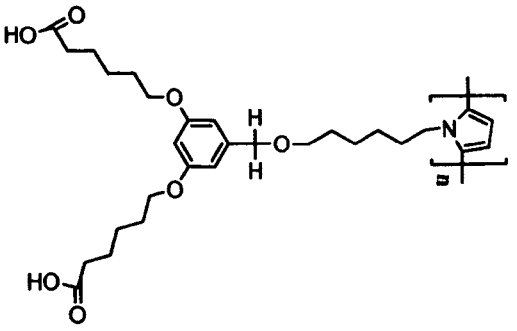
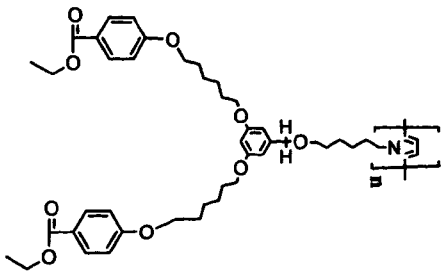
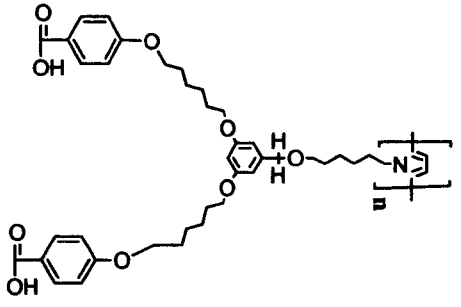
Monomer (5) **IUPAC Name:** diethyl 6,6'-(5-((6-(1H-pyrrol-1-yl)hexyloxy)methyl)-1,3-phenylene)bis(oxy)dihexanoate	 **RMM= 573**	Polymer (5)		**First generation** dendritic, precursor to hydrophilic terminal alkyl chain ester groups to be hydrolysed to COOH after polymerisation (5a)
Monomer (6) **IUPAC Name:** tetraethyl 6,6',6'',6'''-(5,5'-(6,6'-(5-((6-(1H-pyrrol-1-yl)hexyloxy)methyl)-1,3-phenylene)bis(oxy)bis(hexane-6,1-diyl))bis(oxy)bis(methylene)bis(benzene-5,3,1-triyl))tetrakis(oxy)tetrahexanoate	 **RMM = 1301**	Polymer (6)		**Second generation** dendritic, precursor to hydrophilic terminal alkyl chain ester group to be hydrolysed to COOH after polymerisation (6a)

Monomer (7)		Polymer (7)		2nd generation
IUPAC Name: diethyl 4,4'-(6,6'-(5-(2-(6-(1H-pyrrol-1-yl)hexyloxy)propan-2-yl)-1,3-phenylene)bis(oxy)bis(hexane-6,1-diyl))bis(oxy)dibenzoate	 **RMM = 785**			dendrimers with terminally attached LC precursor end groups ester group to be hydrolysed to COOH after polymerisation (7a)

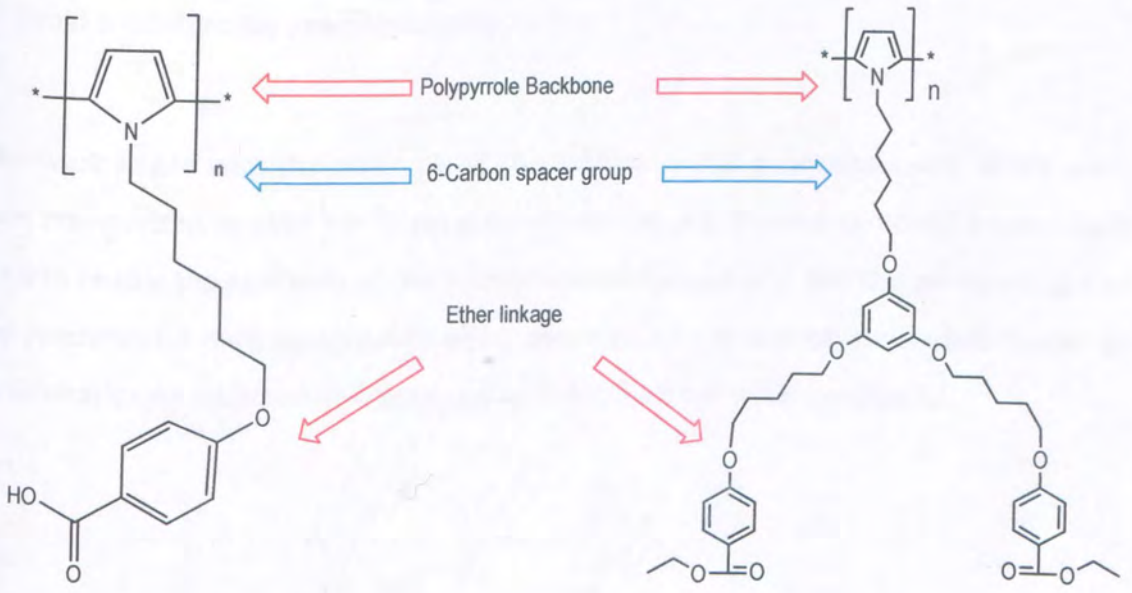
NB: Although only seven polymers are illustrated in table 4.1 above, polymers 1,2,5,& 7 were all hydrolysed to carboxylic acids groups, thus yielding four additional pyrrole polymers, namely 1a,2a,5a,&7a. Polymers 4 & 6 were insoluble so they could not be characterised further. Therefore the final 9 polymers to be discussed in this report are: 1 & 1a, 2 & 2a, 3, 5 & 5a and 7 & 7a. See table 4.2 below.

Table 4.2 Illustration of the final 9 polymers synthesised, characterised and measured in this project

Polymer	Corresponding Carboxylic Acid Polymer
(1) 	(1a) 
(2) 	(2a) 

(3) 	***No Corresponding carboxylic acid polymer**
(5) 	(5a) 
(7) 	(7a) 

The commonality in structure of each monomer and polymer, was an N-substituted pyrrole with a 6-carbon flexible spacer group attached to an aromatic ring via an ether linkage. The aromatic ring was substituted with either a liquid crystal side group laterally or terminally attached, or in some cases a dendritic side group that had potential liquid crystal properties.



Terminally attached liquid crystal precursor

Second generation dendrite with terminally attached liquid crystal precursor end groups

Figure 4.1 **General Structure of N-Substituted polypyrrole with liquid crystal and dendritic side groups**

From table 4.2 above, it can be seen that there were four different types of molecules synthesised:

1. Polypyrrole with terminally and laterally attached liquid crystal side groups (monomers/polymers 1 & 2)
2. Polypyrrole with first and second generation dendritic side groups, with alkyl chains (monomer/polymers 3 & 4)
3. Polypyrrole with first and second generation dendritic polymers with hydrophilic terminated alkyl chains (monomer/polymers 5 & 6)
4. Polypyrrole hybrid material, second generation dendritic polymer with terminal liquid crystal groups (monomer/polymer7)

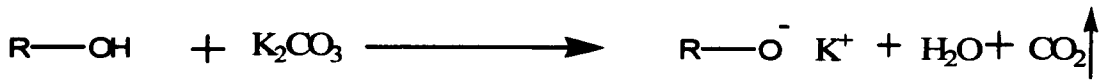
The work began with the synthesis of the monomer and precursor units, which were then polymerised to yield the novel polymer compound. Various synthetic routes were used to enable the synthesis of the monomers and precursors, and the primary stage of the synthesis for each compound began, with the attachment of the flexible spacer to an aromatic ring via an ether linkage, using the Wiliamson ether synthesis.

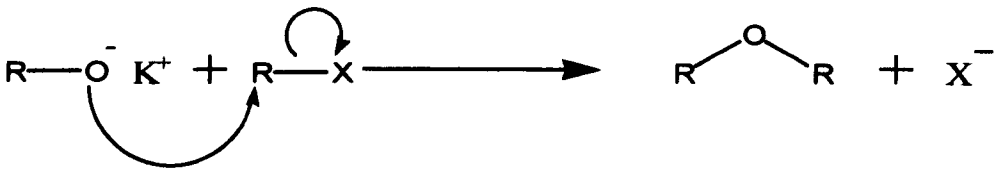
4.1 Williamson Ether Synthesis

Alkylation of the benzyl alcohols and phenols, are often carried out via Williamson Ether Synthesis. This reaction is widely used in both laboratory and industrial synthesis and remains the simplest and most popular method of preparing symmetrical and asymmetrical ethers.

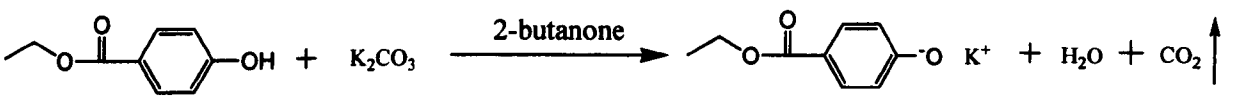
The primary step in the synthesis was the generation of the alkoxide ion by the use of anhydrous potassium carbonate in 2-butanone. This was then reacted with the alkyl halide (1,6-dibromohexane) to produce the ether.

4.2 General Procedure - Williamson Ether Synthesis

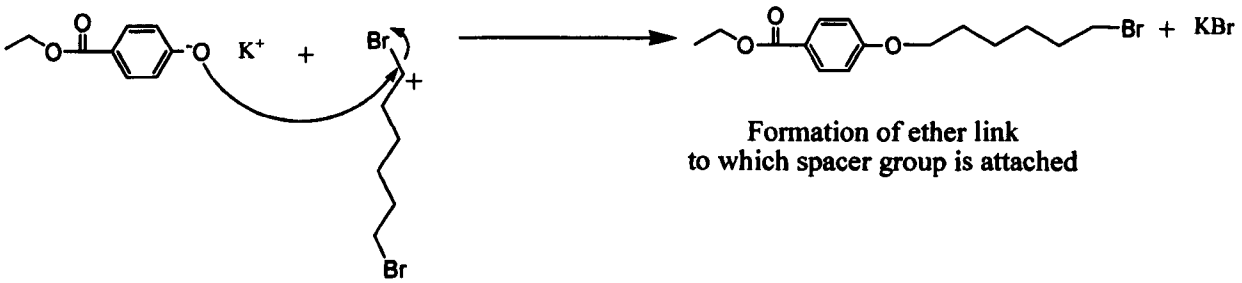
1. 

2. 

Primary stage of synthesis for each compound- Attachment of flexible spacer to aromatic ring via ether linkage. (Example given- Synthesis of Monomer 2)



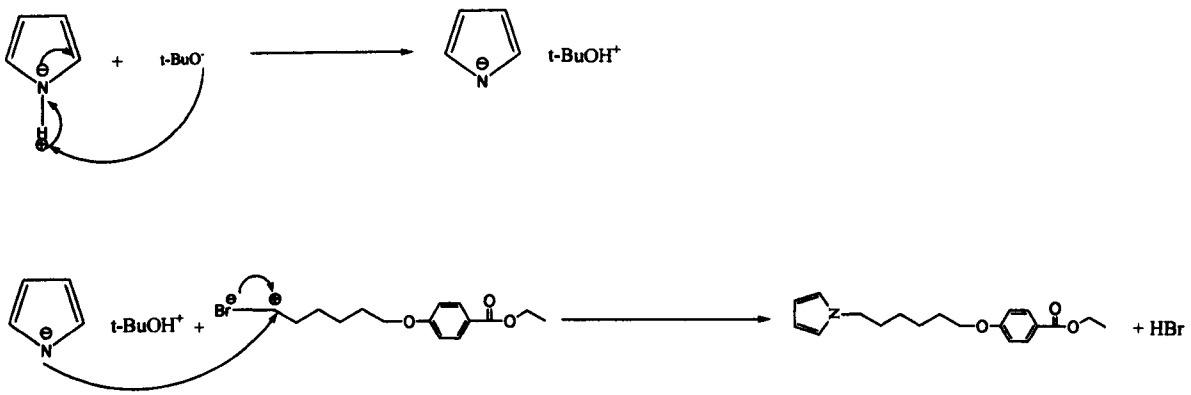
Phenoxide



Formation of ether link
to which spacer group is attached

A vast majority of Williamson synthesis proceeds via an S_N2 mechanism, and can therefore suffer from the associated steric constraints.

The second stage in the synthesis of each compound was the attachment of the flexible spacer to the pyrrole ring. Generally this step was carried out in the presence of 18-crown-6 and potassium *tert*-butoxide in ether. The reaction proceeds via an S_N2 type reaction, where pyrrole is deprotonated followed by the nucleophilic attack on the carbon atom in the alkyl chain.



Monomer (2)

Successful attachment of the spacer group to pyrrole was followed by polymerisation of the monomer compounds, via chemical and electrochemical methods, thus yielding the final polypyrrole materials.

As stated previously, the approach that has been outlined above, was the general procedure undertaken for the synthesis of all the polymers within this project. Each intermediate and monomer compound was characterised using techniques such as ^{1}H NMR, GC/MS, IR, and MS. Lastly physical measurements (conductivity measurements, SEM, hotstage microscopy, solubility testing and DSC) were carried out in order to deduce the general properties and possible applications of the novel polypyrrole materials synthesised in this project.

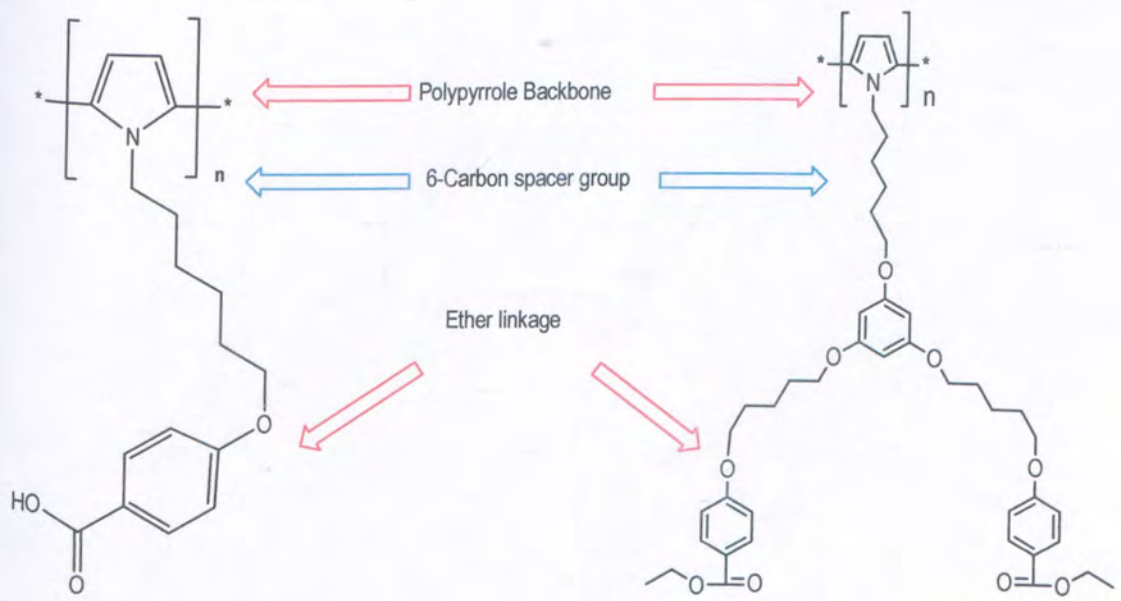
CHAPTER 5

RESULTS & DISCUSSION

CHAPTER 5: Results & Discussion

5.0 Introduction

This chapter will outline the results obtained from the experiments conducted and a discussion of any inferences that can be made, upon interpretation of the data. There were a total of 12 monomers synthesised, of which 9 were subsequently polymerised to yield N-substituted pyrrole polymers. The commonality in structure of each monomer was an N-substituted pyrrole, with a 6-carbon flexible spacer group attached to an aromatic ring via an ether linkage (Figure 5.1).



Terminally attached liquid crystal precursor

Second generation dendrite with terminally attached liquid crystal precursor end groups

Figure 5.1 **General Structure of N-substituted polypyrrole with liquid crystal and dendritic side groups**

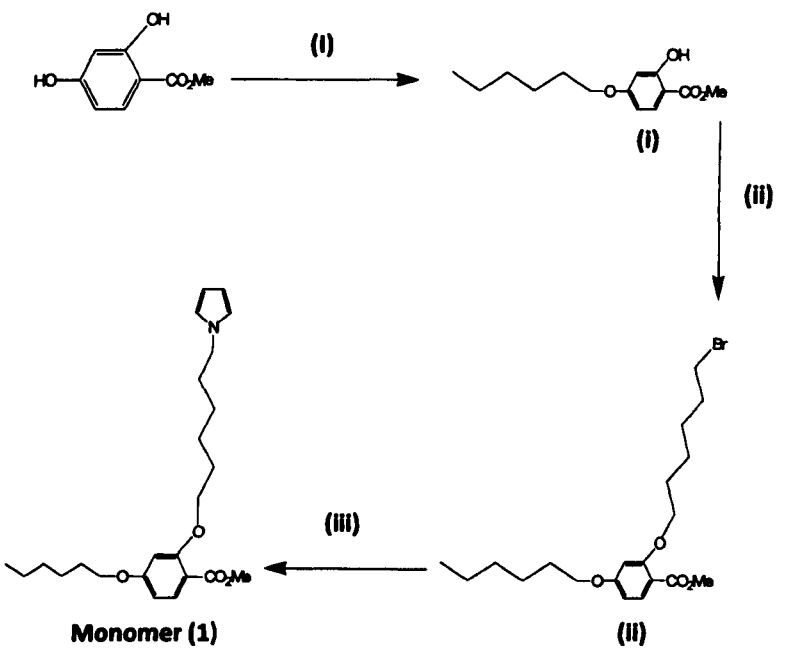
The spacer group was substituted with either a liquid crystal side group laterally or terminally attached, or in some cases a dendritic side group that had potential liquid crystal properties.

There were four different types of molecules synthesised:

1. Polypyrrole with laterally and terminally attached liquid crystal side groups (monomers/polymers 1, 2)
2. Polypyrrole with first and second generation dendritic side groups, with alkyl chains (monomer/polymers 3, 4)
3. Polypyrrole with first and second generation dendritic polymers with hydrophilic terminated alkyl chains (monomer/polymers 5, 6)
4. Polypyrrole hybrid material, second generation dendritic polymer with terminal liquid crystal groups (monomer/polymer 7)

5.1 Monomers with Laterally Attached Liquid Crystals

Reaction Scheme 1 -Synthesis of Methyl 2-(6-(1H-pyrrol-1-yl)hexyloxy)-4-(hexyloxy)benzoate Monomer (I)



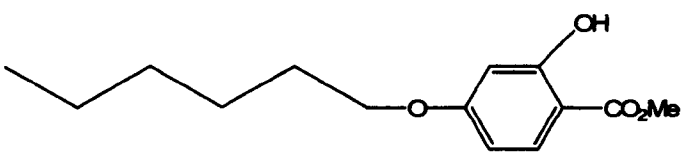
REAGENTS USED

(I) = 1-Bromohexane, anhydrous potassium carbonate, 2-butanone.

(ii) = 1,6-Dibromohexane, anhydrous potassium carbonate, 2-butanone.

(iii) = Anhydrous potassium *tert* butoxide, 18-crown-6, pyrrole, diethyl ether.

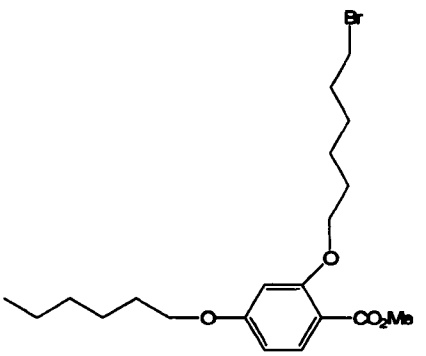
Using the strategy given in reaction scheme 1, methyl 2,4-dihydroxybenzoate was monoalkylated via the method developed by Gray *et al* [Gray], forming methyl 4-*n*-hexyloxy-2-hydroxybenzoate (1) This was carried out via Williamson ether synthesis, involving the treatment of methyl 2,4-dihydroxybenzoate with anhydrous potassium carbonate, to form an intermediate phenoxide ion, which then underwent nucleophilic attack on 1-bromo-hexane. The reaction proceeds via an S_N2 type mechanism, and although there were two possible sites for alkylation (C-2 and C-4), the most preferable position was C-4, as it can undergo facile attack from the nucleophile either above or below the plane, whereas C-2 is less favourable due to steric hindrance arising from intramolecular hydrogen bonding occurring between the OH and CO_2Me groups. The yield of the final product was 79% which improved by 18% on that of the reported work by Gray *et al*, in which the yield was documented as 61%.



(1)

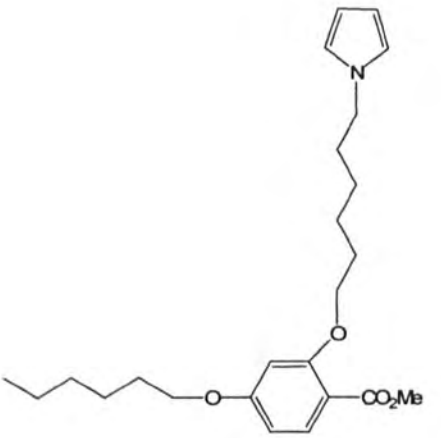
Upon extraction, purification and re-crystallisation of methyl 2-hydroxy-4-*n*-hexoxybenzoate (1), the second step was alkylation of the C-2 OH group. This proceeded by a very similar synthetic route as the first step; however the alkylation of C-2 took longer as it was harder to alkylate this position due to steric hindrance arising from intramolecular hydrogen bonding. In addition, as a large molar excess of 1,6-dibromohexane was required to ensure that the reaction would proceed efficiently, so one of the most time-consuming processes was the removal of this starting material. Due to its high boiling point of 243^0C, it proved quite difficult to remove. The first attempt to remove 1,6-dibromohexane was via column chromatography. Separation did occur but the yield of the product was very low, so it was decided that high vacuum distillation would be the best method of purification. Fortunately

this was an excellent way to separate the product from the starting material and a high yield of 74% was obtained. This step successfully produced a LC intermediate (2), with a 6-carbon spacer group suitable for attachment to pyrrole. Characterisations indicated that compound (2) had been successfully synthesised, and a slight shift in the carbonyl peak was observed in the IR spectrum of compound (2)



(2)

The final stage in the synthesis of monomer (1) involved the attachment of pyrrole by reacting pyrrole with 18-crown-6 and potassium *tert*-butoxide in ether over a period of 24 hours. Potassium *tert*-butoxide was used this time as it is a much stronger base than potassium carbonate, as 18-crown-6 chelates K^+ and increases the basicity of the anion (t-BuO^-). After collecting the crude product, extraction using DCM was carried out and TLC indicated that there were impurities arising from the starting material and side products. So the first attempt to purify monomer (1) was using column chromatography. Separation of the product from impurities did occur but the final yield was very low (45%). Therefore re-crystallisation using various solvents was attempted, but this was unsuccessful as the oily product would not come back out of the solution when cooled. It was therefore decided that although the amount of product yielded from purification using column chromatography was compromised, it was the best method for isolating the product from the impurities.



Monomer (1)

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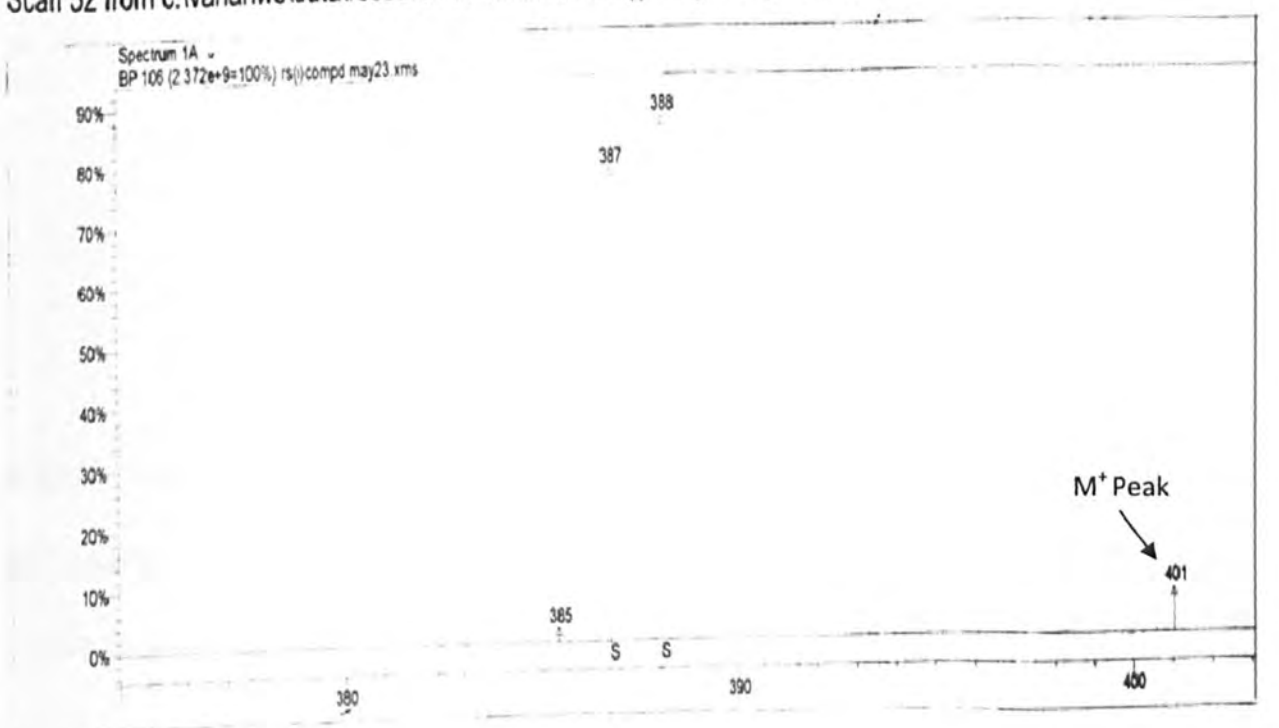
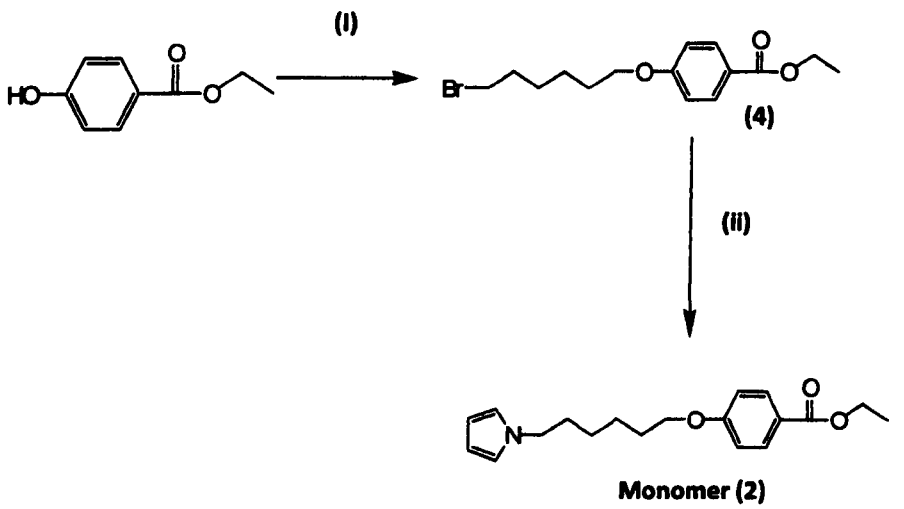


M^+ Peak = 401 indicating that Monomer (1) was successfully synthesised.

