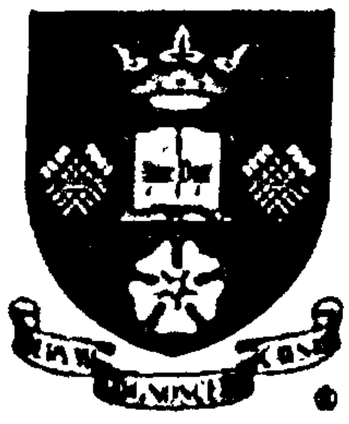
An investigation into the synthesis and characterisation of three materials based on poly (vinyl acetate)



By Stephen Collins

Doctoral thesis submitted in partial requirment for the award of Doctor of Philosophy.

Dept of Chemistry, University of Sheffield

July 2004

Declaration

This thesis is submitted for the degree of Doctor of Philosophy (PhD) at the University of Sheffield, having been submitted for no other degree. It records the research project carried out in the Polymer Centre, Dept of Chemistry, from December 2000 to December 2003. The work is entirely original except where due reference is made.

Signed: [redacted]

Date: 1st July 2024

Acknowledgements

This thesis is dedicated to my parents, without their support and guidance, none of this would have been possible.

I would like to thank my girlfriend Christine, who has managed to keep me sane through the trials of writing this thesis, and the people in the laboratory in which I conducted my research.

I would like to acknowledge Dr B. F. Taylor and S. Bradshaw for 400MHz NMR experiments, and N. Scorah for triple detection SEC.

I would like to thank the effort that John and Dan the departmental glass blowers have put in with construction and repair of high vacuum equipment used in my research.

Special thanks goes to Dr S. Rimmer, my supervisor, for the exemplary guidance, encouragement and supervision he has shown throughout the course of my research.

Abstract

An investigation into the synthesis of three types of material based on poly (vinyl acetate) was performed using three novel polymerisation techniques. The three techniques used were: i) the use of chain transfer to solvent; ii) the use of enzymes to catalyse the synthesis of block copolymers of vinyl acetate and ε-caprolactone; iii) the synthesis of hyperbranched polymers of vinyl acetate and n-vinyl pyrrolidinone, monomers which both propagate through an unstabilised radical.

The first technique has been widely used in order to synthesise polymers and oligomers with solvent derived endgroups. In this work polymers have been synthesised using isopropanol, 2-isopropoxy ethanol and 3-methyl-2-butanone as solvents. All of these have been shown to be active as chain transfer agents in previous studies.

The second technique builds on previous work, performed in the field of enzymatic control of polymerisation reactions. Enzymes can be used to both synthesise monomers and catalyse the polymerisation of monomers. Hydroxy terminated poly (vinyl acetate) was used to control the polymerisation of ε-caprolactone, leading to the formation of block copolymers.

The third technique involves the synthesis of hyperbranched poly (vinyl acetate) and poly (n-vinyl pyrrolidinone). This was achieved through the use of a polymerisable branching agent, also with the ability to act as a chain transfer agent. Through the use of this as a comonomer a hyperbranched polymer can be synthesised without the formation of a crosslinked gel.

Part 1: The synthesis of hydroxy terminated poly (vinyl acetate)

1.Introduction to the synthesis of hydroxy terminated poly (vinyl acetate)

The production of low molecular weight polymers, or oligomers (from the Greek, *oligos* - little/few, *meros* - part), is a goal of many research groups throughout the polymer community. Such polymers exhibit different properties to relatively high molecular weight polymers. The difference between an oligomer and a polymer is often defined in terms of their properties: the properties of oligomers are largely dependent on the end group structures, whereas a polymer's properties are regarded as independent of the end group functionality.

Another aspect is the synthesis and use of telechelic oligomers. The term telechelic is a combination of "*tele*", Greek for "far" and "chelic", which is derived from "*chela*" which are claws or pincers (17^{th} Century New Latin from the Greek *khele*), and indicating that reactive sites are widely separated. The Greek letters α and ω are also used to denote oligomers that have functionality at both chain ends. There are many reported methods of producing telechelic oligomers, a review by Jerome *et al*[1] details many of the methods that can be used to synthesise these useful compounds.