Figure 5.2 MS of Monomer (1)

5.2 Monomers with Terminally Attached Liquid Crystals

Reaction Scheme 2 - Synthetic route for the preparation of ethyl 4-(6-(1H-pyrrol-1-yl)hexyloxy)benzoate - Monomer (2)



Monomer (2)

REAGENTS USED

(I) = 1,6-dibromohexane, K_2CO_3, dry butanone

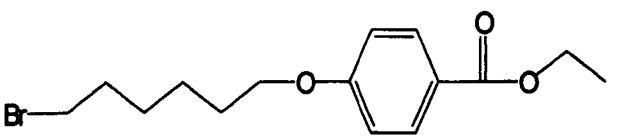
(ii) =18-Crown-6, DEE, potassium *tert*-butoxide, pyrrole.

The synthesis of ethyl 4-(6-(1H-pyrrol-1-y)hexyloxy)benzoate) (monomer 2) involved a two step reaction in which, firstly, ethyl 4-hydroxybenzoate was reacted with 1,6-

dibromohexane, 2-butanone, anhydrous potassium carbonate under reflux for approximately 48 hrs. Through the use of thin layer chromatography and GC/MS it was

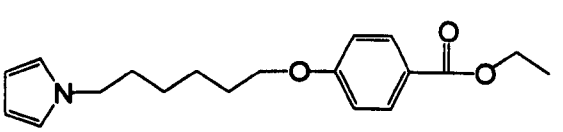
possible to determine the purity of the product and it became apparent that the main impurity was one of the starting materials, 1,6-dibromohexane.

Initial attempts to purify the crude product were carried out via re-crystallisation from IMS, however this proved to be unsuccessful as a large quantity of 1,6-dibromohexane remained. It was therefore necessary to remove the impurity using high vacuum distillation. This proved to be successful, and in terms of green chemistry it provided a useful method of recycling the starting material, which could be used in another reaction.

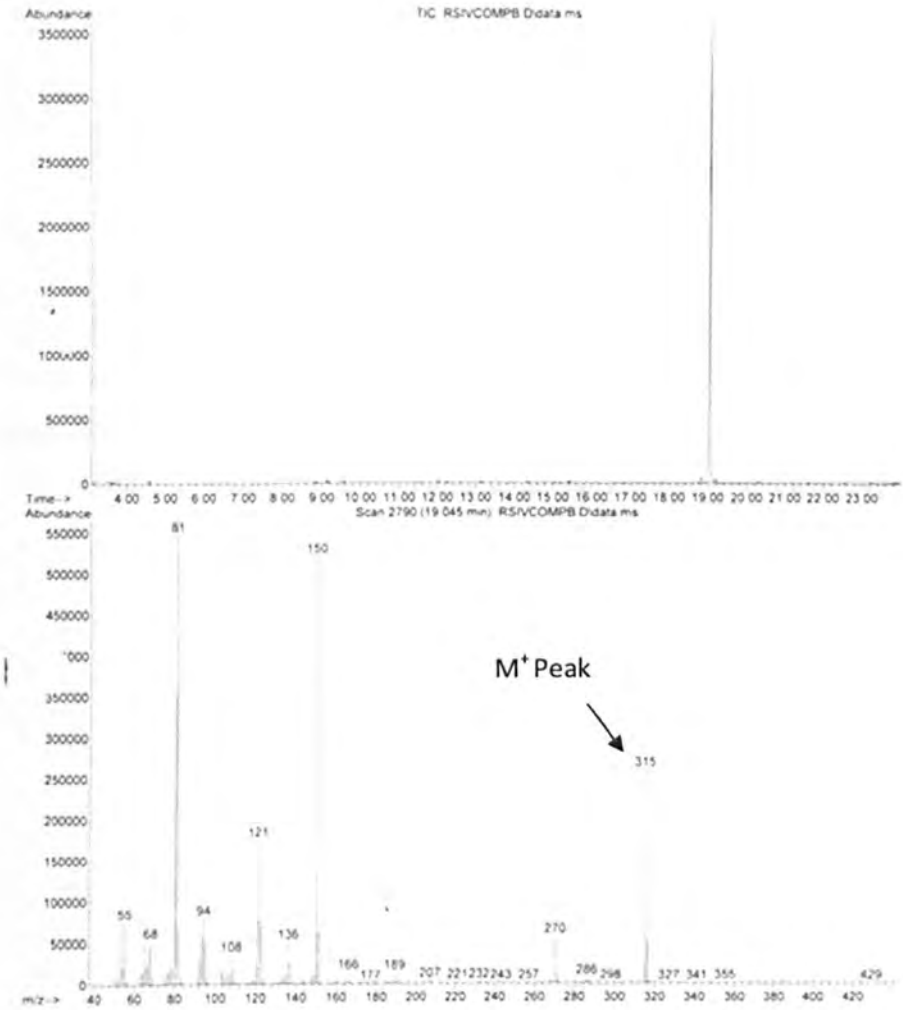


(4)

The second stage of the synthesis involved the attachment of pyrrole. This was carried out using the method outlined previously in which, 18-crown-6 and potassium *tert*-butoxide were dissolved in diethyl ether for 10-15 minutes before pyrrole was added in one portion to the reaction mixture. The end of the reaction was determined by TLC and the crude product was extracted using dichloromethane and purified using column chromatography. GC/MS and ^{1}H NMR determined that the compound (4) had been successfully synthesised and a high yield of 79% was obtained (see figure 5.3). Out of all of the reactions carried out in this project, the synthesis of monomer (2) was the easiest and least problematic as it had the advantage of only two steps, and the attachment of the terminal side group via nucleophilic substitution is more favourable than lateral attachment due to less steric hindrance arising from adjacent side groups.



Monomer (2)

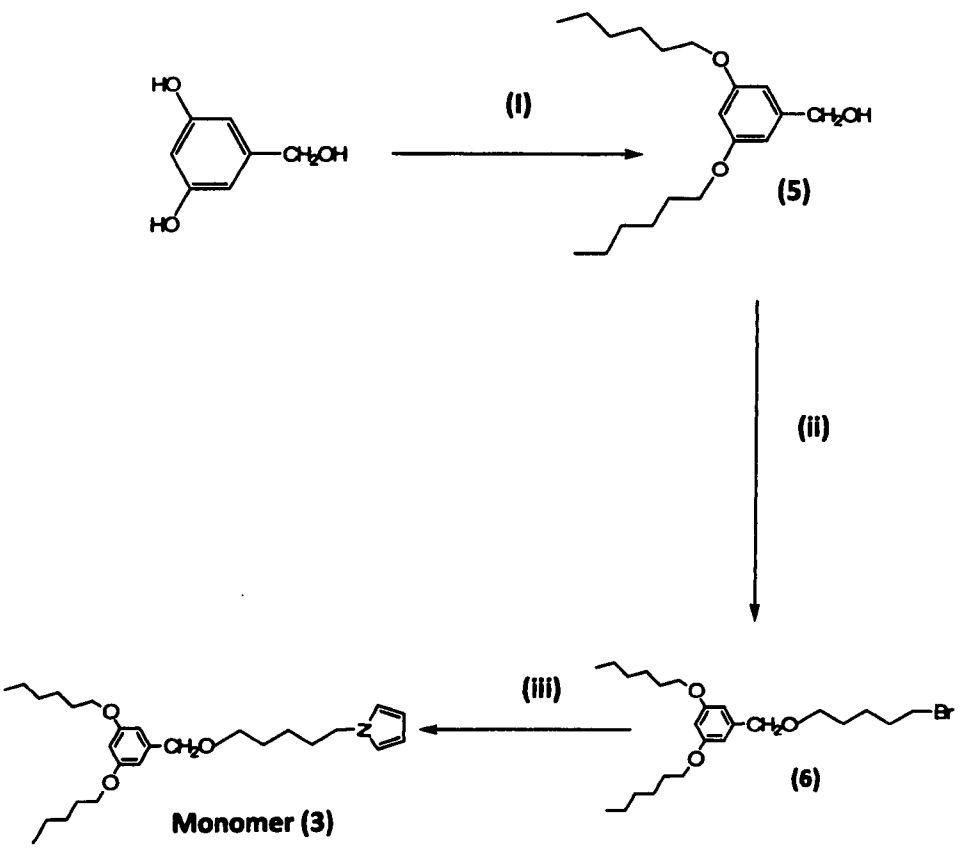


M^+ peak = 315 indicating that monomer (2) was successfully synthesised.

Figure 5.3 GC/MS of Monomer (2)

5.3 Monomers with First & Second Generation Dendrites, with Terminal Alkyl Chains

Reaction Scheme 3 – Synthesis of 1-(6-(3,5-bis(hexyloxy)benzyloxy)hexyl)-1H-pyrrole - Monomer (3)



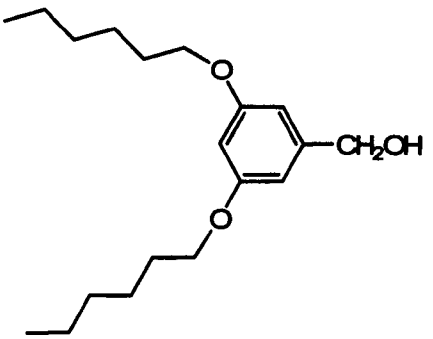
REAGENTS USED

(i)= Anhydrous potassium carbonate, 2-butanone, 1-bromohexane

(ii)=1,6-dibromohexane, potassium *tert*-butoxide, 18-crown-6, DEE

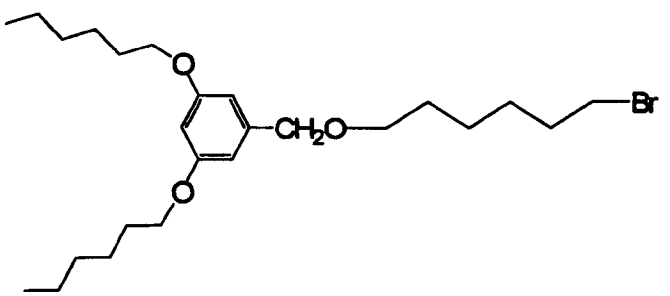
(iii)= Pyrrole, potassium *tert*-butoxide, 18-crown-6, DEE

1-(6-(3,5 bis(hexyloxy)benzyloxy)hexyl)-1H-pyrrole - Monomer (3), was the first dendritic polypyrrole monomer to be synthesised. Dendritic polymers increase in size, by adding branches of similar repeating units around a core. Each successive unit or "branching" is known as a generation and within this project we synthesised first and second generation dendrimers. Monomer (3) is an example of a first generation dendritic monomer. It was synthesised by alkylation of the starting material 3,5-dihydroxybenzyl alcohol. This was carried out by a Williamson ether synthesis in which the two hydroxyl groups were di-alkylated by nucleophilic attack from alkyl halide 1-bromohexane in the presence of anhydrous potassium carbonate and butanone. This reaction proceeded via an S_N2 type mechanism and there were no problems during the work-up of the reaction. Once the reaction had gone to completion, as determined by TLC, the crude product had to be purified as there was evidence of some of the starting material. It was decided that the first approach to separate the starting material from the product should be to carry out an extraction using diethyl ether and washing with water then the organic layer was collected, dried with $MgSO_4$ and the solvent was removed under reduced pressure. This proved to be a very effective way to separate the starting material from the product as characterisation tests indicated that the target compound had been successfully made without any impurities. The overall yield of the final product was 65%.



(5)

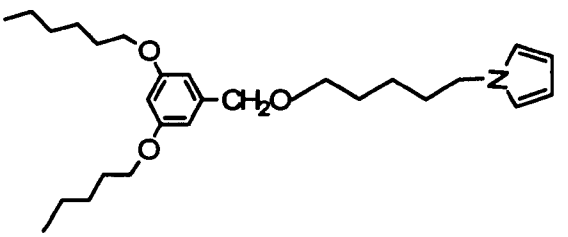
Having alkylated the two hydroxyl groups, the next stage was to alkylate the benzyl alcohol group. This was a straight forward reaction involving an S_N2 type mechanism in which the hydroxyl group was first deprotonated by potassium *tert*-butoxide, thus allowing the remaining oxygen anion to act as a nucleophile and attack the carbon atom of the alkyl halide to achieve substitution of the six carbon chain. From the results of the spectroscopic data, it was confirmed that the target compound had been synthesised, and purification of compound (6) was carried out by high vacuum distillation. (Kugelrohr 0.01mmHg/70^{0}C) was used to remove the excess of 1,6-dibromohexane. The final yield obtained was 61% and the product was a yellow oil.



(6)

The final stage in the synthesis of monomer (3) was the attachment of pyrrole. This was carried out using the previously mentioned method using pyrrole, potassium *tert*-butoxide and 18-crown-6, in diethyl ether. Purification of compound (6) was achieved by column

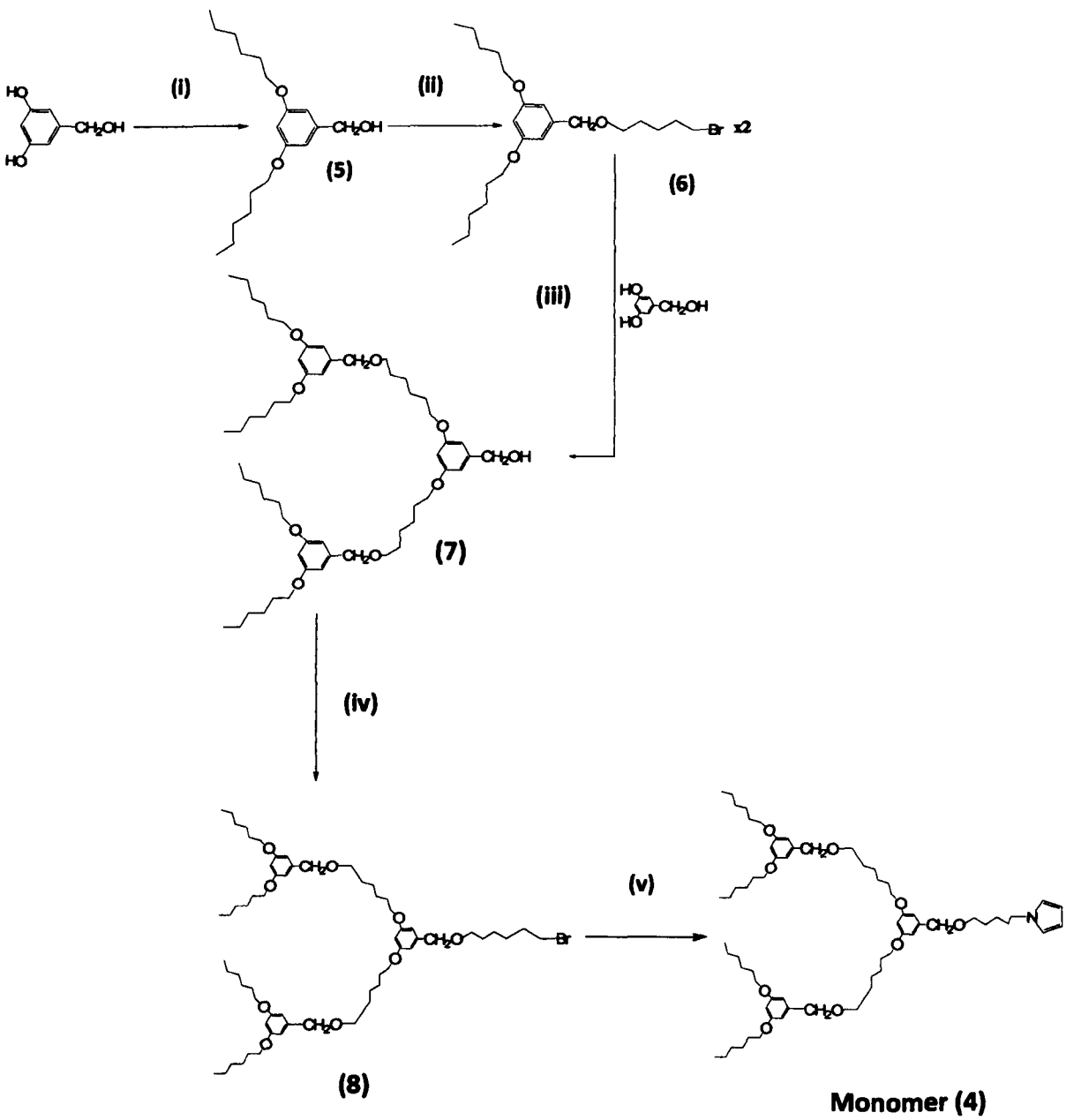
chromatography but the yield was relatively low as some of the product appeared to adhere to the stationary phase (silica gel) of the column. It was thought that the terminal alkyl chains may have had some weak interactions with one another, making the overall structure of the compound bulky and less mobile to travel down the column. The final yield of the monomer (3) was 34%, and was a light brown oil.



Monomer (3)

5.4 Monomers with First & Second Generation Dendrites, with Terminal Alkyl Chains

Reaction Scheme 4 -Synthesis of Monomer (4)



Reagents Used

(I) = 1-bromohexane, anhydrous potassium carbonate, 2-butanone.

(ii) =1,6-dibrohexane, potassium *tert*-butoxide, 18-crown-6, ether.

(iii) =Anhydrous potassium carbonate, 2-butanone

(iv) =1,6-dibromohexane, potassium *tert*-butoxide, 18-crown-6, DEE

(v) = Pyrrole, potassium *tert*-butoxide, 18-crown-6, DEE

Monomer (4) is structurally related to monomer (3) as they both have the same dendritic sub-units, but monomer (4) has one additional tier of branching, making it a second generation dendritic monomer. The relative molecular mass of monomer (4) is 1069, making it one of the largest monomers synthesised in this project. Due to its large size and structure, there were quite a few problems with the synthesis and purification. The above strategy was the first attempt at synthesising monomer (4), and it was carried out using a divergent method (See Figure 5.4), in which the molecule was assembled from the core to the periphery. Each step of the reaction must be driven to full completion to prevent defects in the dendrimer, which can cause trailing generations (some branches are shorter than the others). Such impurities can impact the functionality and symmetry of the dendrimer, but are extremely difficult to purify out because the relative size differences between perfect and imperfect dendrimers are very small.

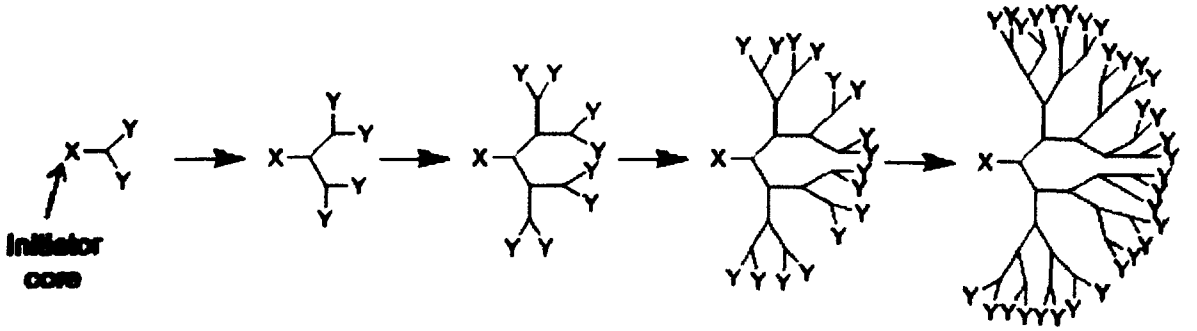


Figure 5.4 Schematic of divergent synthesis of dendrimers

[en.wikipedia.org]

Purification of compounds (7) and (8) proved to be quite challenging due to the size and bulkiness of the compounds and the structural similarity between the impurities and product added to the difficulty in separation. Purification by column chromatography took a long time and the yields of the final compounds were very low (22%, 17% respectively). Another disadvantage with this strategy was that purification of compound (8) had to be carried out via high vacuum distillation in order to remove the excess 1,6-dibromohexane. When the crude product (8) was subjected to this method of purification, great care had to be taken to ensure that firstly the vacuum system had no leaks as a higher temperature would be required to remove the 1,6-dibromohexane, and this in turn would cause the product to char. In addition the removal of the 1,6-dibromohexane took longer than usual, and it was proposed that this may have been due to slight attractive interactions occurring between the terminal alkyl chains of compound (8) and the alkyl chains of excess 1,6-dibromohexane. Also some of the 1,6-dibromohexane may have been trapped within the internal cavities or compound (7) and (8) as dendritic compounds of this structure, have the ability to temporarily host molecules via weak van der Waals interactions, leading to greater difficulty in removing the 1,6-dibromohexane. It was therefore decided that another

strategy would be used to synthesise monomer (4). Below is an alternative strategy for the synthesis of Monomer (4).

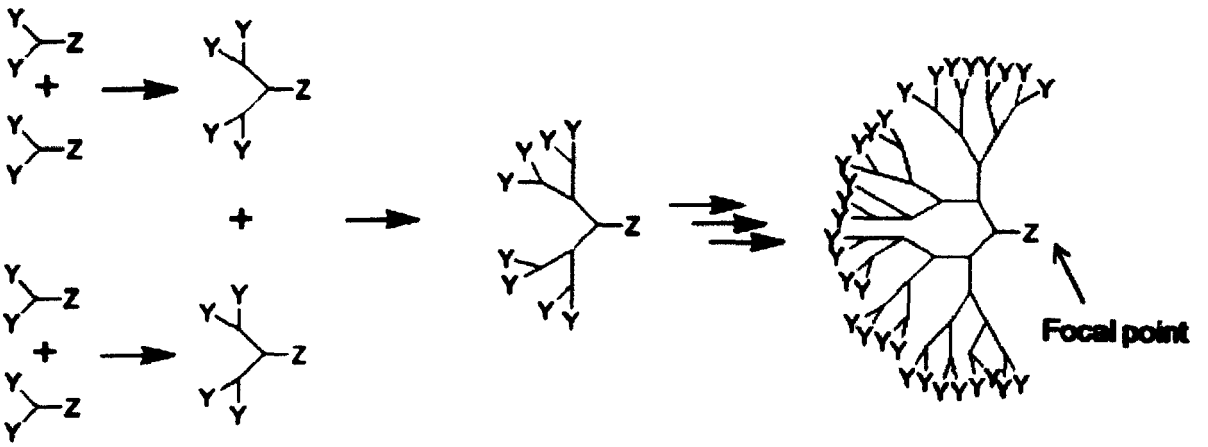
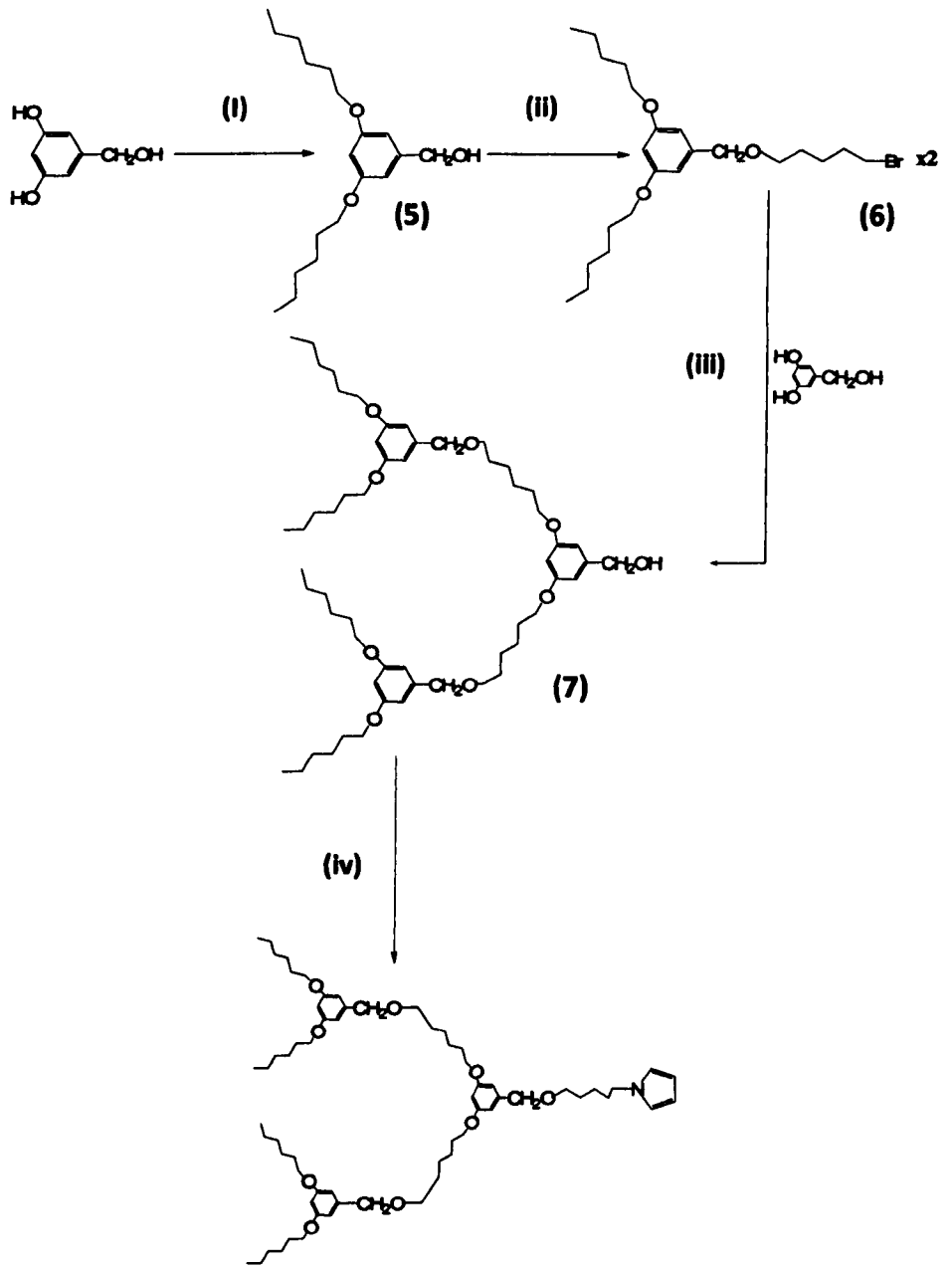


Figure 5.5 Schematic of convergent synthesis of dendrimers

[en.wikipedia.org]

5.5 Monomers with First & Second Generation Dendrites, with Terminal Alkyl Chains

Reaction Scheme (4a) - Alternative Route for synthesis of Monomer (4)



Monomer (4)

Reagents Used

(I) = 1-bromohexane, anhydrous potassium carbonate, 2-butanone.

(ii) =1,6-dibrohexane, potassium *tert*-butoxide, 18-crown-6, DEE.

(iii) =Anhydrous potassium carbonate, 2-butanone

(iv) =Compound (3), potassium *tert*-butoxide, 18-crown-6, DEE

The alternative route for the synthesis of monomer (4) involved the generation of the spacer group 1-(6-bromohexyl)-1H-pyrrole (3). This was achieved using the method outlined previously in reaction scheme 1B. Compound (3) was added to a reaction mixture of 18-crown-6, potassium *tert*-butoxide and compound (7) dissolved in ether. The reaction was left to proceed under gentle reflux for 24 hours. Upon completion of the reaction the reaction was quenched by the addition of water and usual methods of filtration, extraction and washing with a saturated solution of sodium chloride were followed. The product was purified by column chromatography and the final product was a light brown oil with a yield of 28%. Comparison of the TLC plates and GC/MS data for reaction schemes 4 and 4a, indicated that reaction scheme (4a) resulted in a product that had fewer impurities and a higher yield.

After several attempts of repeating the same experiment using the two methods, it was discovered that the attachment of the spacer group (3) via route (4a) took less time than the attachment of pyrrole in route (4). It was also noted that route (4a) yielded fewer impurities than route (4) and it was suggested that the two observations were related. One explanation for this could be due to the fact that with an increase in time and prolonged exposure to heat, the pyrrole monomers began to spontaneously crosslink, therefore producing several unwanted side products. This suggestion was supported by the evidence of black tarry material that remained on the column after washing several times when route (4) was used.

Monomer (4) was successfully synthesised via synthetic routes (4) and (4a); however synthetic route (4a) proved to be a better method of synthesising monomer (4) as the yield

improved by 17%, it took less time for attachment, and there were fewer impurities arising from route (4a) as indicated by TLC and GC/MS. The attachment of the spacer group (3) was incorporated into all of the synthetic routes (figure 5.6), and it was found that this provided a slightly quicker route for synthesis and increase in monomer productivity. In addition the reactions generally yielded fewer impurities when this method was used.

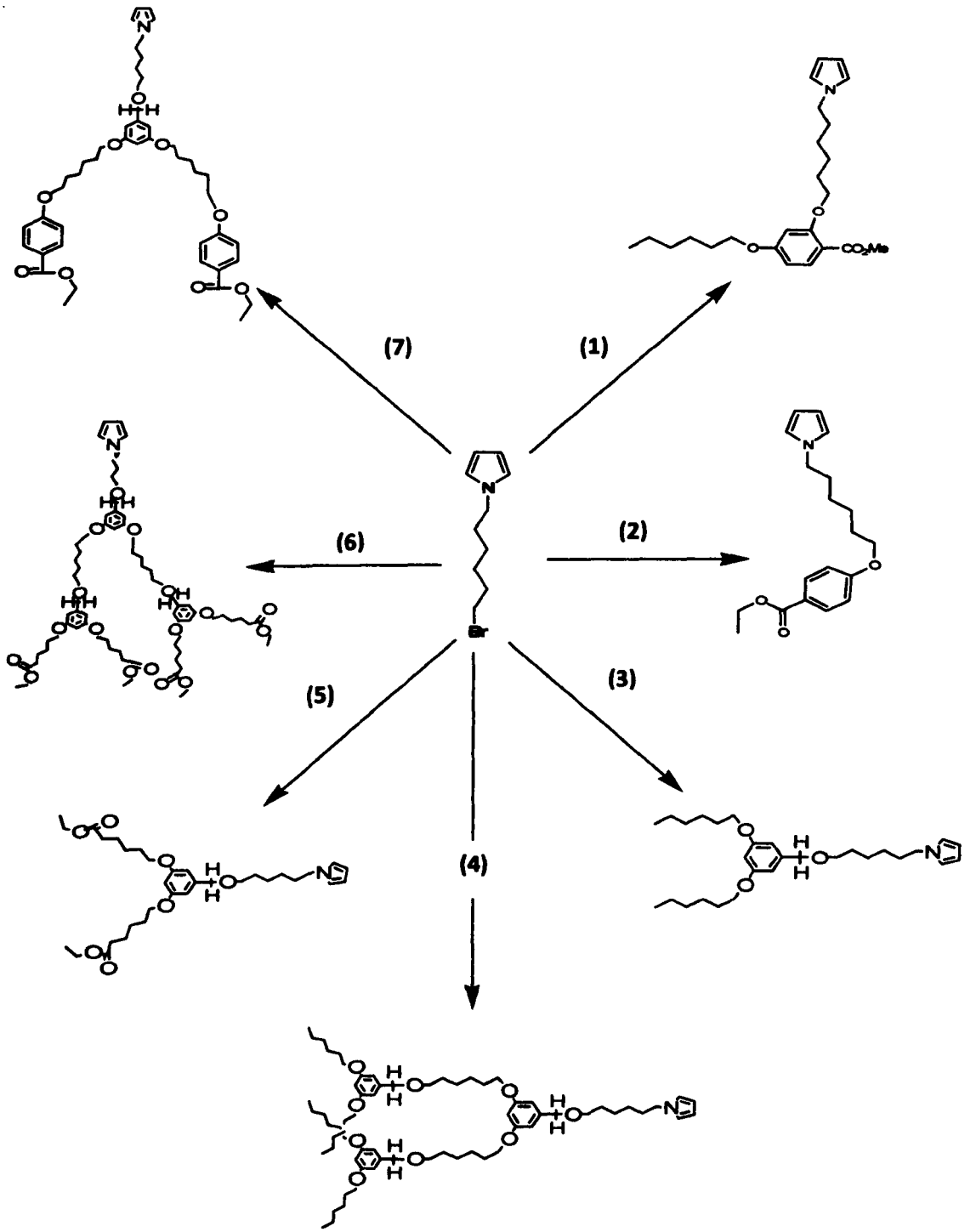
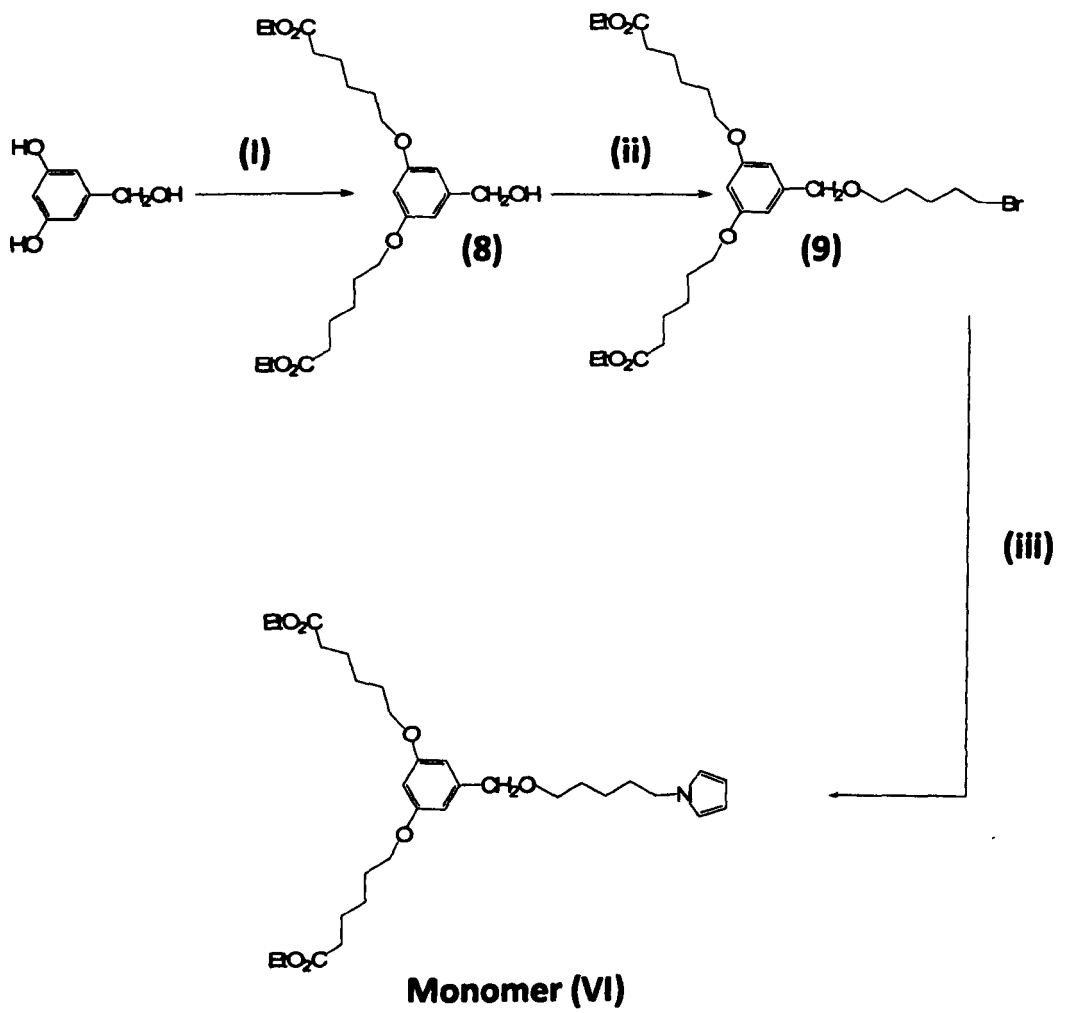


Figure 5.6 The incorporation of Spacer Group (3) into all Synthetic Routes

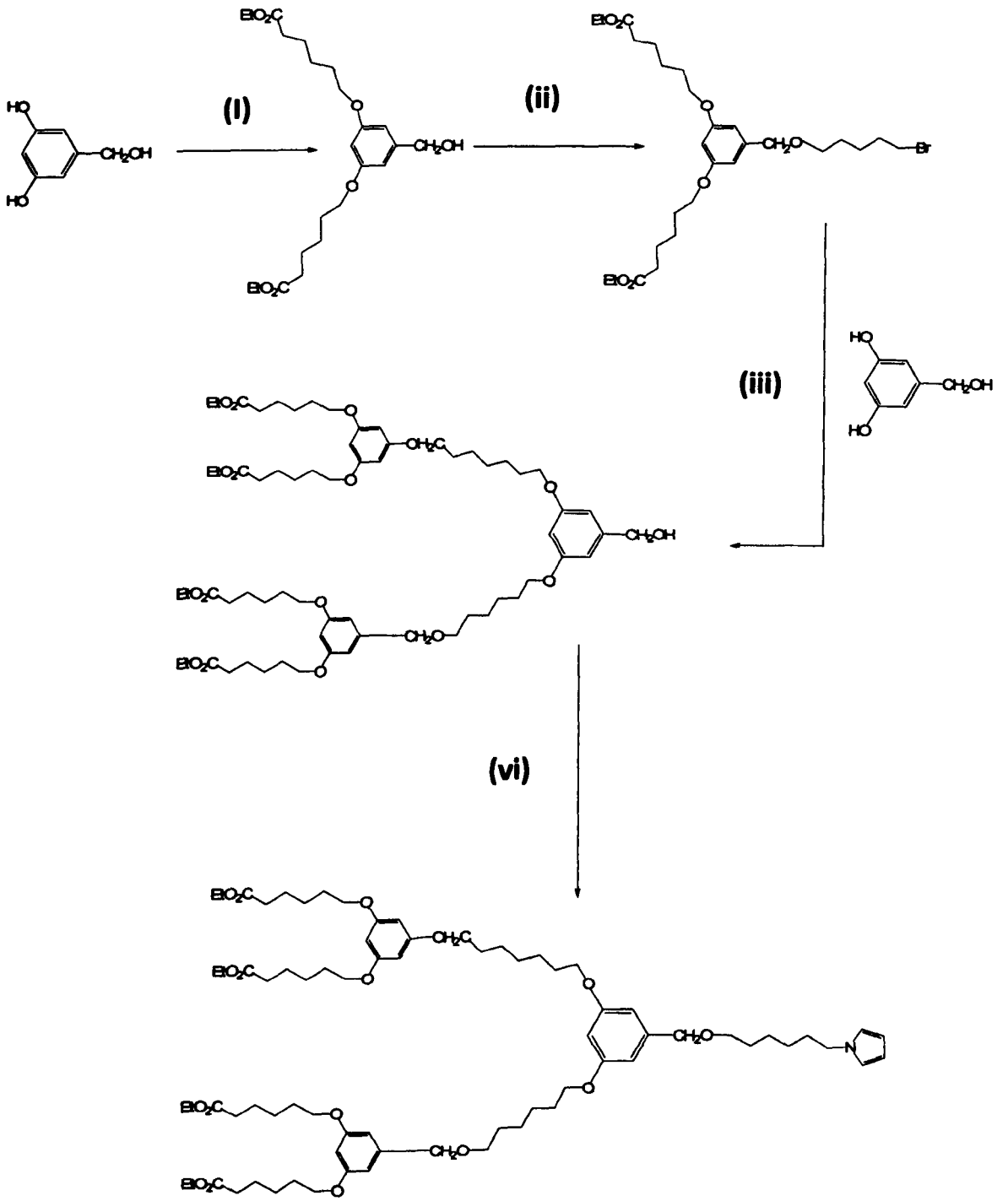
5.6 Monomers with First and Second Generation Dendrites with Potentially Hydrophilic Terminated Alkyl Chains

Reaction Scheme for the synthesis of Monomer 5



Reagents used in each step:
(I)= Anhydrous potassium carbonate, 2-butanone, ethyl-6-bromo-hexanoate.
(ii)= 1,6-Dibromohexane, 18-crown-6, potassium *tert*-butoxide, DEE.
(iii)= Pyrrole, 18-crown-6, potassium *tert*-butoxide, DEE.

Reaction Scheme for the synthesis of Monomer (6)



Reagents used

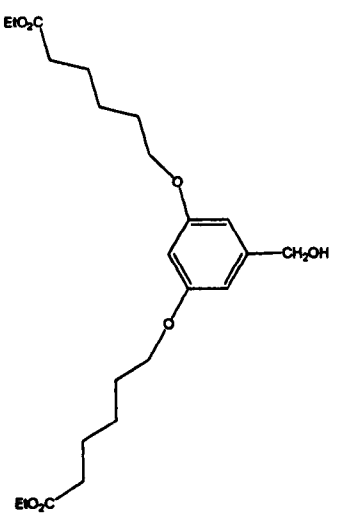
(i) = Ethyl 6-bromohexanoate, anhydrous potassium carbonate, 2-butanone

(ii) = 1,6-dibromohexane, 18-crown-6, potassium *tert*-butoxde, DEE

(iii) = 2x compound (9), anhydrous potassium carbonate, 2-butanone.

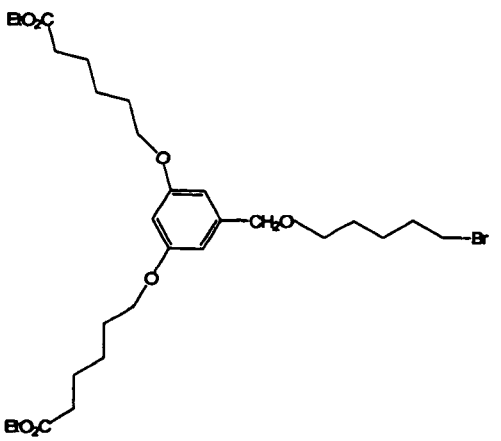
(iv) = Compond (3), 18-crown-6, potassium *tert*-butoxde, DEE

Monomers 5 & 6 are structurally related, as monomer (5) is a first generation dendrite with potentially hydrophilic terminal alkyl chains, while monomer (6) is a second generation dendrite with hydrophilic terminal alkyl chains. The synthesis of both monomers was quite labour intensive as they have relatively high molecular masses with large bulky side groups. The procedure involved a reaction with anhydrous potassium carbonate, dissolved in dry diethyl ether, 3,5-dihydroxy benzyl alcohol and ethyl 6-bromo-hexanoate. Successful completion of step (i) resulted in the synthesis of compound (8) which was characterised by IR, GC/MS and ^{1}H NMR. The product yield was very good (81%) and high vacuum distillation was used to remove the excess ethyl 6-bromohexanoate.



(8)

Step (ii) in the strategy used for the synthesis of monomers (5) and (6) was the same and proceeded via nucleophilic attack by the benzyl oxy-anion on the alkyl halide (1,6-dibromohexane). Alkylation of the hydroxyl group resulted in the formation of the hexyl spacer group, to which pyrrole was attached. Usual methods of high vacuum distillation were carried out to remove the excess 1,6-dibromohexane.



(9)

In the synthesis of monomer (6), Compound (9) became the "branching units" of the 2nd generation dendrite (see figure 5.7). In the next stage of the synthesis, 2 moles of compound (9) were attached to 1 mole of 3,5-dihydroxy benzyl alcohol via nucleophilic substitution. This reaction took a long time to go to completion, but this was expected due to the bulkiness of the side groups causing some degree of steric hindrance. In addition the overall yield was very low (31%), and the reaction had to be repeated several times in order to gain enough product to work up the third step.

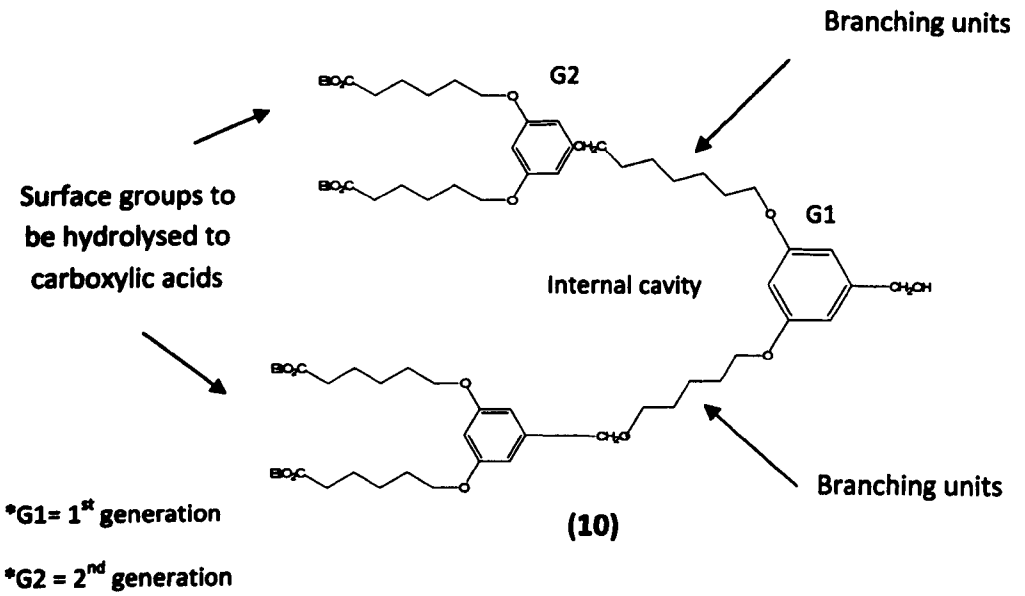
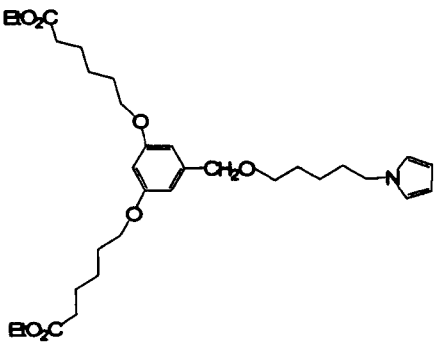


Figure 5.7 Structure of 2nd generation dendrite. Compound (10)

Figure 5.7 illustrates the structure of Compound (10) and highlights the main structural features that contribute to its dendritic architecture. Nucleophilic substitution at positions 3 and 5 of the benzyl alcohol resulted in the formation of 3 main features of the dendritic compound (10):

1) Branching units which radiate outwards from the benzyl alcohol core
2) Internal cavity – Potential ability to encapsulate host molecules
3) Ester surface groups which could potentially be modified to meet various functionalities.

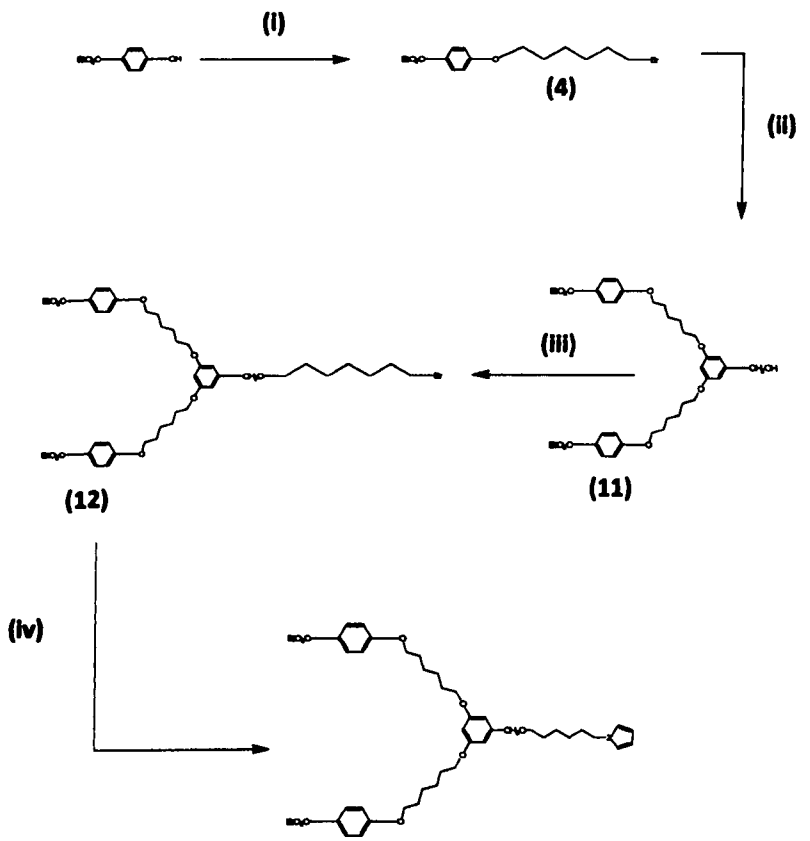
The final stage in the synthesis of monomer (5) was the attachment of pyrrole to the hexyl spacer group. The attachment was successful and proceeded without any major difficulties. Spectroscopic data confirmed that Monomer (5) had been synthesised.



Monomer (5)

5.7 Hybrid Monomers - Second Generation Dendritic Polymer with Terminal Mesogenic Groups

Reaction Scheme 7 - Synthetic route for the preparation of - Monomer (7)



Monomer (7)

REAGENTS:

STEP (i) = 1,6-Dibromohexane, anhydrous potassium carbonate, 2-butanone.

STEP (ii) = 3,5-Dihydroxy benzyl alcohol, anhydrous potassium carbonate, 2-butanone.

STEP (iii) = Potassium *tert* butoxide, 18-crown-6, DEE, 1,6-dibromohexane,

STEP (iv) = Potassium *tert* butoxide, 18-crown-6, DEE, 1,6-dibromohexane, pyrrole.

Using the strategy given in reaction scheme (7), ethyl 4-hydroxybenzoate was monoalkylated to form ethyl 4-(6-bromohexyloxy)benzoate compound (5). This alkylation involved a condensation reaction between the hydroxyl group of the ethyl 4-hydroxybenzoate and 1,6-dibromohexane. Following a review of previous work carried out, it was decided that alkylation of aromatic hydroxyl groups should be carried out in an excess of the alkyl halide, with temperatures above 100^{0}C. However the synthesis of compound (4) did not require such high temperatures, as only one hydroxyl group was present on the starting material and as it was *para*-positioned to the ester functional group. This also meant that neither of the functional groups would suffer from steric hindrance exerted by one another and the reaction could proceed easily at a lower temperature.

After 48 hours of refluxing, the crude product was poured into water and the usual method of filtration, extraction and solvent removal under reduced pressure was carried out. In order to purify the product, high vacuum distillation was used to remove the excess of 1,6-dibromohexane. As indicated by GC/MS and Infrared spectrometry, ethyl 4-(6-bromohexyloxy)benzoate compound (4) was successfully synthesised in a high yield (77%).

The synthesis of compound (11) was carried out by refluxing anhydrous potassium carbonate, compound (4) and 3,5-dihydroxybenzyl alcohol in dry butanone for 48 hours. It was decided that a ratio of 2:1 compound (4): 3,5-dihydroxybenzyl alcohol should be used as there were two hydroxyl groups involved in nucleophilic substitution. This stage of the synthesis was relatively straight forward. Although the progress of the reaction was followed using thin layer chromatography, it was important to determine by the use of qualitative analysis if compound (11) had been synthesised successfully. In most situations GC/MS was used to determine the molecular mass of the product; however the mass

spectrometry use in our department had a limitation of 500 m/z. An attempt was made to see how compound (11) would behave in the G.C column when subjected to varying temperatures over different time frames. It was found that the product fragmented severely and there was no sign of product elution from the column. This was expected, so it was decided that the best method of qualitative analysis would be the use of direct insertion mass spectrometry and the electrospray technique.