The methods available to the polymer chemist for the synthesis of telechelic oligomers can be divided into 6 types of reaction: living anionic; living cationic; controlled radical; radical transfer; constructive degradation; and stoichiometric control. Of these, radical transfer can be divided into 3 types: conventional transfer to a transfer agent; reversible addition fragmentation transfer (RAFT);

and catalytic chain transfer. These reactions are governed by the change in enthalpy when the monomer is converted into polymer. Entropicly the polymerisation reaction is unfavourable, as large ordered molecules are being formed from single molecules in a disordered state. Polymerisation reactions have a ceiling temperature above which they do not occur, because at higher temperature the entropic term is becoming bigger.

1.1. Living polymerisations

Living polymerisation is often used to synthesise polymers of narrow polydispersity in order to investigate their properties. They are used in the main to check the agreement of a theory to the experimental result. In an ideal living polymerisation, the active chain-end remains able to propagate after all the monomer is consumed and the polymerisation is free of chain transfer and termination steps. Addition of more monomer results in further polymerisation, addition of a chain capping or terminating agent kills the living end. A living polymerisation can be distinguished by plotting molecular weight against conversion of monomer; in living polymerisation the molecular weight is directly proportional to the degree of conversion. It was Flory that noted that the degree of polymerisation in a living system would be equal to the concentration of monomer divided by the concentration of the initiator. This allows a good deal of control of the molecular weight produced by such polymerisations. However, for some monomers, chain-end stabilisers are needed, and polymerisations may have to be performed at low temperatures. A good general review of living polymerisation techniques was published by Webster[2].

1.1.1. Living anionic polymerisation

In living anionic polymerisation the propagating species is an anion, this anion remains at the chain end until it is killed by the addition of a proton-containing terminating agent. The major monomer classes to be polymerised by anionic methods includes styrenes, dienes, methacrylates, acrylates, ethylene oxide and lactones, of these styrenic monomers have been studied in depth. For these polymerisations two initiators in use include butyl lithium and sodium napthalenide. Butyl lithium gives a polymer with one active chain end, sodium napthalenide a polymer with two active ends. The use of these initiators with different monomers can lead to the formation of well defined block copolymers. Zune *et al*[3] have performed a study of the propagating centre of methacrylic monomers in anionic polymerisations. In this study the interaction of oligo (*tert*-butyl methacrylate) with lithium 2-(2-methoxyethoxy)ethoxide was investigated. Kobayashi *et al*[4] have studied the synthesis of poly (N,N-diethylacrylamide)s with methacrylamide end functional units. This was achieved through the use of N,N-dialkylmethacrylamides as terminating agents for the anionic polymerisation of N,N-diethylacrylamide.

Group transfer polymerisation (GTP)[5], can be used to synthesise telechelic polymers and oligomers. The use of functional initiators can lead to polymers with similarly functionalised ends. GTP is of particular use for the polymerisation of methacrylic monomers, that usually require low polymerisation temperatures. As with all living polymerisations, the rate of initiation must be greater than the rate of polymerisation in order to achieve control of molecular weight and minimise polydispersity.

1.1.2. Living cationic polymerisation

Living cationic polymerisation is more complex than its anionic counterpart, the carbenium ion chain ends, which are generated by initiation of electron rich monomers with strong protic acids, readily transfer β-protons to start new chains. This results in molecular weights being lower than the predicted values and many dead chain ends. In 1984, a method of avoiding this problem was reported for the polymerisation of vinyl ethers, with the chain ends "stored" as stable covalent iodides. The iodides were activated by Lewis acid catalysts in order to generate small amounts of active complexed carbenium ions. The activated ends insert monomers without chain transfer or termination. More recently a mixture of a strong protic acid and a Lewis base, which acts to stabilise the chain ends has been used in the living polymerisation of alkyl vinyl ethers[6].

Walch *et al*[7] have produced telechelic polyisobutylene with chlorine end-groups by the cationic polymerization of isobutylene in dichloromethane using a difunctional initiator, for example 2,5-dimethoxy-2,5-dimethylhexane and 2,5-dimethyl-2,5-hexanediol diacetate. Boron trichloride and titanium tetrachloride were used as catalysts.