Direct insertion mass spectrometry (D.I.M.S) allows for qualitative and quantitative analysis of samples with minimal or no sample preparation. There are usually two types of probes used: Direct Insertion Probe (DIP) and Direct Exposure Probe (DEP). The DIP requires only a small amount of sample and it introduces the analyte directly into the ion source, overcoming the laborious task of determining what solvent(s) is required. Both solids and liquids can be analyzed, and the sample is placed into a flared glass vial and introduced directly into the GC source. The DEP has similar benefits to the DIP, as it allows direct analysis of a sample on the filament. Polar or thermally labile samples can be analysed without the use of gas chromatography so problems associated with sample fragmentation are overcome.

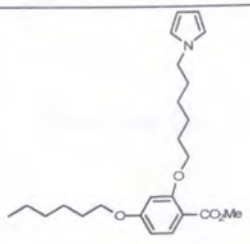
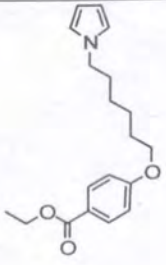
The results obtained from the direct insertion mass spectrometry indicated that the product had formed after 48 hours of refluxing. Thin layer chromatography and ^{1}H NMR were used to determine the purity of the crude product and it was found that the main impurity was arising from the starting material 3,5-dihydroxybenzoate and compound (5). Two extractions were carried out to remove the benzyl alcohol; diethyl ether : water and dichloromethane: water. Due to the presence of the hydroxyl groups on the benzyl alcohol, there was an affinity towards water, and so a more polar solvent such as DCM was used. Compound (11) was subject to column chromatography using a solvent mixture of hexane: ethyl acetate 95 : 5. The synthesis of compound (12) involved the mono-alkylation of the benzyl alcohol using 1,6-dibromohexane, 18-crown-6 and potassium tert-butoxide in diethyl ether. There were no major difficulties with this part of the synthesis, and purification of the crude product was carried out via high vacuum distillation. The final stage in the synthesis of monomer (7) was the attachment of pyrrole. This was carried out via the method outlined

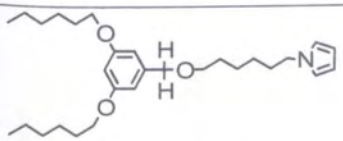
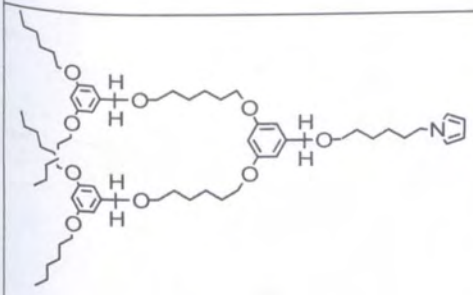
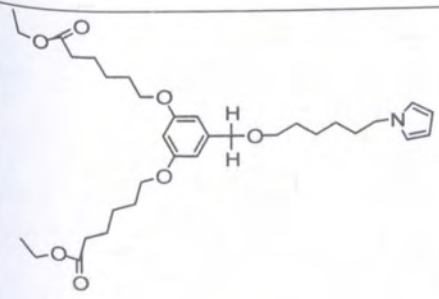
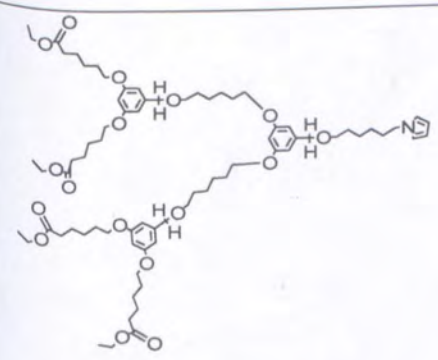
previously and the crude product was subjected to column chromatography using a 50:50 solvent mixture of hexane: ethyl acetate. Although the product was isolated from the starting materials, the final yield was quite low (49%) and it appeared that some of the monomer product may have adhered to the stationary phase of the column. In order to gain a substantial amount of monomer product for polymerisation, it was necessary to repeat the synthesis of monomer (7) several times; this was also the case for most of the monomers with a high relative molecular mass.

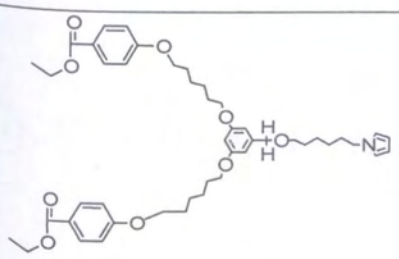
5.8 Mass Spectra for all Seven Monomers

Table 5.1 below illustrates the three mass spectrometry techniques that were used to identify qualitatively the mass of each monomer. The first technique applied was GC/MS; however this method was not suitable for all monomers as the GC/MS instruments had a mass detection limit of 500 m/z. Therefore direct insertion mass spectrometry DI/MS and electrospray were used in such cases as they had a mass detection limit of 1500m/z and 2000m/z respectively. It was only necessary for one of the spectroscopic techniques to accurately identify the mass of each monomer.

Table 5.1 Mass Spectrometry Techniques

Monomer	MS analysis		
	GC/MS	DI/MS	Electrospray
 Monomer (1)	✓ M^+ peak found 408	N/A	N/A
 Monomer (2)	✓ M^+ peak found	N/A	N/A

	315		
 Monomer (3)	✓ M+ peak found 457	N/A	N/A
 Monomer (4)	N/A	✓ M^+ peak found 1069	N/A
 Monomer (5)	N/A	✓ M^+ peak found 573	N/A
 Monomer (6)	N/A	N/A	✓ M^+ peak found 1301

 Monomer (7)	N/A	✓ M^+ peak found 785	N/A

5.9 ^{1}H NMR for all Seven Monomers

The ^{1}H NMR for all seven monomers are listed in Table 5.2 – 5.8 below. The peak integration, chemical shifts and peak assignments indicate that the monomers were successfully synthesised, with adequate purity before polymerisation.

Table 5.2 ^{1}H NMR of Monomer (1)

Chemical Shift (ppm) σ	Integral	Multiplicity	Assignment
8.6	1	Doublet	Aromatic H
7.0	1	Singlet	Aromatic H
6.4	1	Doublet	Aromatic H
6.2	2	Doublet,doublet	Aromatic H of pyrrole
5.7	2	Doublet	Aromatic H of pyrrole
4.1	2	Triplet	CH_2-N
3.9	2	Triplet	Ar-O-CH_2-C
3.7	2	Triplet	C-CH_2
3.5	2	Triplet	Ar-O-CH_2-C
3.3	3	Singlet	O-CH_3
1.9	7	Multiplet	C-CH_2-C-O
1.8	2	Multiplet	C-CH_2-C-O
1.5	6	Multiplet	C-CH_2-C
1.2	2	Quartet	CH_3-CH_2

Table 5.3 **^{1}H NMR of Monomer (2)**

Chemical Shift (ppm) σ	Integral	Multiplicity	Assignment
8.0	2	Doublet	Aromatic H
7.0	2	Doublet	Aromatic H
6.2	2	Doublet,Doublet	Aromatic H of pyrrole
5.7	2	Doublet	Aromatic H of pyrrole
4.2	4	Quartet	-CH_2-O (overlap with Ar-O-CH2)
3.7	2	Triplet	CH_2-N
1.9-1.5	4	Multiplet	-CH_2- CH_2- alkyl chain
1.5	4	Multiplet	-CH_2- CH_2- alkyl chain
1.2	3	Triplet	CH_3-CH_2

Table 5.4 **^{1}H NMR of Monomer (3)**

Chemical Shift (ppm) σ	Integral	Multiplicity	Assignment
7.0	2	Doublet,Doublet	Aromatic H of pyrrole
6.5	1	Triplet	Aromatic H
5.9	2	Doublet	Aromatic H
5.4	2	Doublet	Aromatic H of pyrrole

4.7	2	Singlet	Ar-CH_2-O
3.8	4	Triplet	Ar-O-CH_2 (Overlapping)
3.7	2	Triplet	N-CH_2
3.3	2	Triplet	Ar-O-CH_2
1.8-1.5	12	Multiplet	CH_2-alkyl
1.4-1.2	12	Multiplet	CH_2-alkyl
0.9	6	Triplet	CH_3- CH_2

Table 5.5 **^{1}H NMR of Monomer (4)**

Chemical Shift (ppm) σ	Integral	Multiplicity	Assignment
7.0	2	Doublet,Doublet	Aromatic H of pyrrole
6.5	3	Triplet	Aromatic H
5.9	6	Doublet	Aromatic H
5.4	2	Doublet	Aromatic H of pyrrole
4.8	10	Multiplet	Ar-O-CH_2
4.2	12	Triplet	O-CH_2
3.6	2	Triplet	N-CH_2-
3.0	2	Triplet	CH_2-O-
2.5-1.2	56	Multiplet	-CH_2-CH_2 alkyl chain
1.0	12	Triplet	CH_3-CH_2

Table 5.6 **^{1}H NMR of Monomer (5)**

Chemical Shift (ppm) σ	Integral	Multiplicity	Assignment
6.4	2	Doublet,doublet	Aromatic H of pyrrole
6.2	1	Triplet	Aromatic H
6.0	2	Doublet	Aromatic H
5.7	2	Doublet	Aromatic H of pyrrole
4.9	2	Triplet	Ar-CH_2-O
4.1	4	Quartet	CH_3-CH_2-O
3.8	4	Multiplet	Ar-O-CH_2
3.7	2	Triplet	N-CH_2
3.3	2	Triplet	Ar-CH_2-O
2.5	4	Triplet	CH_2-C=O
1.8	8	Multiplet	-CH_2-CH_2-alkyl chain
1.5	12	Multiplet	C-CH_2- CH_2-alkyl chain
1.3	6	Quartet	CH_3-CH_2

Table 5.7 **^{1}H NMR of Monomer (6)**

Chemical Shift (ppm) σ	Integral	Multiplicity	Assignment
6.4	2	Doublet,doublet	Aromatic H of pyrrole
6.2	3	Triplet	Aromatic H
6.0	6	Doublet	Aromatic H
5.7	2	Doublet	Aromatic H of pyrrole
4.9	6	Triplet	Ar-CH_2-O
4.1	20	Multiplet	CH_3-CH_2.O overlap with CH_2.O-CH_2
3.7	2	Triplet	-N-CH_2
3.2	6	Triplet	O-CH_2
2.5	8	Triplet	CH_2-C=O
1.8-1.5	20	Multiplet	-CH_2-CH_2-alkyl chain
1.4-1.2	28	Multiplet	C-CH_2- CH_2-alkyl chain
1.3	12	Quartet	CH_3-CH_2

Table 5.8 **^{1}H NMR of Monomer (7)**

Chemical Shift (ppm) σ	Integral	Multiplicity	Assignment
8.1	4	Triplet	Aromatic H
7.5	4	Triplet	Aromatic H

6.9	2	Doublet,doublet	Aromatic H of pyrrole
6.4	1	Triplet	Aromatic H
6.0	2	Doublet	Aromatic H
5.8	2	Doublet	Aromatic H of pyrrole
4.7	2	Triplet	Ar-CH_2-O
4.4	4	Quartet	CH_3-CH_2.O
4.0	8	Multiplet	Ar-O-CH_2
3.7	2	Triplet	N-CH_2
3.3	2	Triplet	-O-CH_2
1.8	12	Multiplet	-CH_2-CH_2-alkyl chain
1.5	12	Multiplet	C-CH_2- CH_2-alkyl chain
1.3	6	Quartet	CH_3-CH_2

5.10 Polymerisation of Monomer (1) & (2)

5.10.1 Cyclic Voltammetry

As monomers 1-7 were successfully synthesised, (indicated by mass spectroscopy, IR, and ^1H NMR), the next step was to find a suitable method of polymerisation. Both electrochemical and chemical methods were employed, but generally it was found that chemical polymerisation yielded a larger amount of polymer product, which could be subsequently characterised more easily and the polymer properties were investigated in greater detail. Of the two polymerisation methods, cyclic voltammetry was conducted first. The CV's of polymers (1) and (2) are shown below. No other monomers were polymerised via electrochemical methods, as the polymer films were too thin for analysis.

Cyclic voltammetry is the most widely used technique for acquiring qualitative information about electrochemical reactions. It offers a rapid location of *redox potentials* of the electroactive species [Allen]. During cyclic voltammetric experiments, the electroactive species depleted by the electrode reaction are replenished by diffusion from the solution bulk to the surface of the electrodes prior to the electron transfer reaction. Any soluble products then diffuse back into the bulk solution when the reaction is complete. This movement at the electrodes dictates the shape of the cyclic voltammogram produced.

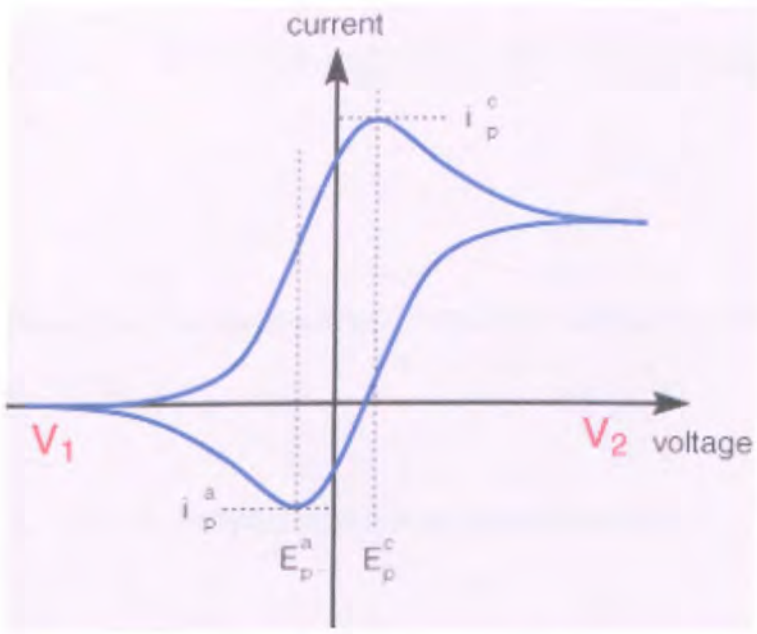


Figure 5.8 Current as a function of working electrode potential for CV

The voltage is swept between two pre-determined values (see Figure 5.8 above) at a fixed rate; however when the voltage reaches V_2 the scan is reversed and the voltage is swept back to V_1. The scan begins from the left hand side of the current/voltage plot where no current flows. A current begins to flow as the voltage is swept further to the right (to more oxidising values), and eventually reaches a peak before dropping. To rationalise this behaviour we need to consider the influence of voltage on the equilibrium established at the electrode surface. Here the rate of electron transfer is fast in comparison to the voltage sweep rate. Therefore at the electrode surface an equilibrium is established close to that predicted by thermodynamics [Allen]. As the voltage is initially swept from V_1 the equilibrium at the surface begins to alter and a current begins to flow. The current rises as the voltage is swept further from its initial value as the equilibrium position is shifted further to the right hand side, thus converting more reactant to product. The peak occurs, since at some point the diffusion layer has grown sufficiently above the electrode so that the flux of reactant to the electrode is not fast enough and the current begins to drop [Allen].

5.11 Cyclic Voltammograms for Polymers (1) & (3)

Polymer (1) - poly-(N-pyrrole)-6-(methyl 4-n-hexyloxy-2-oxybenzoate)hexane

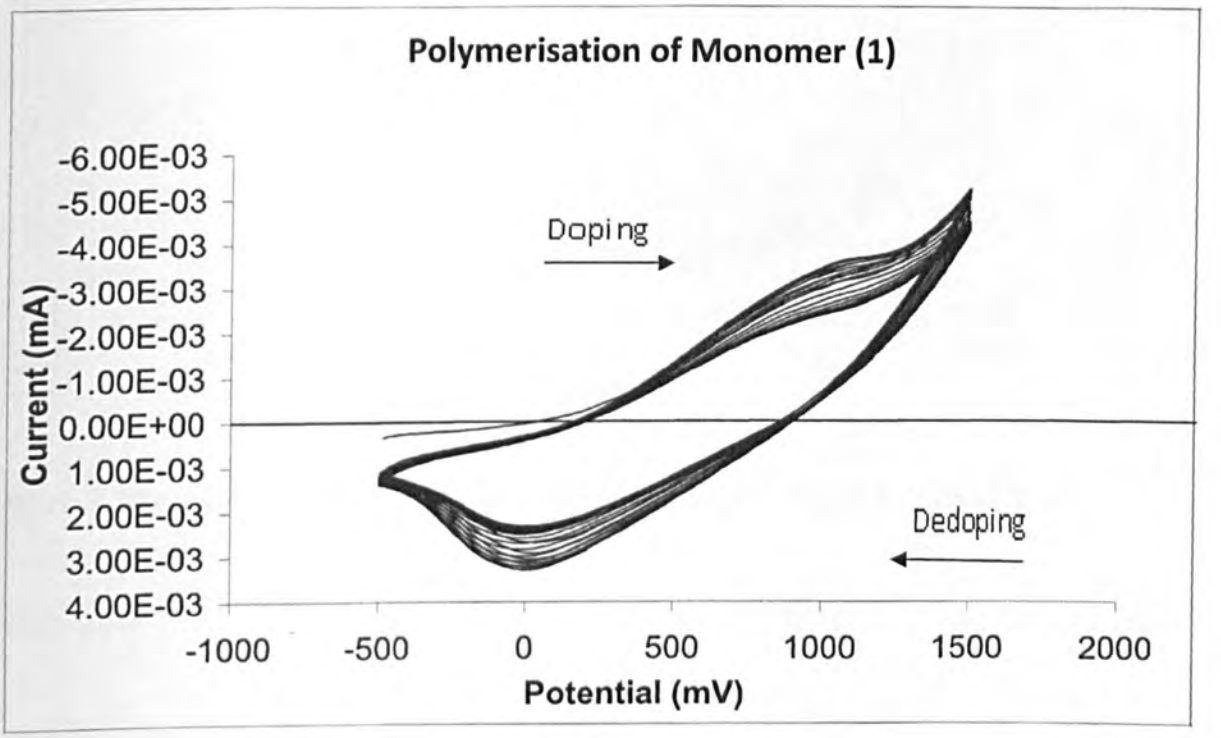


Figure 5.9 **Formation of Polymer (1) – CV of *(N-pyrrole)-6-(methyl 4-n-hexyloxy-2-oxybenzoate)hexane.* TBATFB in *propylene carbonate.***

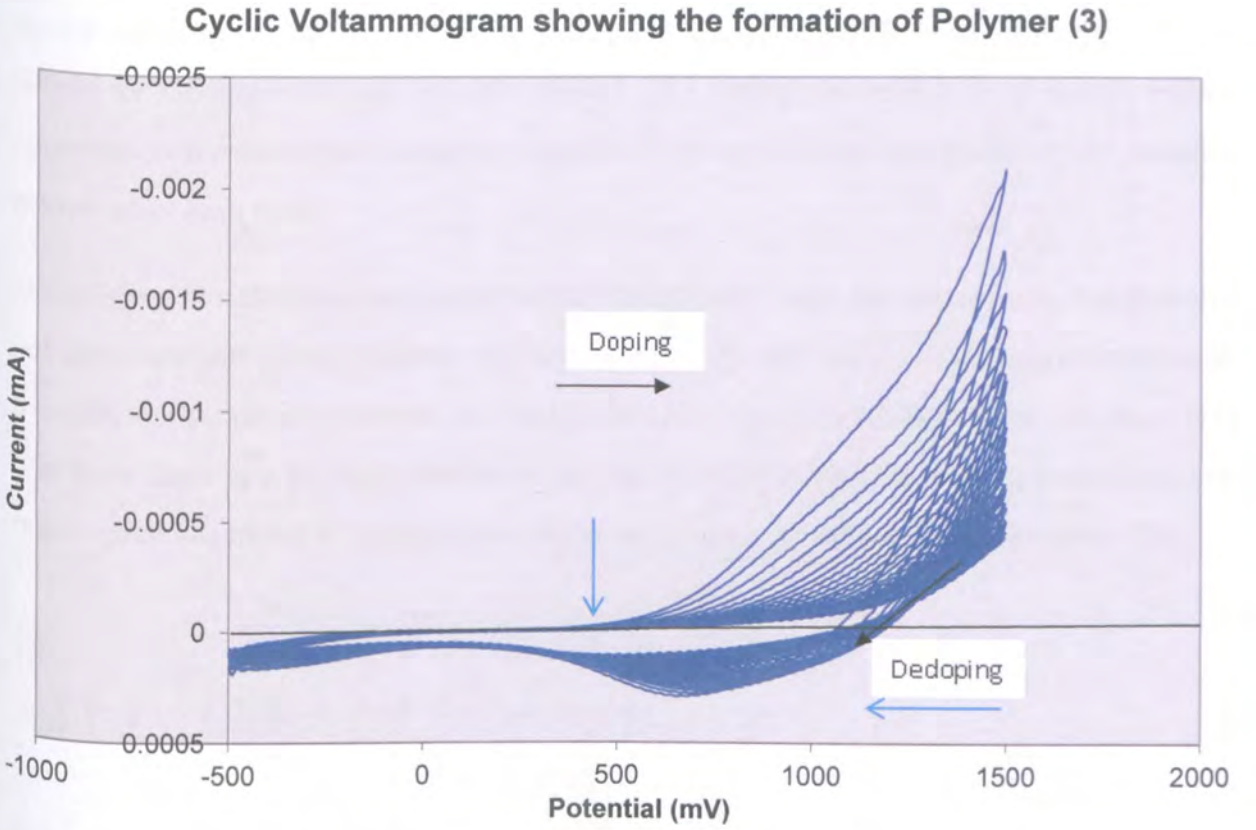


Figure 5.10 A cyclic voltammogram showing the redox properties of monomer (3)

Monomer	Doping Potential (mV)	De-doping Potential (mV)	Oxidation Potential (mV)
(1)	480	50	1500
(3)	1000	500	1500

Table 5.9 Redox Potentials of Monomers (1) and (3), vs SCE

In both voltammograms (See Figures 5.9 and 5.10), the electrode potential was cycled 50 times from – 500 to 1500 vs SCE, at a scan rate of 50mV s^{-1}. In the first half-cycle, oxidation of monomer (1) and monomer (3) started at 480mV and 1000mV vs SCE respectively; as the potential increased, there was an increase in the slope and the polymer films started

growing on the ITO glass. Doping also occurred at that stage. The subsequent reduction (dedoping) of the resulting thin polymer film was observed at 50mV for monomer (1) and 500mV for Monomer (3) (see table 5.9 above). The doping occurred at progressively higher potentials in the successive oxidative stages, as the resistance of the dedoped film became greater after each cycle.

The polymer film thickness was expected to increase with each successive cycle, but this was not observed with either polymer (1) or (3). Although the cyclic voltammogram indicated that polymerisation of monomer (1) and (3) did occur, the polymer films were very thin. This may have been due to steric hindrance arising from the bulky side groups, preventing the regioregular alignment of the polymer chains, which would produce a homogeneous film.

5.11.1 Chemical Polymerisation

The second method of polymerisation was carried out chemically using ferric chloride (anhydrous iron III chloride) as the oxidizing agent. The specific details of the chemical polymerisation of monomers 1-7 are given in the experimental section (8.5). As mentioned previously, chemical polymerisation yielded a larger amount of polymer products, which were dark brown/ black, granular powders. In order to ascertain whether or not chemical polymerisation had taken place, it was necessary to carry out characterisation tests such as IR and ^{1}H NMR on the novel polypyrroles.

5.12 Solubility Parameter

In order to determine the structure and properties of the novel polymer materials, it was necessary to characterise and conduct physical measurements. The first prerequisite was to find a suitable solvent that would sufficiently dissolve each polymer. Instead of going through a process of trial and error, to ascertain what solvent would be the most suitable, it was decided that the best approach would be to calculate the solubility parameter of each polymer.

The general observation of solubility is that like dissolves like, hence polar polymers most readily dissolve in polar solvents and aromatic polymers in aromatic solvents and so on. However, not all polymers are capable of being dissolved. In principle, only linear polymers have the capacity to dissolve. Crosslinked polymers are not soluble in the fullest sense of the word although they may swell in appropriate solvents. There are factors which may increase the resistance of a given polymer to dissolve. These include, crosslinking, crystallinity, hydrogen bonding or the absence of chain branching.

The quantity δ, is known as the solubility parameter, having subscripts s and p referring to solvent and polymer respectively. The solubility of a polymer can be favoured by ensuring that the solubility parameters for polymer, δ_p and the solubility parameter for solvent, δ_s of solvent are very similar.

While the solubility parameters for solvents, δ_s can be determined by various methods [Nicholson], the solubility parameters for most polymers, δ_p can only be determined indirectly.

The group contribution method is the most popular methods where the values of assigned numbers to each group in the involved polymer repeat unit need to be totalled. The numbers are called molar attraction constants and they are obtained semi-empirically.

The molar attraction constants, F have the SI unit in $(J.cm^{-3})^{1/2}$ $cm^3.mol^{-1}$. The various F terms are listed for each F group, under the heading F_i, and if there are two identical groups in the

polymer repeat unit, the F value for the group is doubled. The solubility parameter of a polymer, $\delta_p[(J.cm^{-3})^{1/2}]$, can be calculated by using Equation 1.1

$$\delta_p = [\rho \times \sum F_i] / M_o$$

Where ρ is density of polymer $[g.cm^{-3}]$, M_o is formula weight of the polymer repeats unit [g.mol-1] and $\sum F_i$ is the sum of all groups' attraction constants in polymer repeat unit

$[(J.cm^{-3})^{1/2}\ cm^3.mol^{-1}]$. Molar attraction constants, F_i of some common groups may be found in literature [Nicholson]. (See Table 5.10)

Table 5.10

Molar attraction constants of common groups $(J\text{-}cm^3)^{1/2}\ mol^{-1}$

---CH_3	303
--CH_2-	269
>CH-	176
-CH =	249
>C =	173
-O- in ether	235
-COO-	668
>C = O	537
>N -	125
NH_2	463
-NH-	368
Six membered ring	-48

Five membered ring	43
Ortho	-19
Meta	-13
Para	-82
>C = aromatic	200
-CH = aromatic	239

Table 5.11 Values of Solubility Parameter for Some Common Solvent [δ_s]

Solvent	**Solubility Parameter $(J/cm^3)^{1/2}$**
n-hexane	14.8
Carbon tetrachloride	18.3
Benzene	18.7
Toluene	18.3
Acetone	19.9
Water	47.9
Methanol	29.7
Styrene	19.0
Vinyl chloride	16.0
Diisopropyl ketone	16.4
Aniline	21.1
Pyridine	21.9
Chloroform	19.0

Dipentene	17.4
Xylene	18.0
Tetrahydrofuran (THF)	19.0
Dichloropropane-2, 2	16.6

Table 5.12 Values of Solubility Parameter for Some Polymers [δ_p]

Polymer	**Solubility Parameter $(J/cm^3)^{1/2}$**
Polyethylene	16.2
Polypropylene	16.6
Polystyrene	17.6
PMMA	18.6
PVC	19.4
Polyethylene terephthalate (PET)	21.9
Nylon 6,6	27.8
PTFE	12.7

Where there is no specific interaction between the polymer and the solvent and neither has a tendency to crystallise, the polymer will generally dissolve in the solvent if (δ_s - δ_p) is less than 4.0 (see Tables 5.11 and 5.12). If it is much above 4.0, the polymer is insoluble in the solvent. However, when hydrogen-bonding occurs, a polymer of greatly differing δ value may dissolve in a given solvent [Nicholson].

5.12.1 Solubility Parameter Value Calculation for Main Materials

The polymers prepared in this work were soluble in chloroform which has a solubility parameter of 19.00 $[(J.cm^{-3})^{1/2}$. The solubility parameter of three of these polymers - polymer (1), (2) and (3) – were calculated using the Molar Attraction constants (see Table 5.13).

5.12.2 Calculation of Solubility Parameter Values from Molar Attraction Constants for Polymer (3)

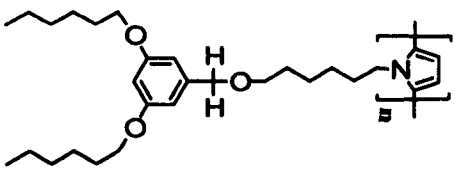


Table 5.13 Molar Attraction Constants

Group	F_i $[(J.m^{-3})^{1/2}.m^3]/mol$	Number of Group	$\sum F_i$ $[(J.m^{-3})^{1/2}.m^3]/mol$
---CH_3	303	2	606
--CH_2-	269	17	4,573
>CH-	176	3	
-CH =	249	3	
>C =	173	3	

-O- in ether	235	3	705
-COO-	668		
>C = O	537		
>N -	125	1	125
NH_2	463		
-NH-	368		
Six membered ring	-48	1	-48
Five membered ring	43	1	43
Ortho	-19		
Meta	-13	2	-26
Para	-82		
>C = aromatic	200	2	1000
-CH = aromatic	239	2	717
			$\sum F_i = 7695$

Details of Calculation, weight of pressed pellet = 0.0260g; thickness = 0.124cm

(1) Density of polymer (3) = ρ = *weight/volume* = *1.069 [g.cm^{-3}]*

(2) $\delta_p = [\rho \times \sum Fi\,]/\,M_0 = [(1.070 \times 7695)]/[457] = 18.02\ [(J.cm^{-3})^{1/2}]$

From the calculations above, polymer (3) has a δ_p value of 18.02 $[(J.cm^{-3})^{1/2}]$. In this work, the solvent, chloroform, with the δ_s value of 19.0 $[(J.cm^{-3})^{1/2}]$ was used to dissolve this polymer. With a (δ_s - δ_p) of 0.97$[(J.cm^{-3})^{1/2}]$ which is much less than 4.0. The calculation for polymer (3) indicates solubility in chloroform.

Other potential solvents of polymer (3) with a (δ_s - δ_p) less than 4.0 are: Carbon tetrachloride, benzene, toluene, acetone, and styrene.

5.12.3 Solubility Parameter Value Calculation for Polymers (1) and (3)

Details of Calculation for Polymer (1); weight = 0.0189g; thickness = 0.099cm
(1) Density of polymer (1) = ρ = *weight/volume = 0.885 [g.cm^{-3}]*
(2) $\sum Fi$ = 6909
(3) M_0 = 401
(4) $\delta_p = [\rho \times \sum Fi]/ M_0 = [(0.885 \times 6909)]/[401] = 15.25$ [(J.cm^{-3})$^{1/2}$]

Details of Calculation for Polymer (2); weight = 0.0360g; thickness = 0.143 cm
(1) Density of polymer (2) = ρ = *weight/volume = 1.284 [g.cm^{-3}]*
(2) $\sum Fi$ = 4987
(3) M_0 = 315
(4) $\delta_p = [\rho \times \sum Fi]/ M_0 = [(1.284 \times 4987)]/[315] = 20.33$ [(J.cm^{-3})$^{1/2}$]

From the solubility parameter calculations, suitable solvents for polymer (1) [δ_p = 15.25 [(J.cm^{-3})$^{1/2}$] with a (δ_s - δ_p) less than 4.0 include: n-hexane, carbon tetrachloride, benzene, toluene, vinyl chloride, diisopropyl ketone, chloroform, dipentene, xylene, tetrahydrofuran (THF), 2,2-dichloropropane and styrene.

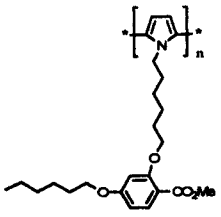
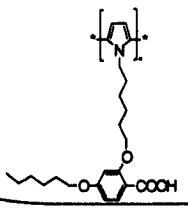
Again, suitable solvents for Polymer (2) - [δ_p = 20.33 [(J.cm^{-3})$^{1/2}$] – with a (δ_s - δ_p) less than 4.0 include: carbon tetrachloride, benzene, toluene, acetone, chloroform, dipentene, Aniline, pyridine, chloroform, xylene, tetrahydrofuran (THF), 2,2-dichloropropane and styrene.

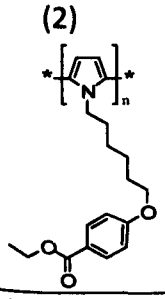
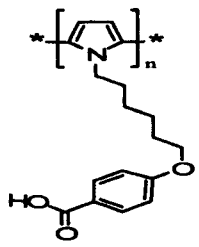
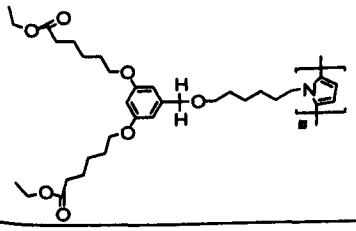
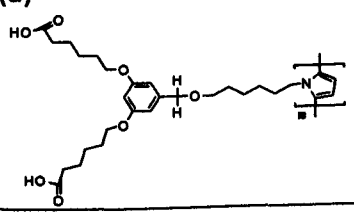
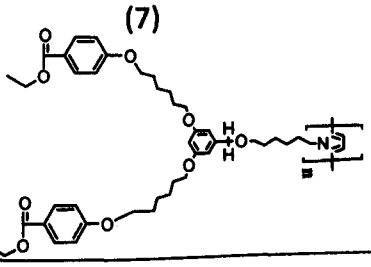
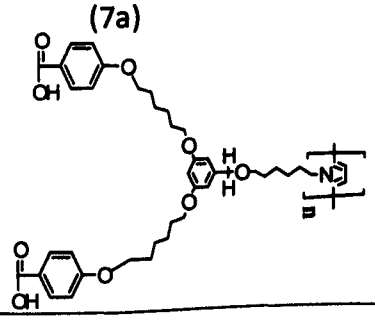
In this work, the solvent, chloroform (δ_s = 19.00 [(J.cm^{-3})$^{1/2}$) was used to dissolve polymer (1) and polymer (2).

5.13 IR analysis of Polymers 1-7

Infra red spectroscopy can be useful in the identification of organic compounds, as the stretching vibrations for various functional groups appear at specific wavelengths within the spectrum. Potassium bromide discs were prepared for each polymer, and analysed by infra red spectroscopy over a range of 4000 to 500 cm^{-1}. The spectra produced were all quite similar (see Figures 5.11 and 5.12 below), however a noticeable difference in the carbonyl (C=O) shifts occurred as the polymers were hydrolysed to their corresponding carboxylic acids. Hydrogen bonding occurring in carboxylic acids weakens the carbonyl bond, so it absorbs at a lower frequency. This trend was observed for polymers 1-7, see table 5.14 below:

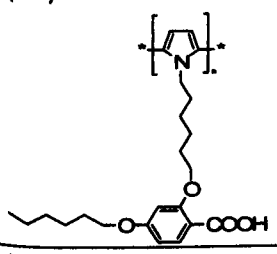
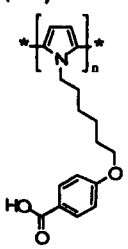
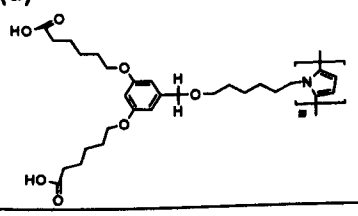
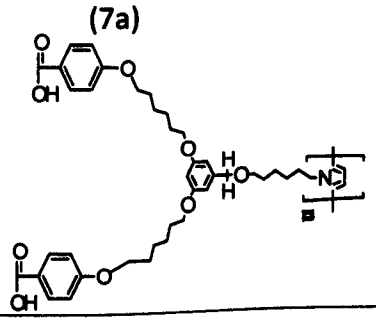
Table 5.14 IR of Polymers 1 – 7; Ester and carboxylic acids

Polymer	Carbonyl Peaks (C = O) cm^{-1}	
	Theoretical Region	Actual Region
(1) 	1750 – 1735	1711
(1a) 	1730 – 1700	1705

(2) 	1750 – 1735	1732
(2a) 	1730 -1700	1705
(5) 	1750 – 1735	1740
5(a) 	1730 – 1700	1700
(7) 	1750 – 1735	1739
(7a) 	1730 -1700	1728

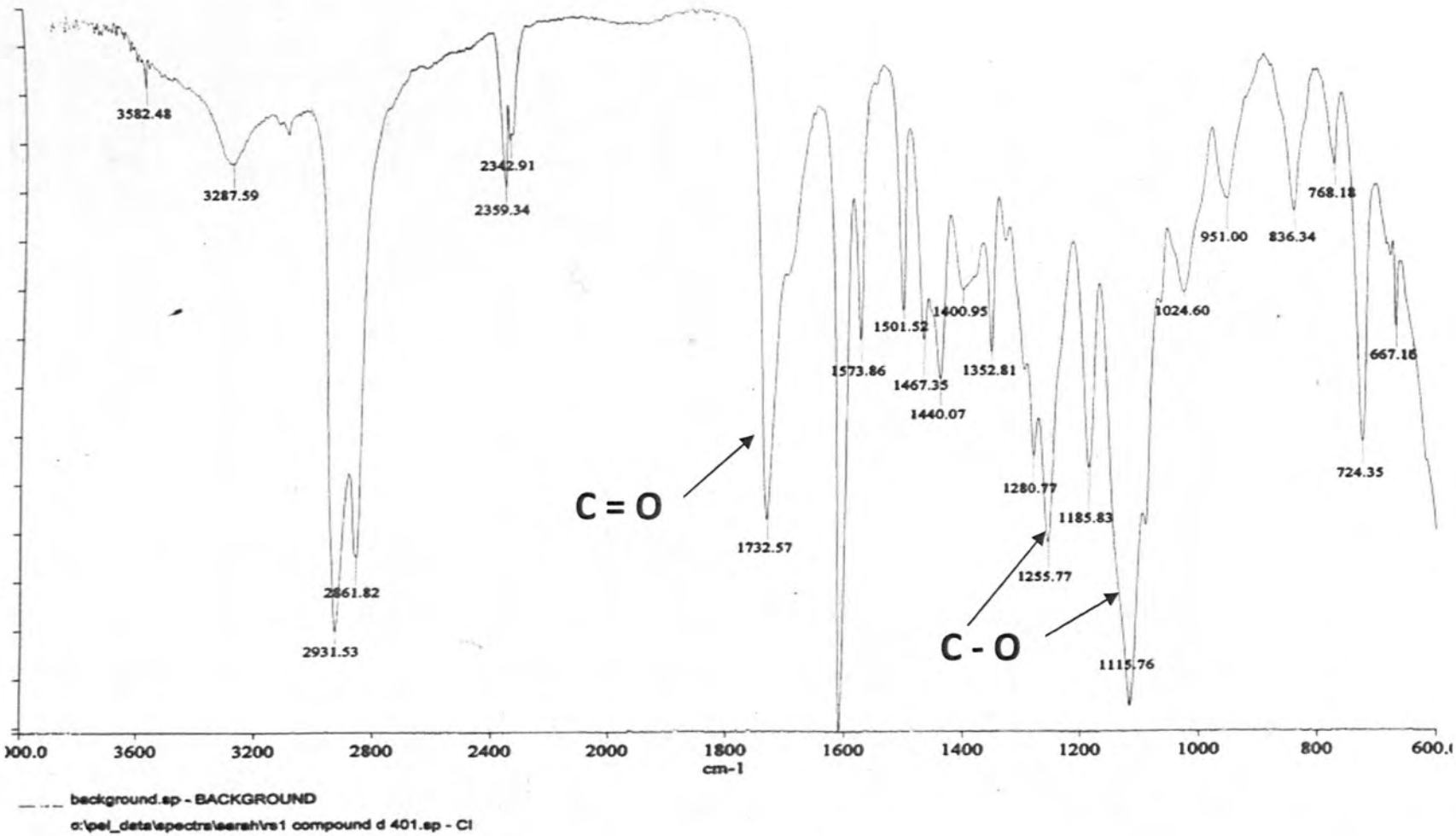
Carboxylic acids can also be further identified by the presence of a broad O-H stretch in the region of 3400 – 2400 cm^{-1}. In addition a third peak can also be observed in the region of 1320 – 1210 cm^{-1} for the C-O. Table 5.15 below illustrates the actual peaks found in the IR for the O-H and C-O bonds for the carboxylic acid polymers. The combination of all three peaks in an IR spectrum would almost certainly indicate that a carboxylic acid functional group is present in the polymer structure.

Table 5.15

Polymer	Actual OH stretch cm^{-1}	Actual C-O Stretch cm^{-1}
(1a) 	2500	1285
(2a) 	2942	1293
5(a) 	2875	1224
(7a) 	2600	1305

Generally all three characteristic peaks of carboxylic acids were observed in the IR spectras of each hydrolysed polymer, therefore indicating that the acid polymer had been synthesised.

Figure 5.11 Infrared spectrum of polymer (2), in its ester form.



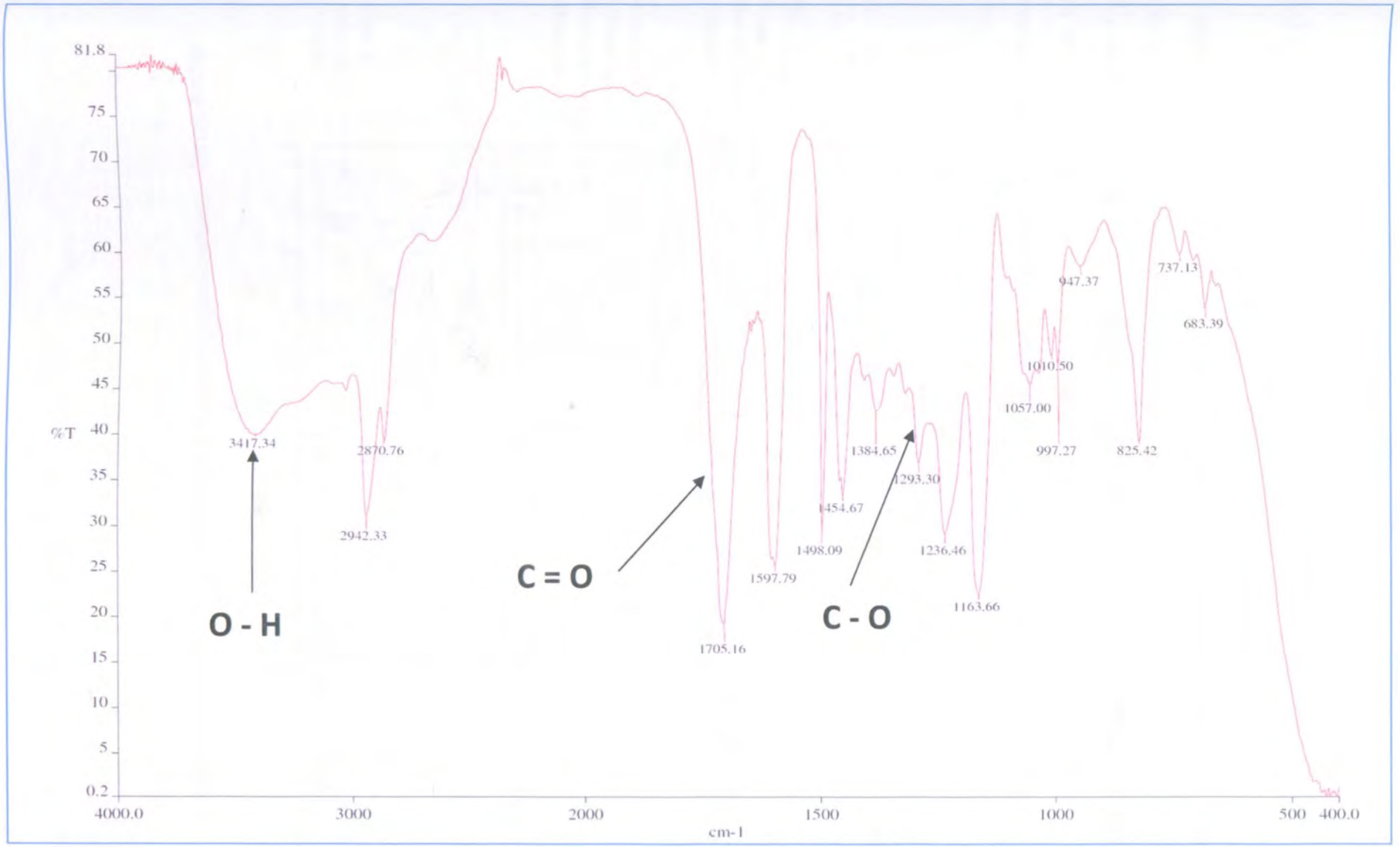


Figure 5.12 Infrared Spectrum of Polymer (2a) (Acid) The O-H stretch of COOH starts at 2500-3417 cm^{-1}

5.14 ^{1}H NMR OF POLYMERS

^{1}H NMR was useful in determining whether successful attachment of pyrrole had occurred when synthesising the monomer compounds. This was indicated by the presence of α- and β-hydrogens of pyrrole in the region of 6.5 and 5.8ppm respectively. After polymerisation, the α-hydrogens at 6.5ppm were no longer visible, indicating that polymerisation had occurred, and the 2,5 hydrogens were involved in the polymerisation process (see Figure 5.13).

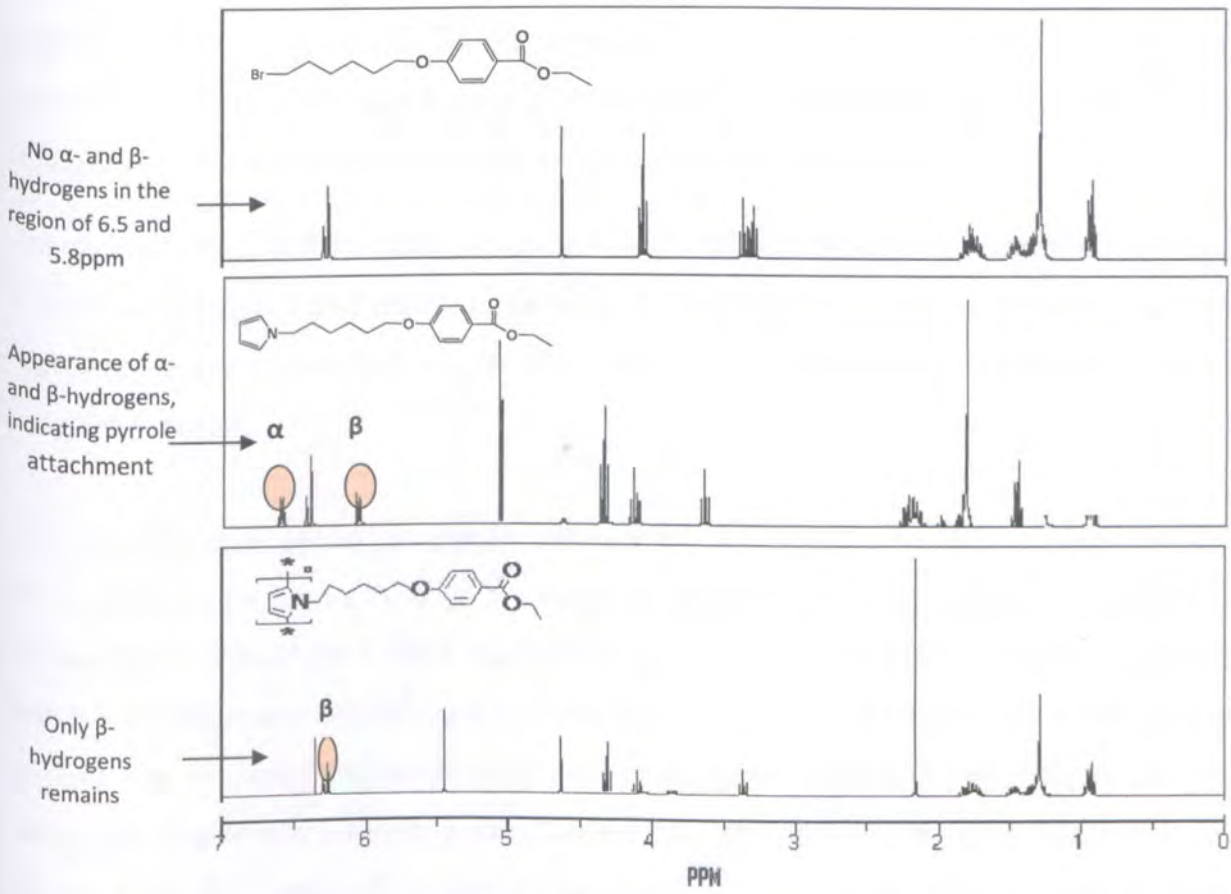


Figure 5.13 Comparison of ^{1}H NMRs of precusor, monomer and polymer (2)

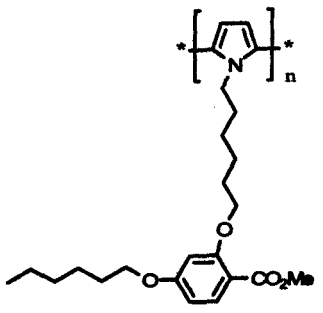
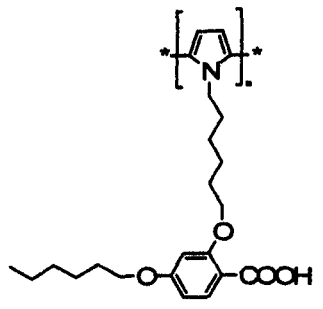
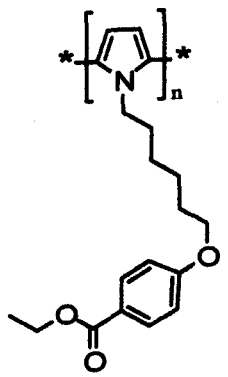
5.15 Conductivity Determination

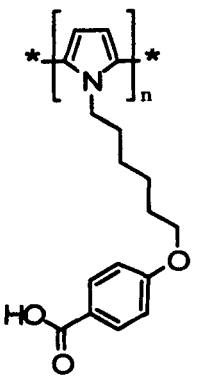
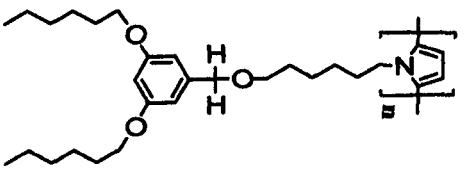
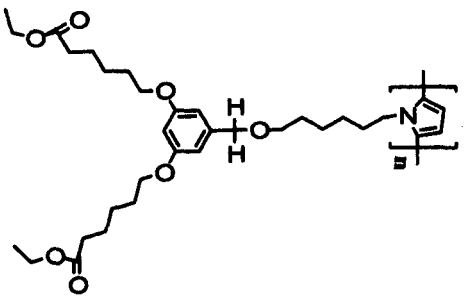
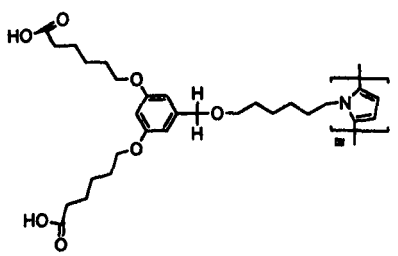
Conductivity measurements were performed on all 9 polymers (see Table 5.16). Each polymer was ground to a fine powder using a freezer mill, and then placed on a watch glass in a desiccator with iodine crystals inside it. The iodine was vaporised by gentle warming to 50^0C [Pratt] for 1 hour. The polymer was then left in the saturated iodine atmosphere for a further 12 hours at room temperature. The doped polymer material was then removed from the desiccator and left on the bench for 2-3 minutes to prevent corrosion by surface iodine when coming into contact with the metal pressing machine. Using a KBr disc-pressing machine, under a pressure of 10 tons, the polymer material was formed into a pellet. The pellet then underwent further doping by re-exposing to iodine for a further 12 hours [Pratt] and the pellet thickness was measured using an electronic micrometer.

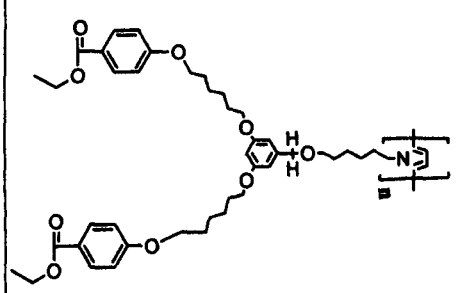
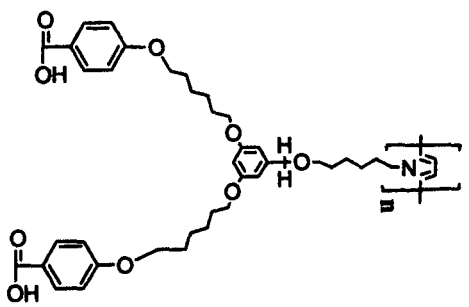
The conductivity was then measured using Van der Pauw 4- probe or 2-probe method using a pellet holder with 4 or 2 metal contacts for the pellets. The samples were connected to a Keithley programmable electrometer and Keithley 224 programmable current source under computer control.

The conductivity of all the samples and its reproducibility were checked. We can measure the resistance of a conductor if we can measure the current through it and potential across it, by using R = V/I: where V is the applied voltage, I is the current flowing through the circuit and R is the resistance offered by the conductor to the moving electrons that constitute the current. The geometry-independent measure of resistance is given by resistivity (ρ) and the reciprocal of resistivity is known as conductivity σ which is given by the equation: $\sigma = L/AR$, where 'L' is the length of a certain conductor and 'A' is the area of cross section. Conductivity of some of the materials were also measured using four probe method. This method is used for measurements of conductivity in metals, semiconductors and conducting polymers [Van de Pauw].