Lang and Rimmer[8], have reported the synthesis of telechelic oligo(isobutyl vinyl ether)s using a technique known as *ab initio* cationic polymerization. In this work silyl enol ethers are alkylated by the propogating carbocation and this yields functionalised oligomers. All the reagents are added at the beginning of the reaction and the method relies on the rate of capping being only slightly less than the rate of propagation.

1.2. Controlled radical polymerisation

The main feature of conventional radical polymerisation is the simultaneous process of initiation, propagation chain transfer and termination reactions that it is subject to. Attempts have been made to control these reactions through the use of compounds that complex with the active radical to decrease its chances of reacting with anything other than monomer.

One method of controlling radical polymerization is the use of nitroxide to mediate the polymerization reaction. In 1994 Matyjaszewski's group published work on the "living" polymerization of vinyl acetate[9]. They used triisobutylaluminium complexed with 2,2'-bipyridyl and TEMPO; as the initiator.

A first order plot of conversion against time, gave straight lines, and this was taken as an indication of first order kinetics with respect to monomer, thus the monomer is involved in the rate limiting step. These plots also indicate that the active species concentration is constant. In order to get high a molecular weight polymer the reaction had to be taken to high conversion ≈80%, though the polydispersity remained low at around 1.3. However attempts to replicate this work have failed to confirm these results[10].

Another method of controlling free radical polymerisation is the use of a technique called atom transfer radical polymerisation (ATRP). In this technique transition metal catalysts are used to control the polymerisation reaction. Matyjaszewski and Sawamoto[11] have both performed much work in the field of ATRP. The use of ATRP to control the polymerization of vinyl acetate has long been a goal since the work of Matyjaszewski and Sawamoto *et al*[12]. More

recently work by Yang *et al*[13], Meyer *et al*[14], Haddleton *et al*[10, 15, 16] and Armes *et al*[17] have proved the usefulness of this technique.

1.3. Radical transfer polymerisation

In a radical polymerisation, the highly reactive propagating radical at the polymer chain end is prone to transfer, thus starting a new chain, whilst leaving a dead chain as result of the transfer. Unless the transfer is intramolecular, i.e. a backbiting reaction, the polymerisation results in low molecular weight polymers. The different types of transfer reactions that are used in the production of low molecular weight polymers are: Conventional chain transfer; Reversible addition-fragmentation transfer; and catalytic chain transfer.

1.3.1. Conventional chain transfer

Radical polymerisations are known to undergo transfer to several species, these include, transfer to solvent, transfer to polymer, transfer to monomer, and transfer to a chain transfer agent. There are many transfer agents in use, and these are often used as additives. Transfer agents are often organic compounds that contain labile bonds to hydrogen or, less frequently, other atoms. For example dodecanethiol (DDT) is commonly used[18] and the transfer constants for DDT and other well-studied agents have been published[19-21]. The transfer of the propagating radical will lead to a lower molecular weight polymer, if the transfer occurs to solvent, monomer or chain transfer agent. Branched polymers can occur when the transfer is to either another polymeric chain, or if the radical is transferred to a site on the same chain, the latter process is known as "back biting". Back biting occurs when the growing polymer chain, bends back on itself

and abstracts a proton from the chain. This terminates the growing radical but leaves a new radical site on the backbone of the chain. From this site the polymerisation continues, leaving a short section of polymer as a branch. Vinyl acetate is known to "back bite" and leads to short chain branching[22]. This reaction is increased at increasing temperature. Hence many workers polymerise vinyl acetate at as low a temperature as possible to minimize the branching, although it cannot be completely suppressed. For this reason, some workers have attempted to produce unbranched, syndiotactic PVAc from poly (vinyl pivalate)[23]. Here the bulky side groups force the polymer into a syndiotactic conformation. The polymer chain is then acetylated, to give PVAc. In this case the polymerisation was performed at 0°C, and a photo active initiator was used, AIBN, which is also used as a temperature activated initiator.