Table 5.16 **Conductivity Values (Sm^{-1}) for undoped & doped polymers at room temperature 25°C**

Polymer	*Conductivity σ (Sm^{-1})*	
	Undoped	***Doped***
(1) 	1.1×10^{-10}	6.6×10^{-8}
(1a) 	4.8×10^{-8}	2.2×10^{-4}
(2) 	6.71×10^{-11}	7.1×10^{-10}

(2a) 	$5.2x10^{-9}$	$6.7x10^{-5}$
(3) 	$3.4x10^{-10}$	$8.3x10^{-9}$
(5) 	$6.6x10^{-11}$	$7.9x10^{-9}$
(5a) 	$8.0x10^{-9}$	$3.1x10^{-6}$

(7) 	$6.3x10^{-11}$	$8.4x10^{-9}$
(7a) 	$1.3x10^{-9}$	$7.8x10^{-5}$

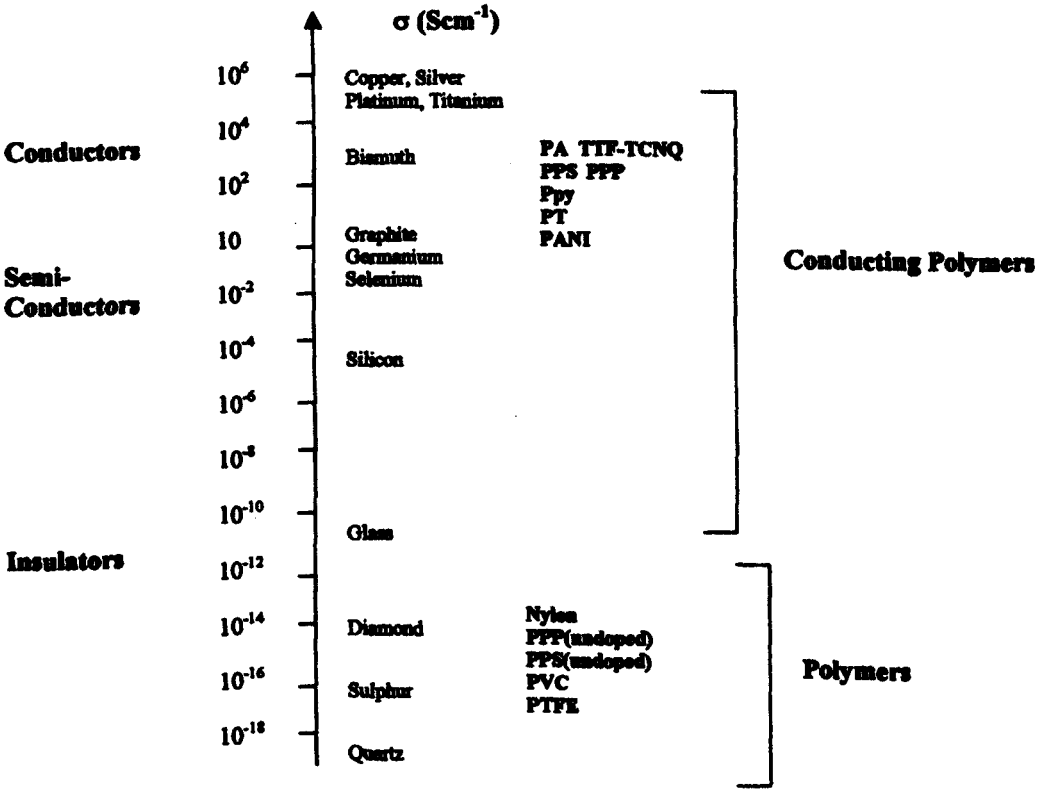


Figure 5.14 Material Conductivities

From table 5.16 above which shows the conductivity values for all nine polymers, several inferences can be made. Upon doping, each polymer showed a modest increase in conductivity of approximately two orders of magnitude. This indicates that subjecting the polymer materials to iodine vapour proved to be a successful method of chemical doping. Generally p-type doping using iodine is one of the most popular dopants because of its ease of handling, availability and effectiveness. N-substituted polypyrroles have been studied extensively, and they usually exhibit much lower conductivities than the doped materials. The reason may be due to sterically twisting of the aromatic ring out of planarity.

Another observation found was that the hydrolysis of the ester functional groups to the corresponding carboxylic acid polymers resulted in an increase in conductivity for doped and undoped polymers. Polymer (1) exhibited a conductivity value of $1.1x10^{-10}Sm^{-1}$ (undoped), and $4.8x10^{-8}Sm^{-1}$ upon hydrolysis to its corresponding acid (1a) (undoped). However an even larger increase was observed upon doping. In the doped state polymer (1) exhibited a conductivity value of $6.6x10^{-8}Sm^{-1}$ and its corresponding acid (1a) increased to $2.2\ x10^{-4}Sm^{-1}$, which classifies it as a semi-conductor. This trend was also observed with polymer (7); $6.3x10^{-11}Sm^{-1}$ (ester/undoped) which increased upon hydrolysis to its corresponding acid (7a) $1.3x10^{-9}Sm^{-1}$(acid/undoped). Then a further increase in conductivity was observed upon doping; (7) $8.4x10^{-9}Sm^{-1}$(ester/doped), (7a) $7.8x10^{-5}Sm^{-1}$ (acid/doped), this also classifies polymer (7a) as a semi-conductor.

In comparison N-substituted polypyrroles behave similarly to polythiophenes. Previous work carried out by Foot, Brown *et al* found that polythiophenes with laterally and terminally attached ester side groups, showed a dramatic increase in conductivity upon hydrolysis to their corresponding carboxylic acids, transforming the insulating materials into semi-conductors. Poly[(1-(3-thiophenemethoxy)-6-(methyl-4-n-oxybenzoate)hexane)-co-(3-hexylthiophene)] was found to have a conductivity value of $4x10^{-7}Sm^{-1}$ and upon hydrolysis to its corresponding acid the conductivity increased to $7.1x10^{-4}Sm^{-1}$. This was also observed for polymer (29) in which the conductivity values was $8.19x10^{-8}Sm^{-1}$ before conversion to the acid and $1.4\ x10^{-2}Sm^{-1}$ afterwards (29a).

It was suggested that the phenomena observed in the increase in conductivity values, upon conversion of the esters to carboxylic acids, may be due to hydrogen bonding. As strong intermolecular hydrogen bonding occurs between adjacent carboxylic groups, a pseudo ring is formed (see figure 5.15). This characteristic is believed to improve conjugation of the polymer backbone by preserving planarity - thus increasing the flow of electrons along the polymer chain, which in turn increases the overall conductivity of the polymer material.

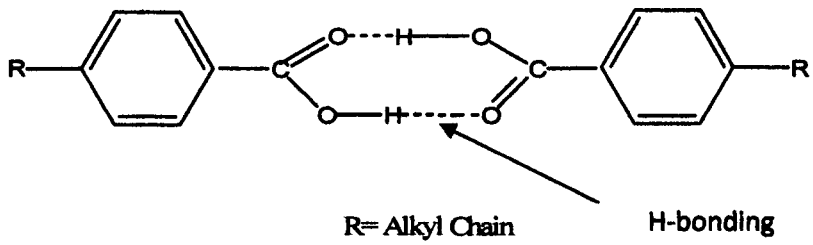


Figure 5.15 Formation of Pseudo Ring

The lower conductivity values observed in polymers (2) and (5), may be due to bulky groups causing steric hindrance, therefore reducing the planarity of the polymer backbone.

5.16 Scanning Electron Microscope (SEM)

The morphologies of the novel polymer materials are very important in relation to their applications as drug carrier molecules. Ideally for a polymer material to have the ability to accommodate or transport a host material around the body, it needs to have the ability to allow the migration of compounds from within the internal cavities of polymer to the surroundings. SEM can provide useful information about the porosity and pore size of the polymer material under investigation.

The images taken for polymers (1a), (3), (5a) (6a) and (7a) are displayed in figures 5.16 – 5.20 below.

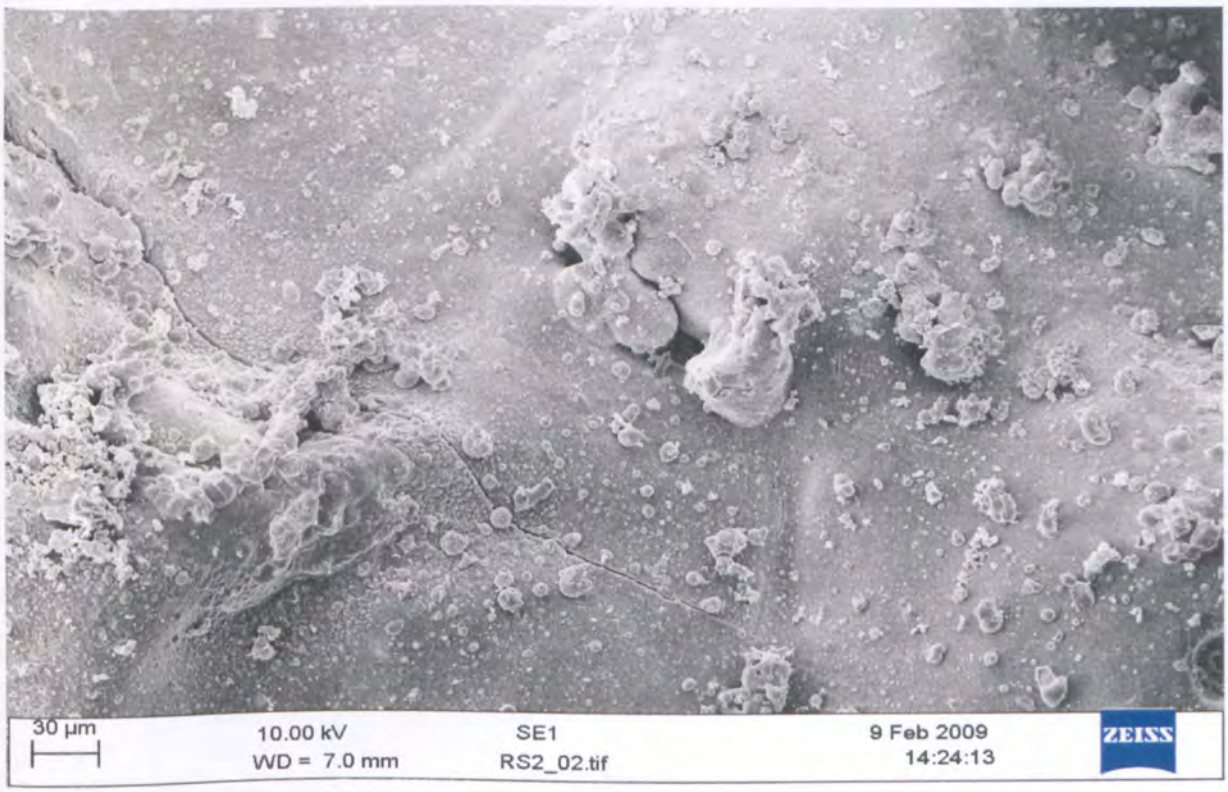


Figure 5.16 Polymer (1a) - Polypyrrole with laterally attached liquid crystal side groups caste on a coverslip.

From the image it can be observed that polymer (1) has a combination of a smooth morphology with round, textured nodules on the surface. The smooth continuous morphology may suggest that the polymer chains were able to pack closer together, forming a continuous layer.

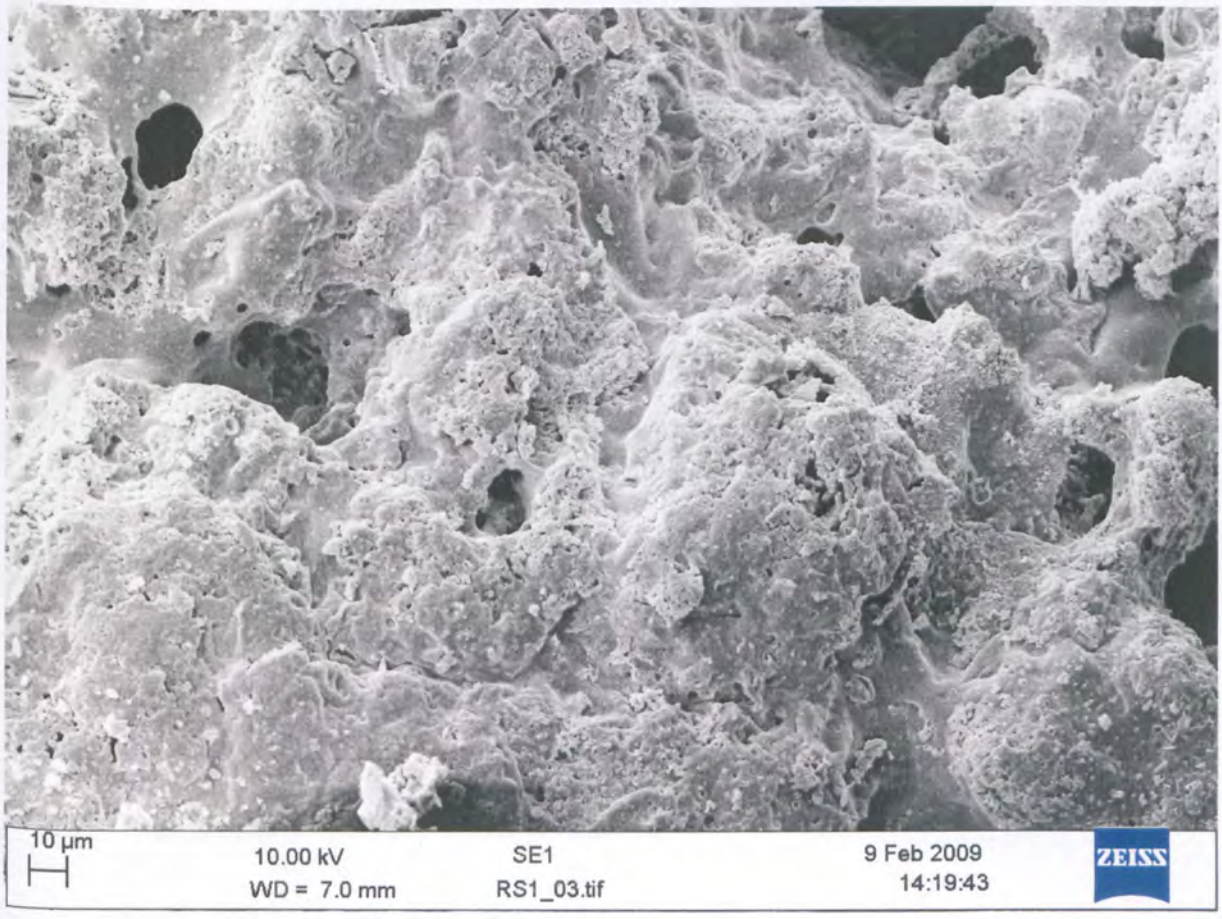


Figure 5.17 Polymer (3) - Polypyrrole with first generation dendritic side groups, with alkyl chains.

From the image it can be observed that polymer (3) has a more porous morphology than polymer (1a), with micropores varying in size throughout the polymer matarial. As it is a dendritic polymer it may suggest that the polymer chains may align themselves further apart than the molecules in polymer (1), creating space and generating small pores.

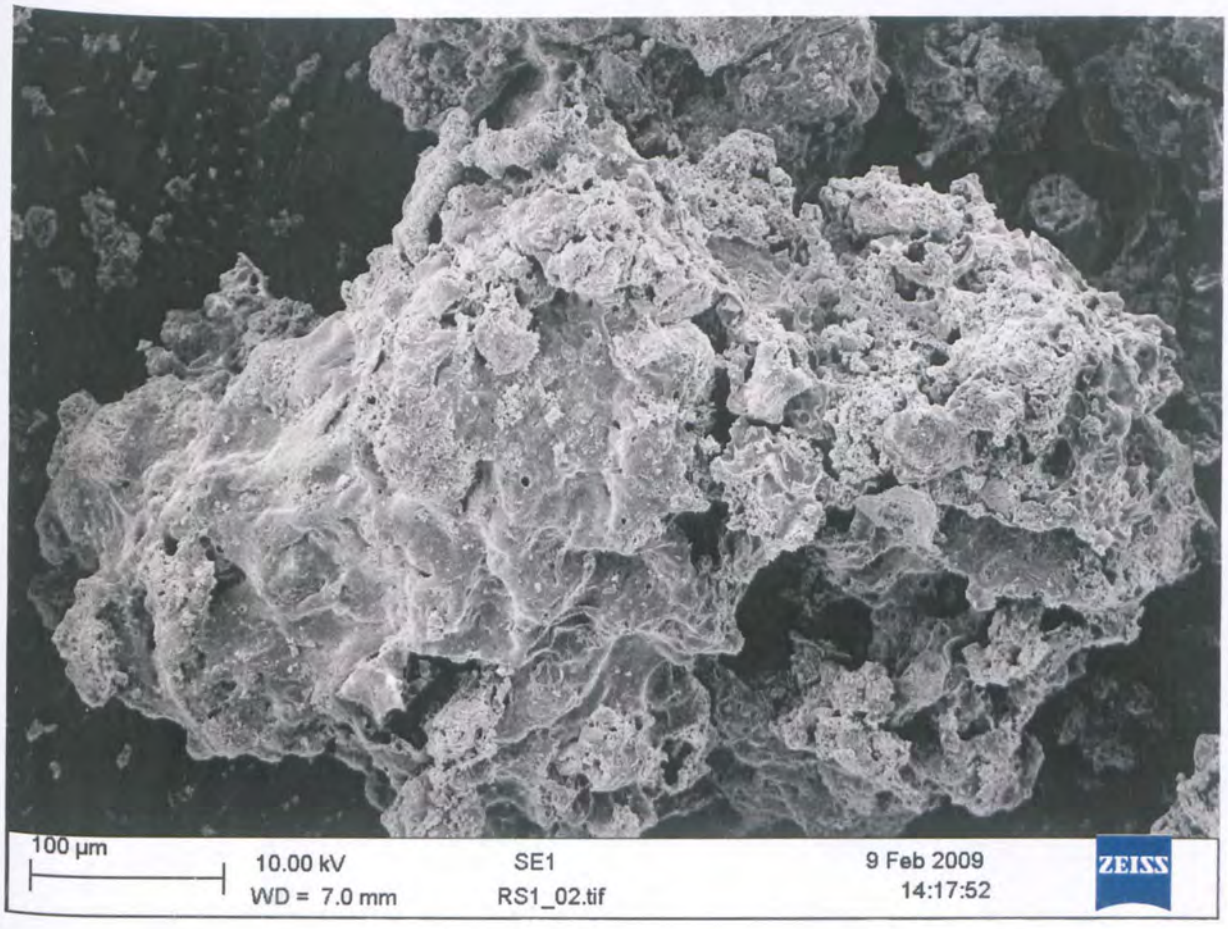


Figure 5.18 Polymer (5a)-Polypyrrole with first generation dendritic polymers with hydrophilic terminated alkyl chains.

The image illustrates a rough and uneven morphology for polymer (5a). Micropores of various sizes can be observed, and some areas have more densely packed clusters, while other areas are more continuous.

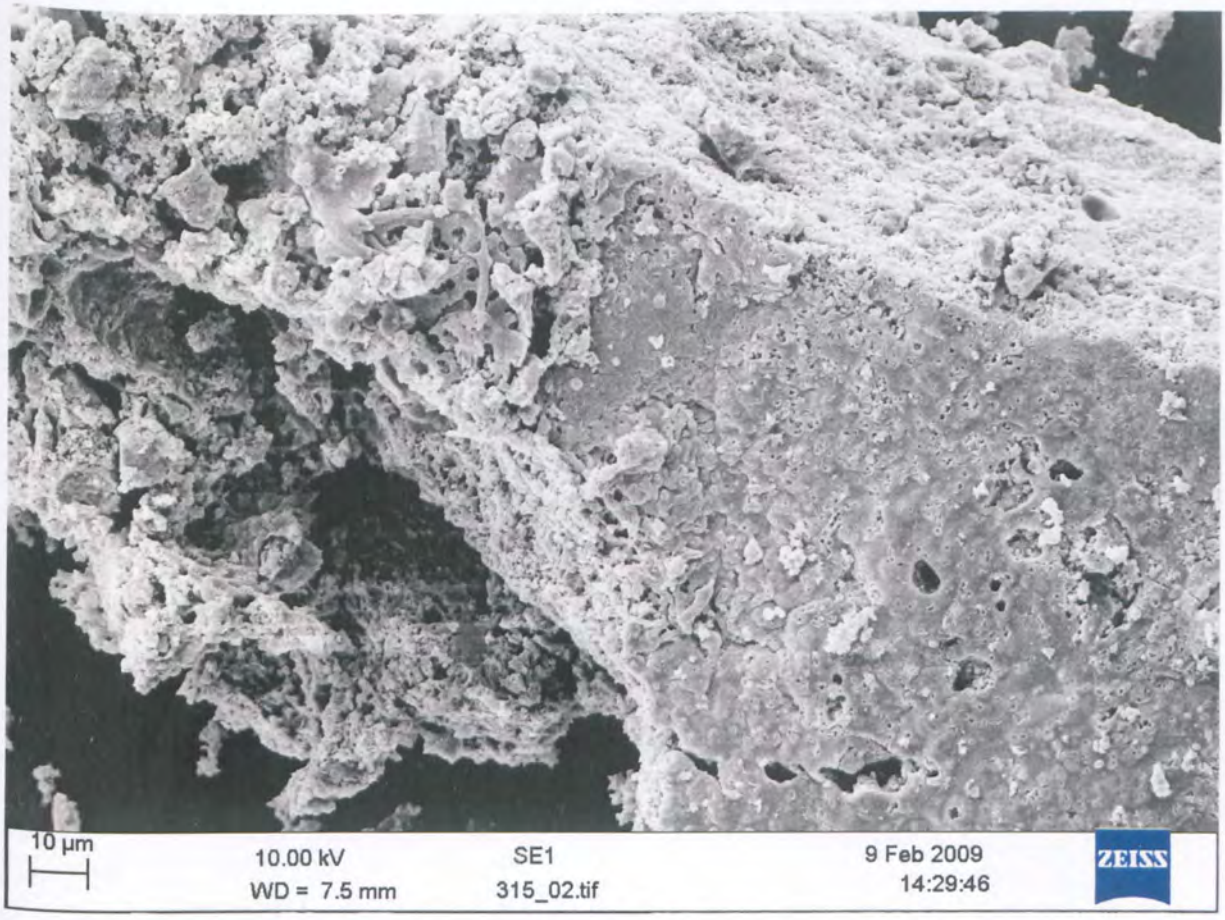


Figure 5.19 Polymer (6a) - Polypyrrole with second generation dendritic polymers with hydrophilic terminated alkyl chains

From the image it can be observed that polymer (6) had a morphology with a combination of rough, porous clusters and a continuous layer with smaller pores on the surface.

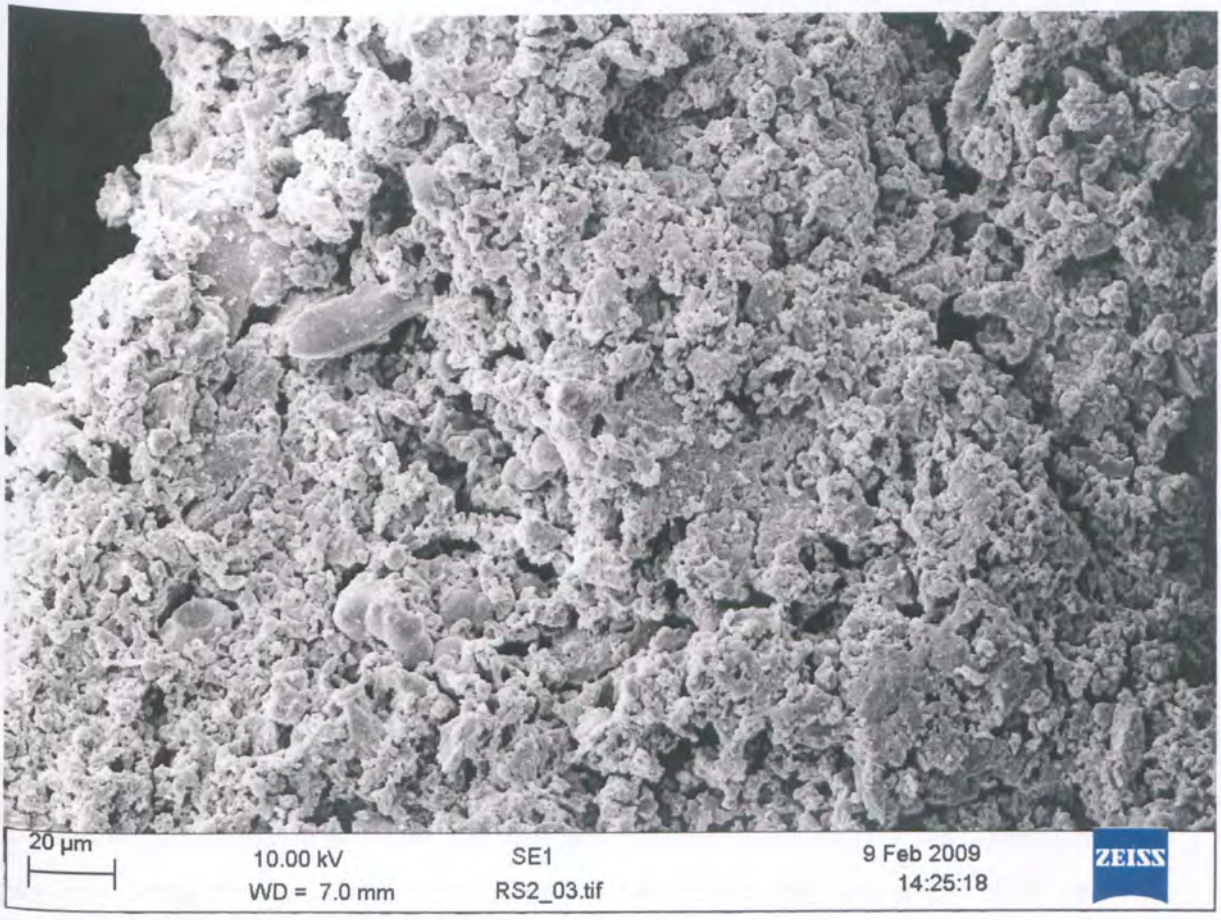


Figure 5.20 Polymer (7a) - Polypyrrole hybrid material, second generation dendritic polymer with terminal liquid crystal groups

From the image it can be observed that polymer (7a) had a very porous morphology, in which micropores of various sizes where clustered together. This may indicate that the polymer chains may align themselves in such a way that small pores of similar size may be formed. Interestingly, polymer (7a) was also found to have an unexpectedly high conductivity value ($7.84 \times 10^{-5} Sm^{-1}$). It was suggested that due to the porous nature of the polymer material, better p-type doping could occur; as the iodine molecules could penetrate the between the micropores and come into closer contact with the polymer material.