A study by Hill *et al*[24] has investigated the phenomenon of transfer to solvent, in polymerizations of N-maleimides in THF. In this work it was discovered that the initiator, AIBN, fragmented and transferred to the solvent, forming solvent radicals, which then initiated the polymerisation. The polymers were analysed by ^{13}C NMR and MALDI-TOF mass spectrometry. It was found in the NMR that there were no peaks due to AIBN fragments, only THF fragment peaks were observed, the same also held true for the MALDI-TOF mass spectrometry, the peaks only showed the presence of THF fragments as the end groups of the polymer, with a hydrogen atom at the terminal end. This hydrogen was thought to come from a transfer to solvent, as there were no double bond peaks evident in the NMR, so termination by bimolecular disproportionation was ruled out. The molecular weight of the polymers was low and this was also taken as an indication of transfer to solvent.

Liu *et al*[25] note that the use of anionic polymerization, followed by capping the "living polymer" with suitable agents was previously used to synthesize telechelic

oligomers. Their work, however, is centered around the use of free radical polymerization and chemical modification. Here the authors performed a free radical polymerization of butyl methacrylate with thioglycolic acid as a chain transfer agent. The resulting mono-functional oligomer was then subjected to hydroxide-mediated saponification in order to give a telechelic polymer.

It has been noted that the three methods of introducing end functionality usually associated with free radical polymerization are: i) the use of functional initiators, ii) the use of functional termination agents and iii) control of the termination reaction. The incorporation of initiators into the polymer chain has been studied by Bevington *et al*[26] by the use of N^{15} NMR.

1.3.2. Reversible addition-fragmentation transfer (RAFT)

The principle behind RAFT polymerisation is that there are repeated reversible transfer events taking place throughout the course of the polymerisation, but the concentration of free radicals is constant. This has the effect of inducing equilibrium between dormant and living chains. Whilst RAFT can produce polymers of a pseudo living character similar to ATRP, it has been found that the two methods are complimentary. The techniques can be used to control the polymerisation of different monomers and in different media. An example would be the use of RAFT in heterogeneous reactions such as emulsion polymerisation. Another advantage of RAFT is it can be used to control the polymerisation of monomers bearing acidic groups. The synthesis of RAFT mediators however is not facile when compared with the synthesis of their ATRP initiator counterparts. Recently work by Wager *et al*[16] has looked into the conversion of ATRP initiators into RAFT mediators.

1.3.3. Catalytic chain transfer

Recently Boileau *et al*[27] have published work on the synthesis of telechelic polydimethylsiloxanes, which have terminal acetylenic groups. These oligomers were synthesized using a phase-transfer catalysis method. The reaction scheme is shown below.

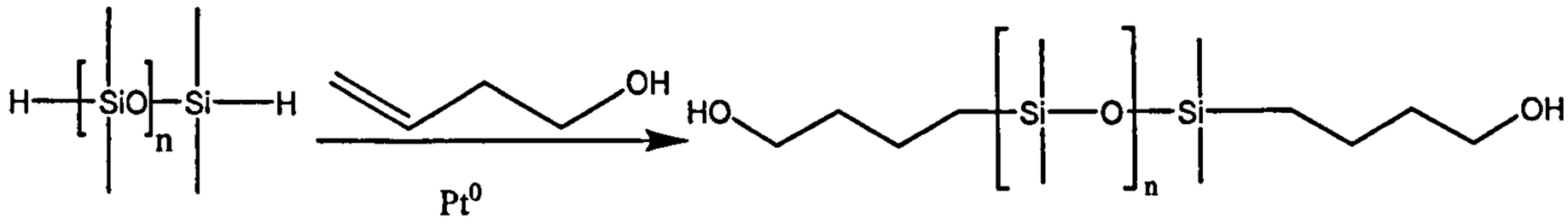


Figure 1-1 Reaction scheme showing synthesis of polydimethylsiloxanes

Gagne and Korn[28], have recently patented a method for the production of telechelic oligomers. Here the authors use a chain transfer agent and a catalytic amount of a alkali metal alkoxide to break down a polymer chain into smaller segments. The chain transfer agents used are esters in which the pK_a of the corresponding alcohol is in the same range as the pK_a of the primary leaving group of the polymer being depolymerised or broken down. By selecting a suitable chain transfer agent it is possible to react the oligomers further to form block copolymers.