5.17 UV-Visible Spectra of Polymers (1) & (3)

The films of polymers (1) & (2) grown by electrochemical polymerisation were analysed using UV-visible spectrophotometry (See Figures 5.21, 5.22 and 5.23). A reference electrode of ITO glass was used, and the scans were run from 800 -200nm. In addition polymer (1a) was also analysed to study what effect hydrolysis of the ester (1) to the corresponding carboxylic acid (1a) would have on the energy gap (Eg) of the polymer. For this a thin film of polymer (1a) in its undoped form was dissolved in chloroform, cast upon a cover slip and the solvent was evaporated. As most of the polymers only partially dissolved in chloroform, and formed a solution of suspended particles as well as some of the polymer materials going into solution, most were unable to form homogenous films. Analysis of the polymers using UV-Visible spectrophotometry was restricted to polymer (1) & (3) as very thin films had been grown previously by cyclic electrochemical oxidation and (1a) was analysed in order to compare the ester (1) to the acid (1a). The results are recorded in table 5.17 below.

Table 5.17 UV-Visible Values for Polymers (1), (1a) and (3)

Polymer	*λmax (nm)*	*λ (nm)*	*Eg (eV)*	*Inference*
(1)	*270*	*315*	*3.9*	*π-π* transition*
(1a) Peak (a)	*450*	*500*	*2.48*	*π-π* transition*
(1a) Peak (b)	*710*	*698*	*1.8*	*polaron*
(3) Peak (a)	*240*	*250*	*4.96*	*π-π* transition*
(3)Peak (b)	*325*	*330*	*3.75*	
(3) Peak (c)	*360*	*417*	*2.97*	*π-π* transition*

The optical spectrum provides useful information about the π-orbital overlap. There is a direct relationship between the extent of conjugation and observed energy of the π-π* transition. As the λ_{max} value increases, the extent of conjugation in the backbone increases, and the size of the band gap (Eg) decreases. The relationship between the extrapolated wavelength of absorption onset (λ_0) and energy gap (Eg) is derived from Planck equation:

$$1/\lambda_0 = Eg/hc$$

$$Eg = hc/\lambda_0$$

Where:

c = speed of light ($3x10^8 ms^{-1}$)

h = Planck constant ($6.6x10^{-34} Js$)

Eg = Energy gap

λ_0 = wavelength of photon equivalebt to band gap Eg

$1eV = 1.6x10^{-19} J$

Calculation of the Energy Gap of polymers (1), (1a) and (3), indicated that the ester form of polymer (1) was in the region of insulators as it was found to have an Eg of 3.9eV. However, the corresponding acid (1a) was found to have a smaller Eg of 2.48eV undoped and 1.8eV doped, indicating that the extent of conjugation in polymer (1a) is greater than polymer (1), making it a semi -conductor.

University of Kingston
School of Chemistry & Pharmaceutical Sciences
Penryn Road
Kingston

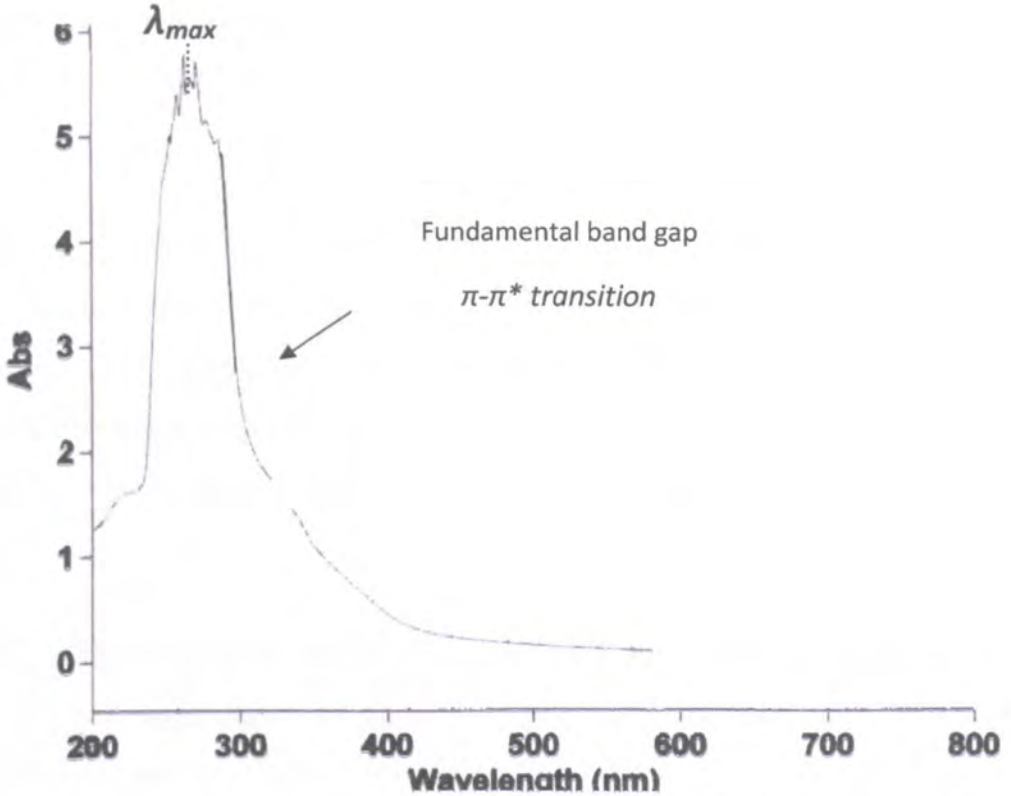


Figure 5.21 UV- Visible Spectrum of Polymer (1)

Figure 5.21 is the UV-visible spectrum of de-doped polymer (1) on ITO glass. It features a strong π-π* peak at 270 nm, and an absorption edge at 315nm (3.9eV). When the energy gap of polymer (1) is compared to the literature value of the parent polymer, polypyrrole (2.38eV) [Yang] it indicates that polymer (1) is likely to have less conjugation that that of polypyrrole. This was to be expected, as large substituent's such as the ester groups present in polymer (1), are not likely to preserve the planarity of the polymer backbone, therefore increasing the band gap. However when polymer (1) is hydrolysed to its corresponding

carboxylic acid (1a) the band gap becomes much smaller (2.48eV at 450nm) and resembles an energy gap value much closer to that of polypyrrole. See figure 5.22

The reduction in the band gap upon conversion from the ester to carboxylic acid may be due to hydrogen bonding, which somewhat improves the overall planarity and extent of conjugation in polymer (1a).

Figure 5.23 is the UV-visible spectrum of de-doped polymer (3) on ITO glass. It features a strong π-π^*peak at 360nm, an absorption edge at 417nm (2.97eV) from the data in table. It is apparent that polymer (3) has a smaller band gap (2.97eV) than polymer (1a), but a larger band gap than polymer (1a). This indicates that polymer (3) is likely to have a greater degree of conjugation than polymer (1), but less conjugation than polymer (1a) and polypyrrole.

In contrast, polymers (1) and (1a) can be compared to corresponding polythiophenes with laterally attached ester groups which were subsequently hydrolysed to carboxylic acids. Previous work carried out by Foot, Brown *et al* reported that poly[(1-(3-thiophenemethoxy)-6-(methyl 4-n-hexoxy-2-oxybenzoate)hexane)-*co*-(3-methylthiophene)] (28b) and poly[(1-(3-thiophenemethoxy)-6-(methyl 4-n-hexoxy-2-oxybenzoic acid)hexane)-*co*-(3-methylthiophene)] (29b) were found to have an energy gap of 3.4eV and 2.4ev respectively. These reported values were almost identical to the Eg values of polymer (1) and (1a) which indicates that hydrogen bonding occurring in the carboxylic acids plays an important role in the conjugation and planarity of the polymer backbone, which in turn reduces the energy gap of the polymer material. This feature of hydrogen bonding may improve the conductivity of the polymer material and can transform insulators to semi-conductors. By convention, a material of band gap greater than 3eV is considered an insulator and below about 0.2eV, a conductor [Brett].

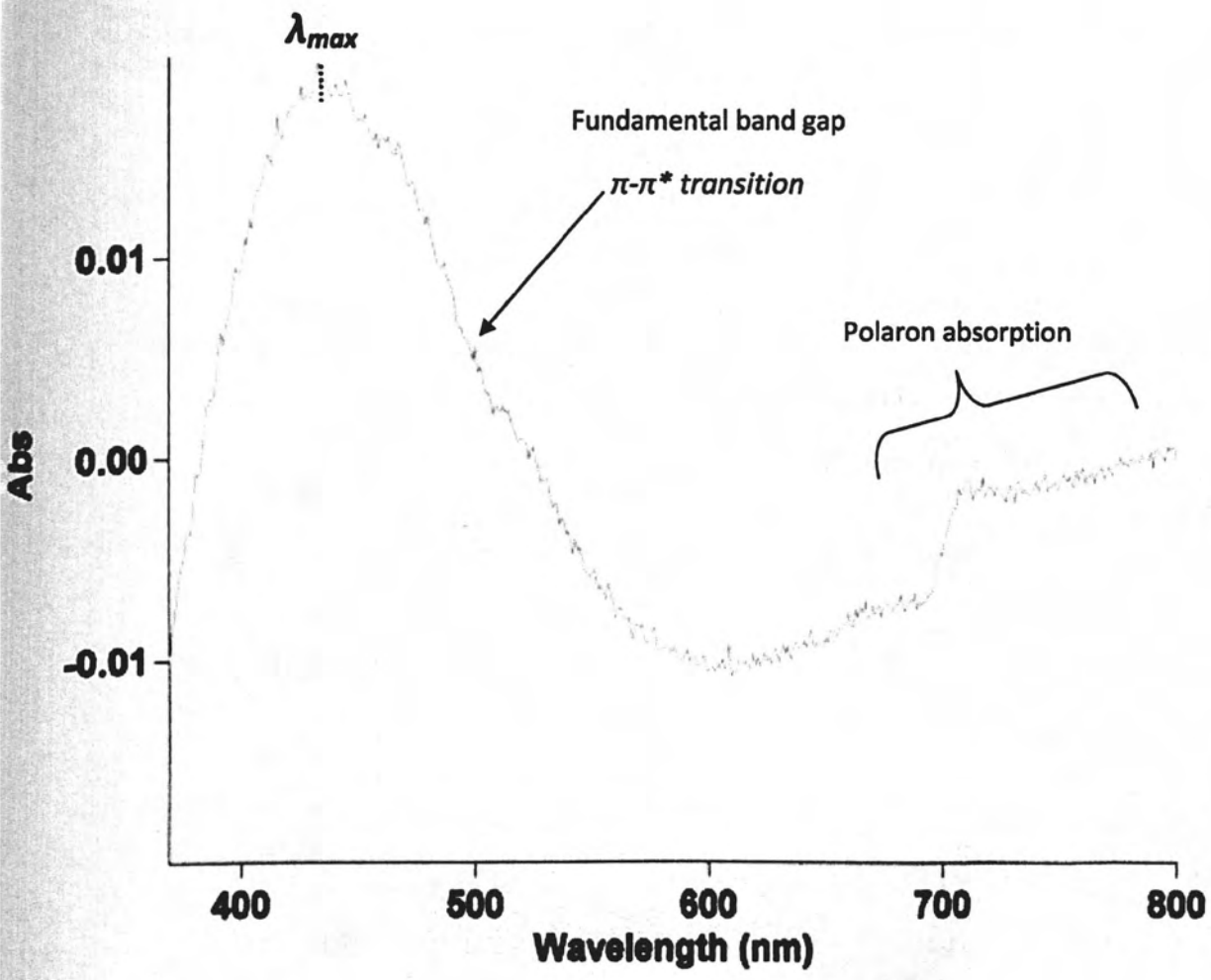


Figure 5.22 UV-Visible Spectrum of Polymer (1a)

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University of Kingston
School of Chemistry & Pharmaceutical Sciences
Penrhyn Road
Kingston

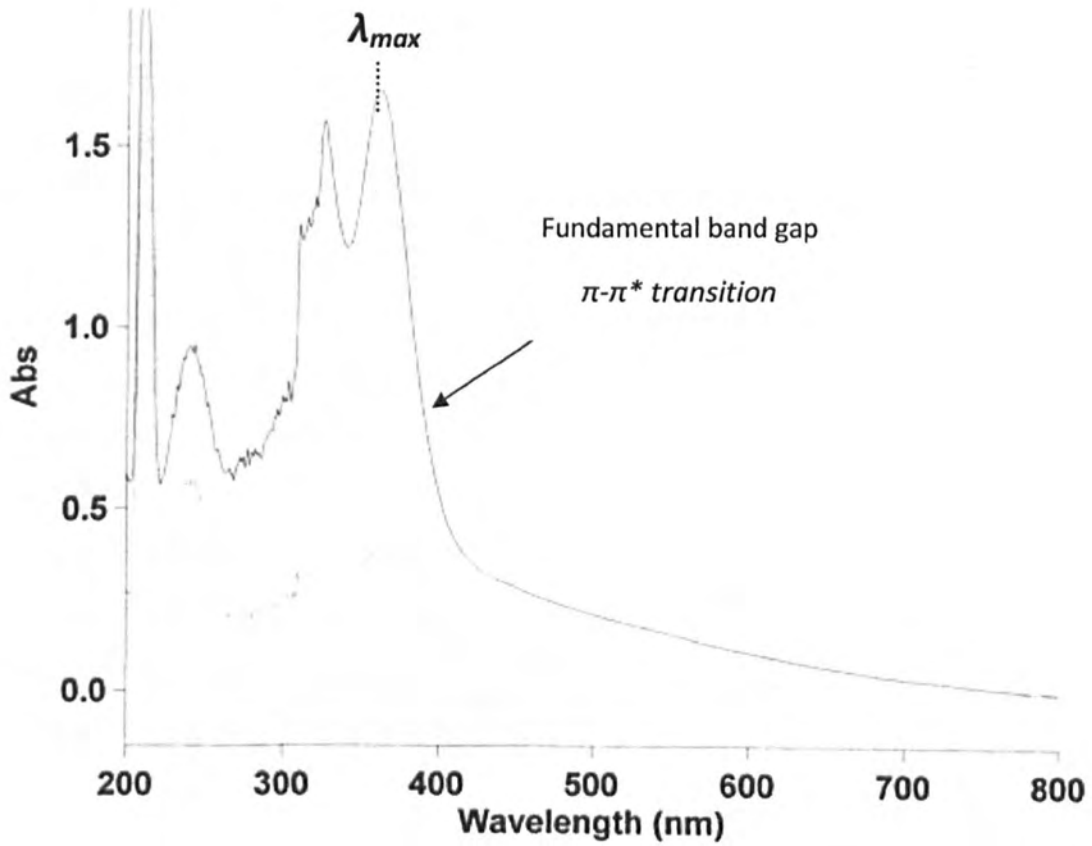


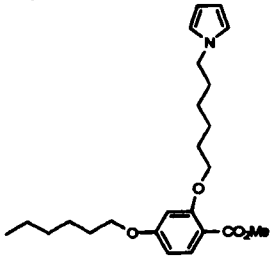
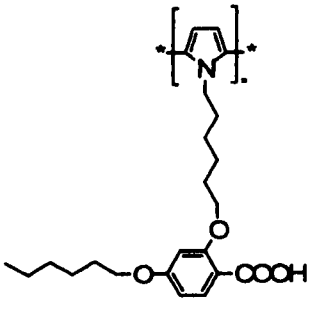
Figure 5.23 UV Visible Spectrum of Polymer (3)

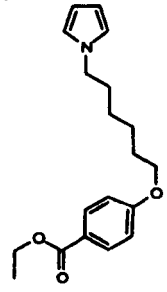
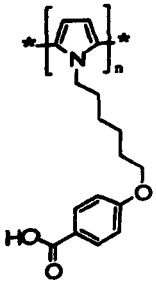
5.18 DSC – Differential Scanning Calorimetry

DSC is a technique in which the difference in heat flow to the sample and reference are monitored against temperature [Lambe]. It can be very useful in the detection of multiple transitions of a given monomer or polymer material, and the DSC's obtained can indicate whether endothermic, exothermic or entropic processes are occurring. When investigating the phase transitions of potential liquid crystal compounds, DSC and Hot-stage Microscopy are generally used in conjunction. The DSC trace will tend to give an approximate temperature region where a phase transition may be occurring, by the presence of a large or small peak depending on what phase the molecules within the material are undergoing transition to and from. Generally, large peaks will indicate that a high energy transition is occurring, which may suggest that material is undergoing a phase transition from a something like a crystalline solid to a nematic phase (highly ordered – random less order structure). Alternatively, smaller peaks will indicate that a small energy transition is occurring , and it is likely to be a transition occurring within a phase, such as smectic A – smectic B.

As we were most interested in investigating the phase transitions of the potential liquid crystal polymers, it was decided that our approach would be to focus on the lower molecular weight monomers/polymers (monomers (1) & (2) and polymers (1) & (2)) as previous studies reported that lower molecular weight polymers with less bulky substituent, were more likely to give liquid crystal phases [Ibison]. In addition particular attention was placed on the ester polymers which were hydrolysed to acids, as they were most likely to exhibit liquid crystal phases. Therefore the DSC's of monomers (1) & (2), polymers (1) & (2) and their corresponding acids (1a) & (2a) were carried out. Table 5.18 below illustrates the results obtained from DSC.

Table 5.18 DSC's of Polymers (1) & (2) and Corresponding Acids (1a) & (2a)

Monomer/Polymer	*Transition Temperature* (°C)			*Assignment/inferences*
	1st	*2nd*	*3rd*	
Monomer (1) - Methy2-(6-(1H-pyrrol-1-yl)hexyloxy)-4-(hexyloxy)benzoate 				No major phase transitions were observed 1st peak = 75 °C - Likely to be solvent evaporation of ethyl acetate from column chromatography 2nd peak = 160°C Clearing Point where monomer has melted.
(1a) – Acid Polymer of Monomer (1) 	60 Melting	100-105 I→N	105-249 (N→N) 240 (N→I)	At 60 °C polymer may begins to soften/melt. 100-105 °C further melting, polymer is likely to be liquid 105-248 °C polymer likely to enter nematic phase and remains in the nematic phase (N→N). May see subtle movement or possible transitions within the nematic phase. 240 °C Polymer becomes liquid (N→I) Peaks α and β are likely to be radical formation due to bond breaking – Endothermic (ether linkage C→O) γ- Decomposition.

Monomer (2) – Ethyl 4-(6-(1H-pyrrol-1-yl)hexyloxy)benzoate 				No phase transitions were observed. 1st peak = 160 °C Clearing Point where monomer has melted. 2nd Peak = 280 °C – Decomposition. Endothermic process possible bond breakage.
(2a) – Acid Polymer of Monomer (2) 	65 Soften	75-105 (I)	105-170 (N→N) (N→I) 180-230 (I→C) 180-230	At 65 °C polymer begins to soften. (Tg baseline shift) 75-105 °C – Further melting polymer may become liquid 105-170 °C – Expect to observe Nematic phase 180 °C – Polymer looses order and becomes a liquid again. (N→I) 180-230 °C – Polymer regains some degree of order (Exothermic process) possibly re-crystallisation or degradation. (I→C) 240 °C - Decomposition. Endothermic reaction

From the DSC 2-3 peaks were observed, which indicated that polymer (1a) and (2a) undergo liquid crystal phase transitions (see Figures 5.24, 5.25, 5.26 and 5.27). The assignment of each peak is outlined in table 5.18 above with details of the transition temperatures. In order to get a better picture of what the exact transitions were, hot-stage microscopy was used to study the liquid crystallinity of each polymer.

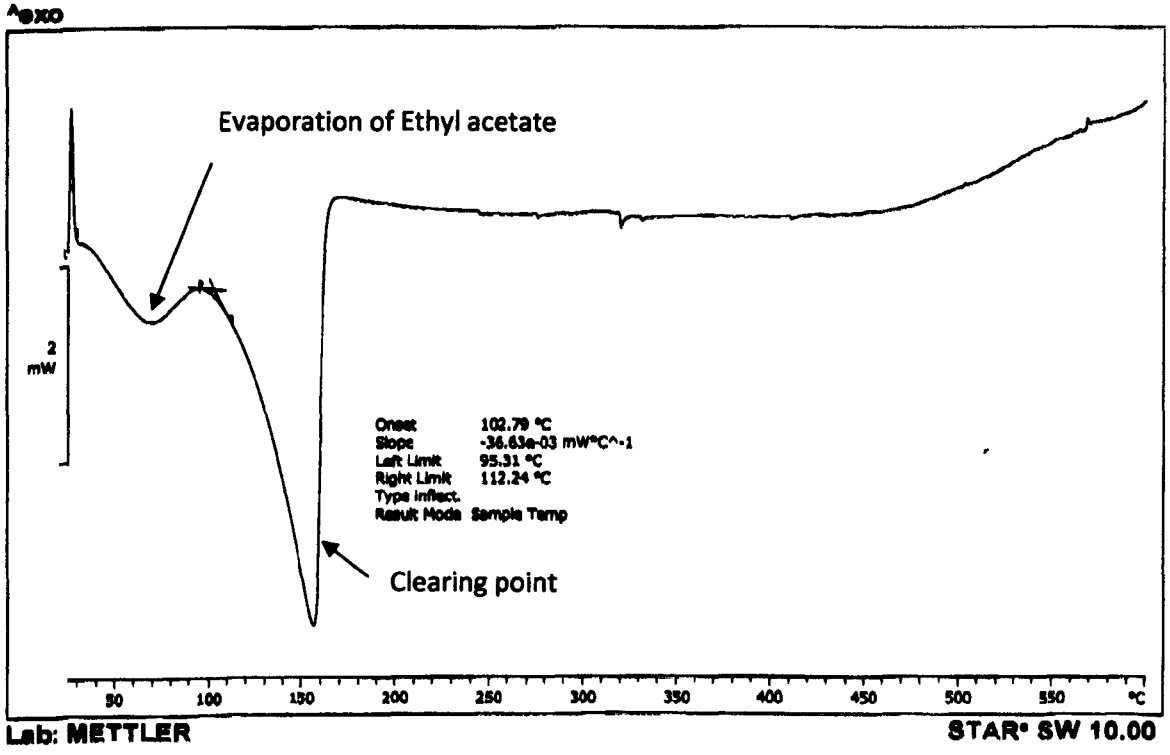


Figure 5.24 DSC of Monomer (1)

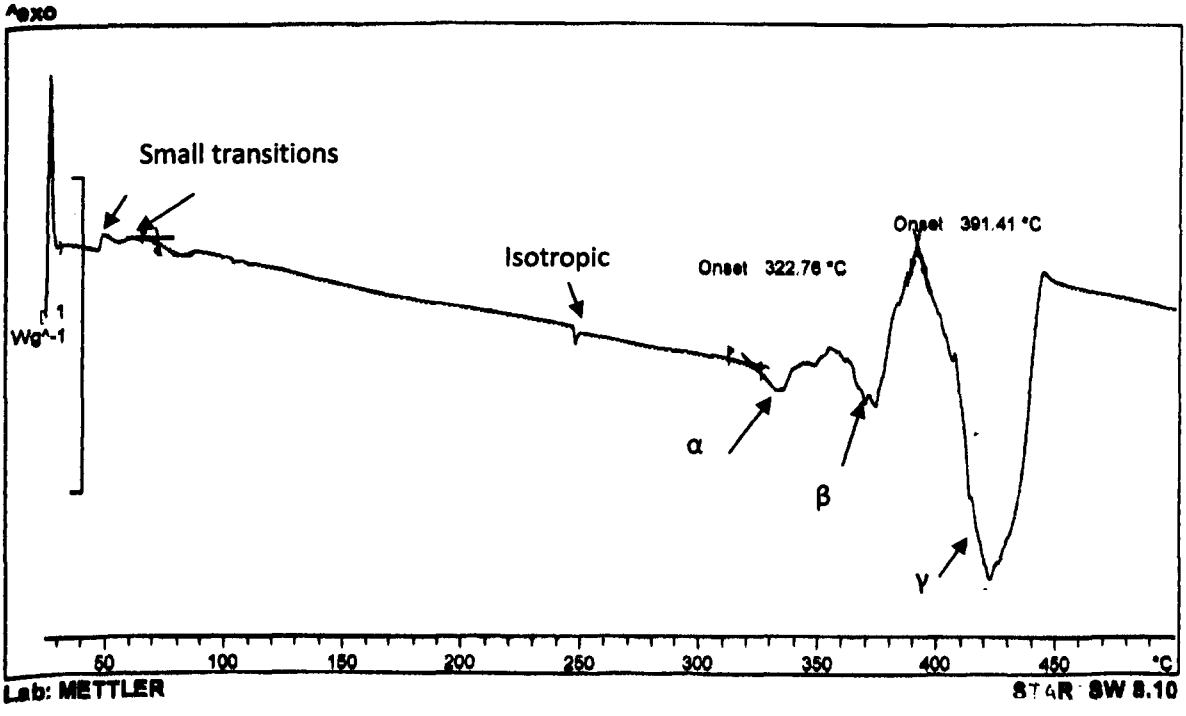


Figure 5.25 DSC of Polymer (1a)