1.4. Condensation reactions

Oligomers can be synthesised via the use of stoichiometric control of a condensation reaction. This method is used in the pre-polymer method of producing polyurethanes. A similar method has been followed by Hiltunen *et al*[29], who have synthesized lactic acid telechelic oligomers by the condensation polymerization of L-lactic acid and 1,4-butanediol or adipic acid, in the melt using tin octoate as a catalyst. Reaction with 1,4-butanediol leads to hydroxyl-

terminated oligomers, whereas reaction with adipic acid leads to carboxy terminated oliogmers. Prepolymers were synthesized with molecular weights in the range 2,800-18,000 $gmol^{-1}$, dependant on the amount of 1,4-butanediol, or adipic acid added.

1.5. Constructive degradation

Ebdon *et al*[30-34], have used ozonolysis of internal double bonds in order to create functionalised oligomers. In this procedure, methyl methacrylate was polymerized with 1,3-butadiene, to form a polymer containing internal double bonds. These double bonds are susceptible to cleavage through the use of ozone. The resulting ozonides were subject to reductive workup by the use of zinc powder in acetic acid at 0°C, to leave hydroxyl or aldehyde terminated methyl methacrylate oligomers, whereas an oxidative workup using sodium periodate yielded carboxyl or ketone endgroups.

1.6. Other methods

Sawaguchi *et al*[35, 36], have used controlled thermal degradation in order to form telechelic oligomers with isopropenyl end groups from polyproplyene. Here the polymers are degraded at 370°C for time periods between 30-90 mins. It was discovered that the functionality of the formed oligomers decreases with decreasing molecular weight of the parent polymer, to this end work was performed on measuring any increase in functionality of the oligomers by increasing the initial molecular weight of the starting polymers.

Helminen *et al*[37-39] have worked on crosslinked polymers synthesized from dimethacryl ε-caprolactone, L-lactide or D,L-lactide oligomers. These oligomers were then crosslinked thermally with dibenzoyl peroxide at 120°C.

1.7. Applications to vinyl acetate

It must be noted that none of the above mentioned methods for the production of oligomers can be applied to vinyl acetate at the present time. Living anionic and living cationic are of little use as the monomer is unable to support the propagating ion. It is only recently that Sawamoto[12] has reported the use of an iron-based catalyst that is applicable to vinyl acetate polymerisation. Conventional transfer techniques are also not suitable to use with vinyl acetate. Transfer agents such as DDT have mismatched transfer rates with respect to those of vinyl acetate, and therefore need to be fed in to the reaction gradually. Constructive degradation is of little use owing to its reliance on the copolymerisation of vinyl acetate with another monomer, usually a diene, which gives a random distribution of double bonds along the backbone of the polymer. However, dienes are not suitable comonomers in vinyl acetate copolymerisation. Similarly stoichiometric control is of little use.

Because of the above reasons, a different method has been employed in an attempt to synthesise end-functional vinyl acetate oligomers. The method used is known as chain transfer to solvent. Here a propagating solvent radical initiates a chain, the solvent is also acting as a transfer agent, but since the rate of transfer is comparatively low there is no need to feed the transfer agent into the reaction over time.

Research in the field of end-functionalised poly (vinyl acetate) is detailed herein. Previous work in this area [40-42], has focused on the enzyme modification of low molecular weight polymers. Here the polymers were reacted with various enzymes in order to try and cleave only one or two of the acetate groups from the polymer chain-end, leaving a polymer functionalised at both ends of the chain. It is thought that these polymers could then be further reacted in order to form amphiphilic networks, although the difficulty in forming block copolymers from vinyl acetate is reflected by a lack of published work in this area.

A general reaction scheme is shown below, with the transfer reactions highlighted. This shows the basic scheme by which the reaction is thought to occur. Initiator, I → two primary radicals, R·. A secondary radical S· can react with another radical, in which case the reaction does not proceed. The radical could also react with a monomer unit, M. The addition of monomer continues until another reaction causes it to end. The three reactions considered in the scheme below are disproportionation, combination and chain transfer. Of these three, combination and chain transfer occur with the most frequency.

When combination occurs, two polymer radicals terminate to give a polymer with mass equal to the sum of the two polymer radical molecules. When chain transfer occurs, the radical on the polymer chain abstracts a labile atom, Y (in this case hydrogen) from the chain transfer agent, S-Y, this terminates the polymer chain, and gives rise to a new transfer agent based radical.