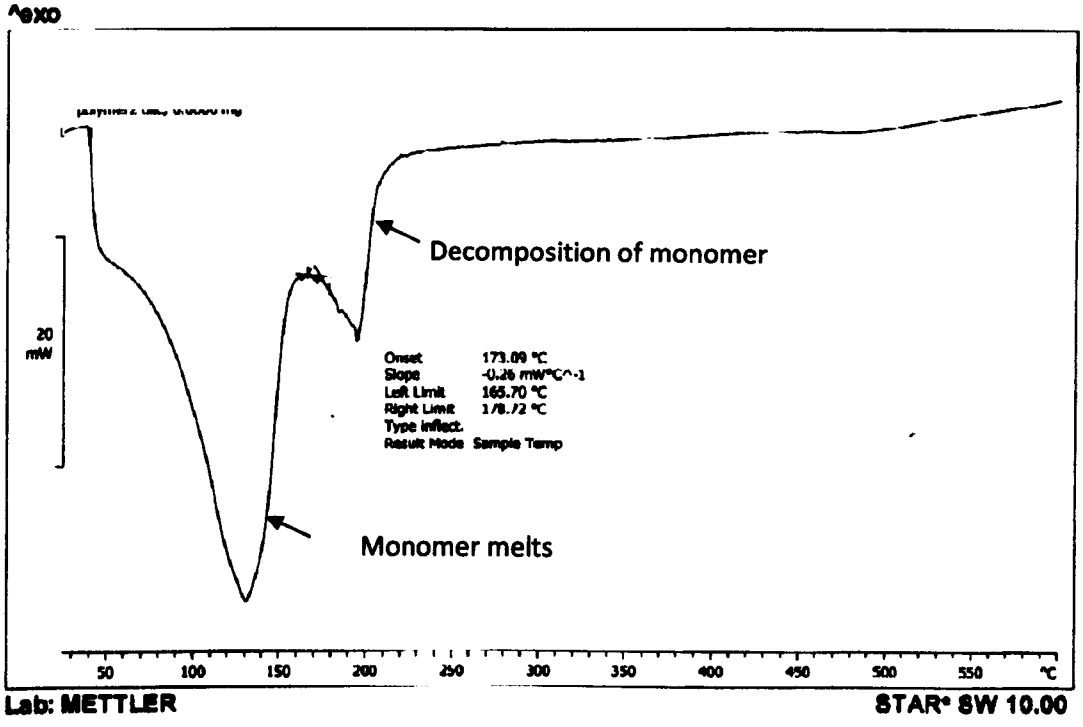


Figure 5.26 DSC of Monomer (2)

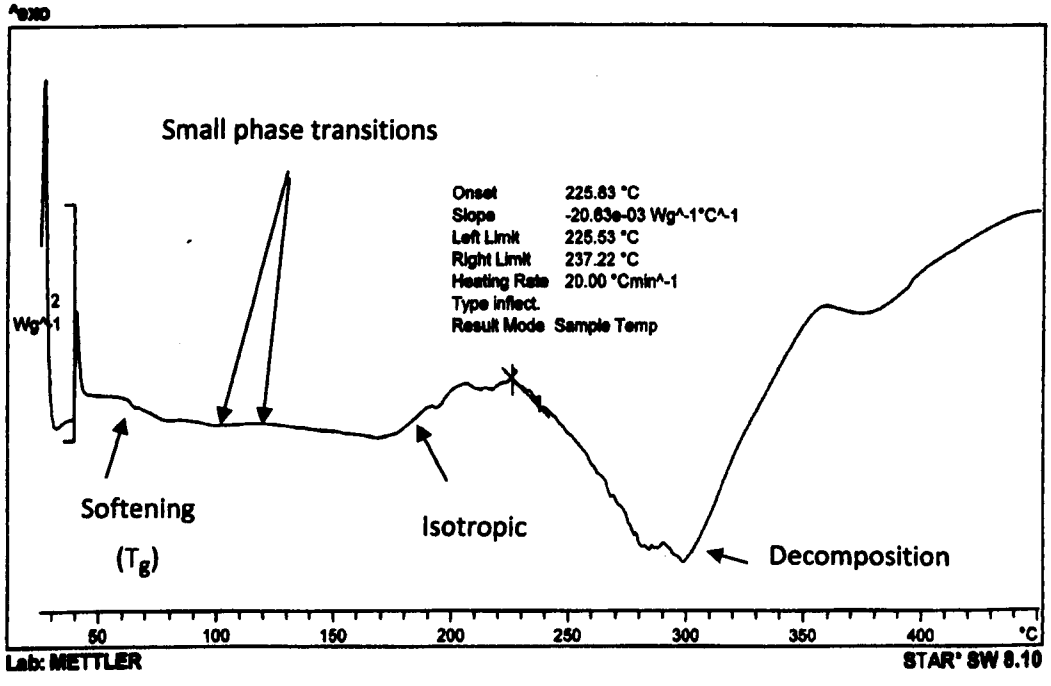


Figure 5.27 DSC of Polymer (2a)

5.19 Hot-Stage Microscopy

The liquid crystallinity of polymers (1a) and (2a) and monomers (1) and (2) were studied using hot-stage microscopy. Each monomer/polymer was cast on a cover slip and subjected to a temperature range of 25-300 ^{0}C, at a heating rate of 20 ^{0}C /min. The images of the different phase transitions and textures were recorded and some have been illustrated below (Figures 5.28 -34). As expected no phase transitions were observed in the case of monomers (1) and (2); however interesting nematic textures were observed for polymers (1a) and (2a). Cross polarisers were used to observe the colours and textures and also to determine when the polymers had reached the isotropic state, when no light could pass through the material and a dark/black image was observed. The isotropic phase is when the polymer has become a liquid due to complete loss of order. Liquid crystals can move in and out of the isotropic phase before the formation of a new phase occurs.

Polymer (1a) – Images taken

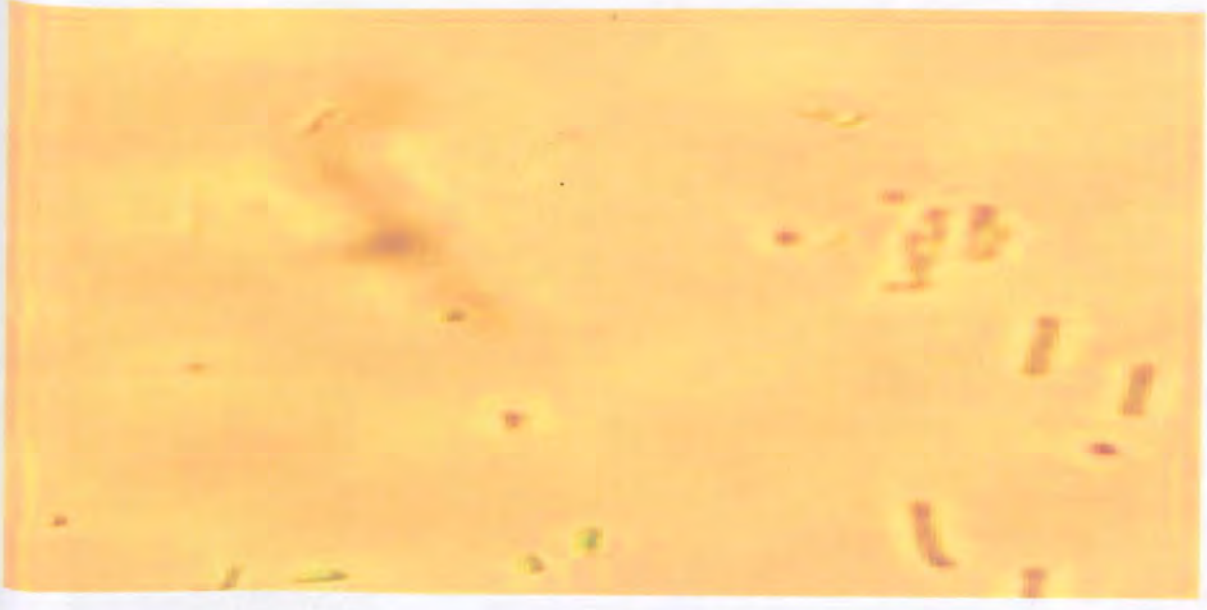


Figure 5.28- Polymer (1a) At room temperature. [image (x50)]

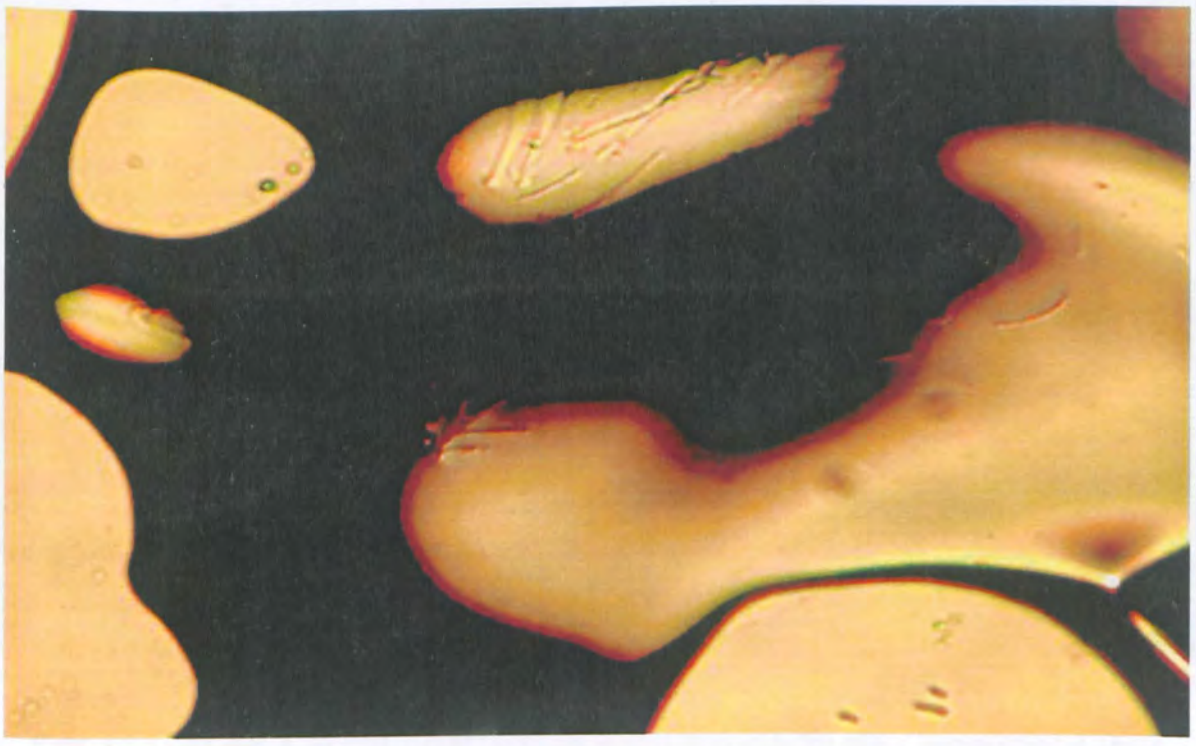


Figure 5.29 At 70^{0}C polymer (1a) begins to soften/melt, gradual loss in order. [image (x50)]

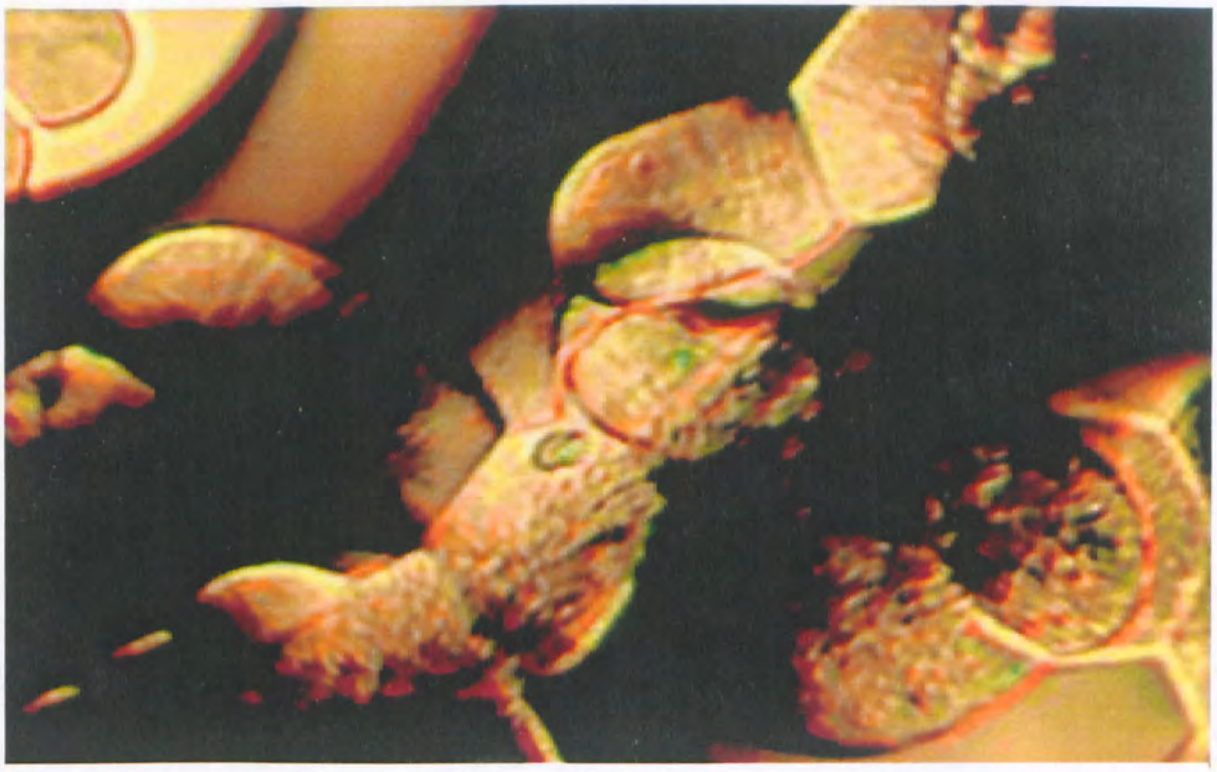


Figure 5.30 120-230 ^{0}C Polymer (1a) displays Nematic textures. More ordered than isotropic phase and colours and textures can be observed. Transition from Isotropic to Nematic was quite acute and sharp. [Image (x50)]

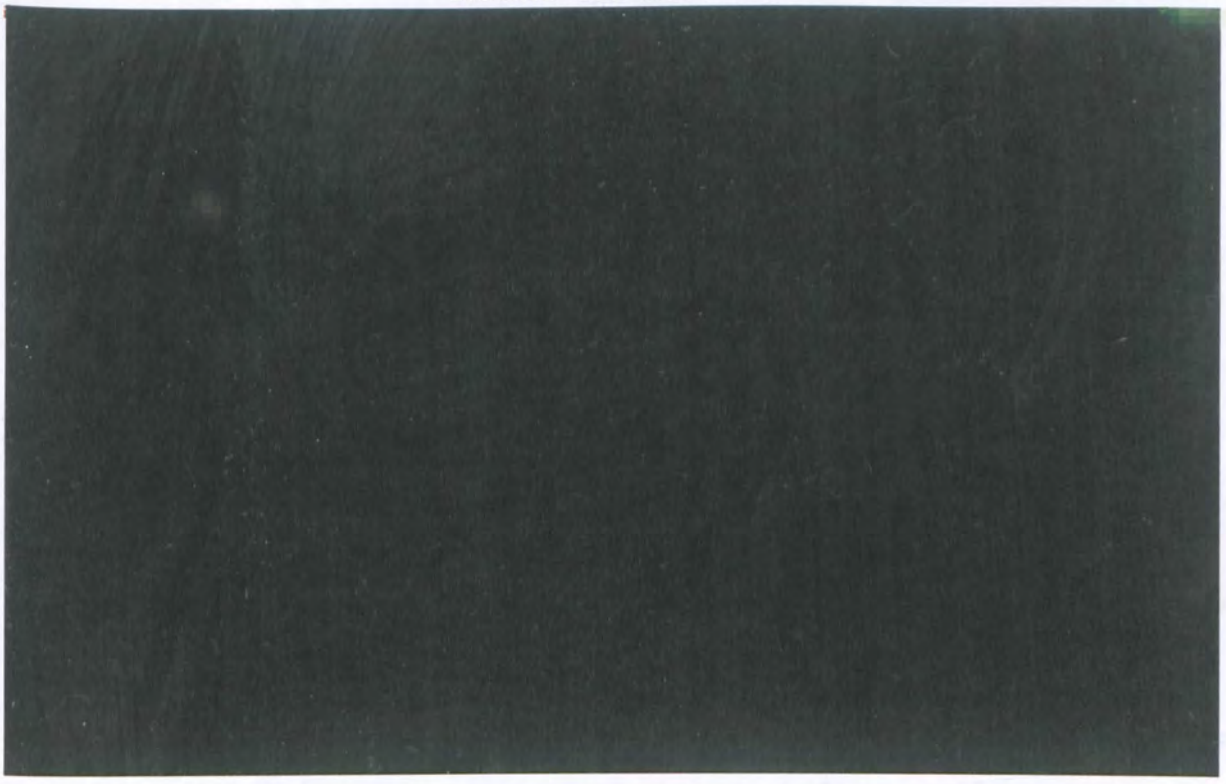


Figure 5.31 At 245 ^{0}C Polymer (1a) becomes isotropic liquid. No other liquid crystal phase transitions were observed above this temperature. This can defined as the clearing point of polymer (1a). [Image (x50)]

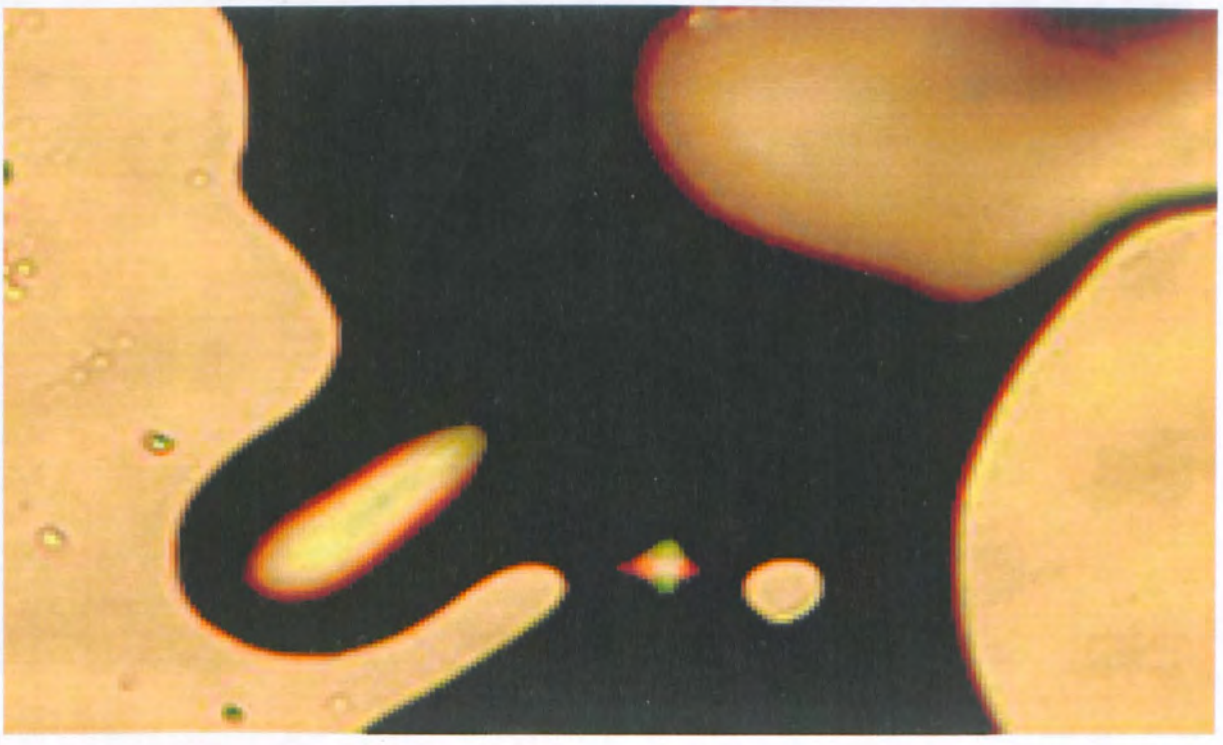


Figure 5.32 At 75 ^{0}C, Polymer (2a) begins to soften. [Image (x50)]

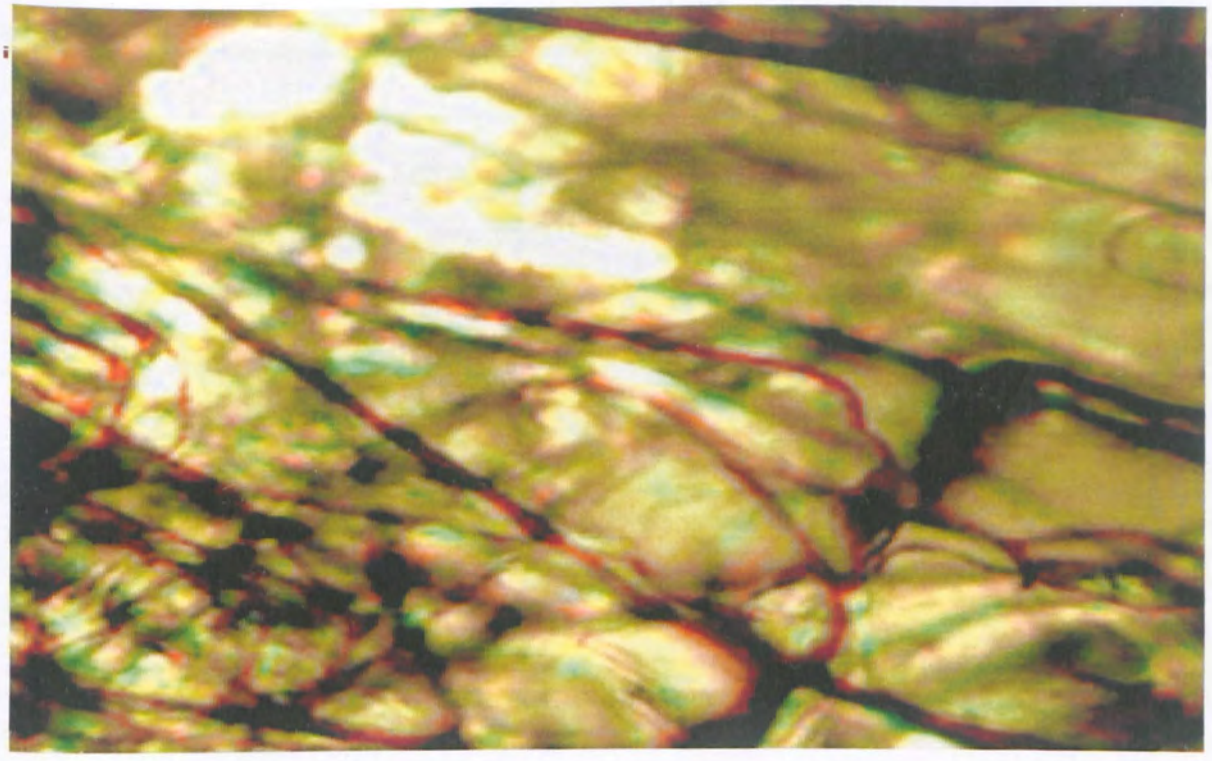


Figure 5.33 At 110-175 ^{0}C – Textured Nematic phase observed. More ordered than polymer (1a). Transition from Isotropic to Nematic was quite acute and sharp. [Image (x50)]

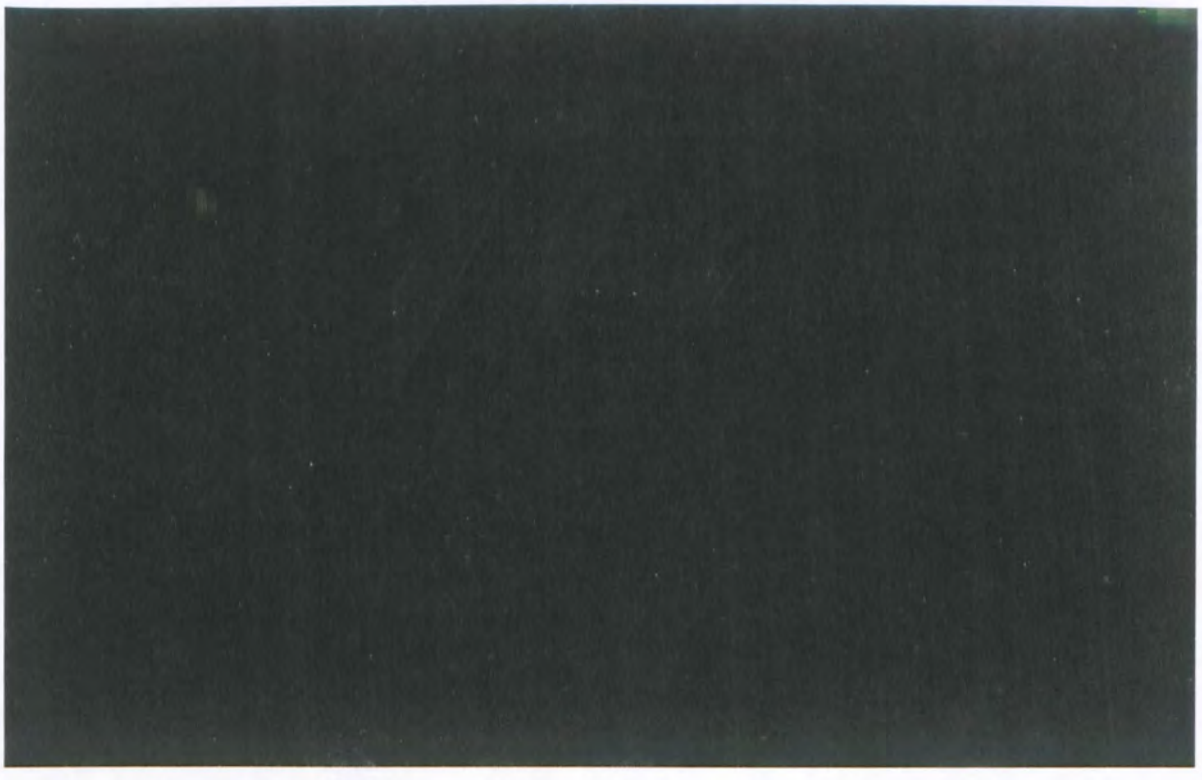


Figure 5.34 At 195 ^{0}C – Polymer (2a) loses order and becomes a liquid again. (N→I). [Image (x50)]

The images observed using hot-stage microscopy were consistent with the results of the DSCs. However polymer (2a) was expected to undergo an additional phase transition, approximately at a temperature of 180-230 ^{0}C. The DSC curve began to rise indicating that an exothermic process was occurring. It was predicted that polymer (2a) may undergo a transition from the nematic phase to a crystalline state but this was not observed under the hot-stage microscope. It was suggested that this peak may have been due to carbon dioxide formation or free radical formation as the polymer decomposes, both of which are exothermic processes.