$I \rightarrow 2R^{\bullet}$ $\quad$ $R^{\bullet} + S\text{-}Y \rightarrow S^{\bullet} + R\text{-}S$

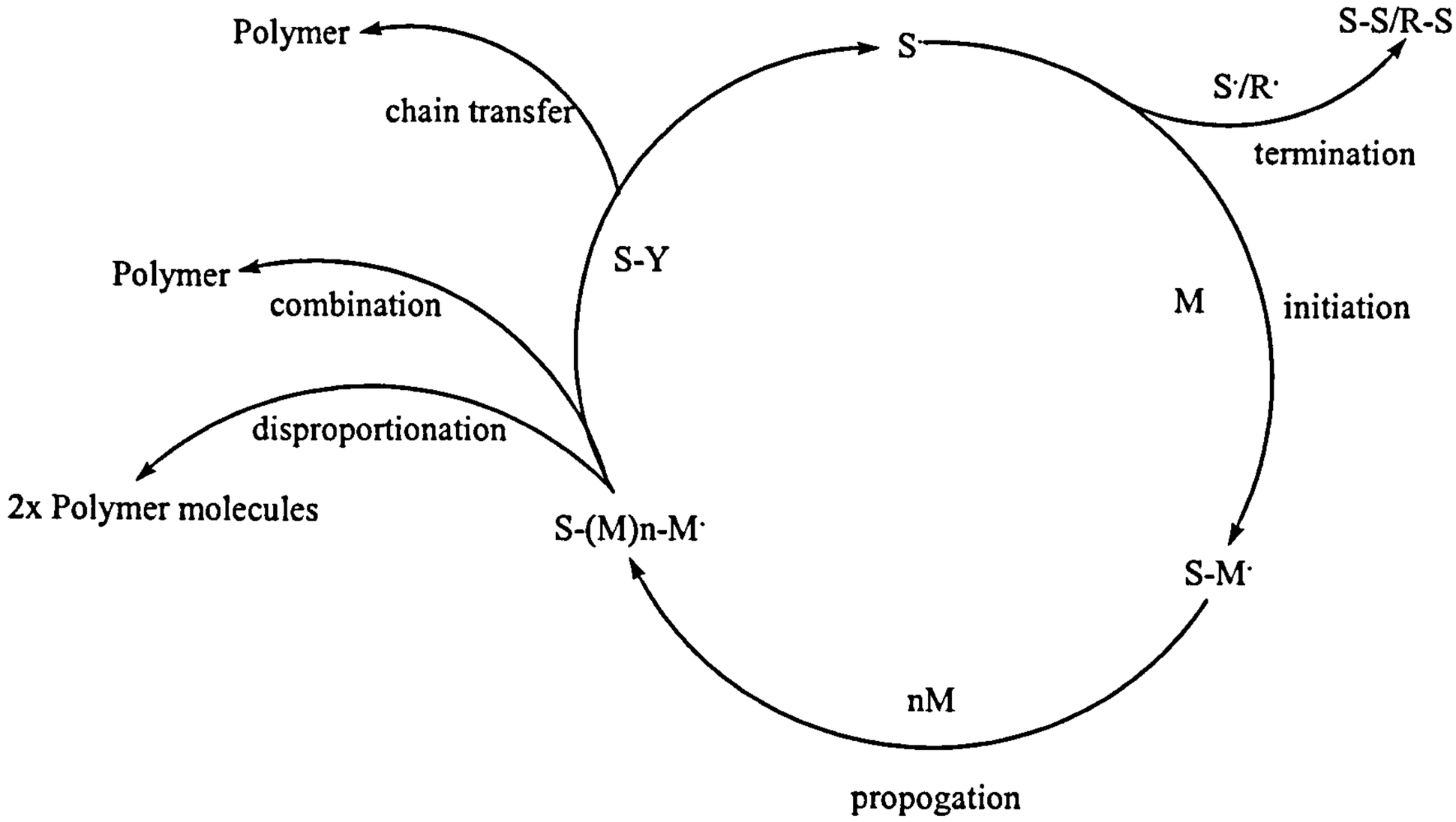


Figure 1-2 General reaction scheme for radical polymerisation

In the case of vinyl acetate, the general scheme is translated into the following reaction sequence, where the solvent is isopropanol.

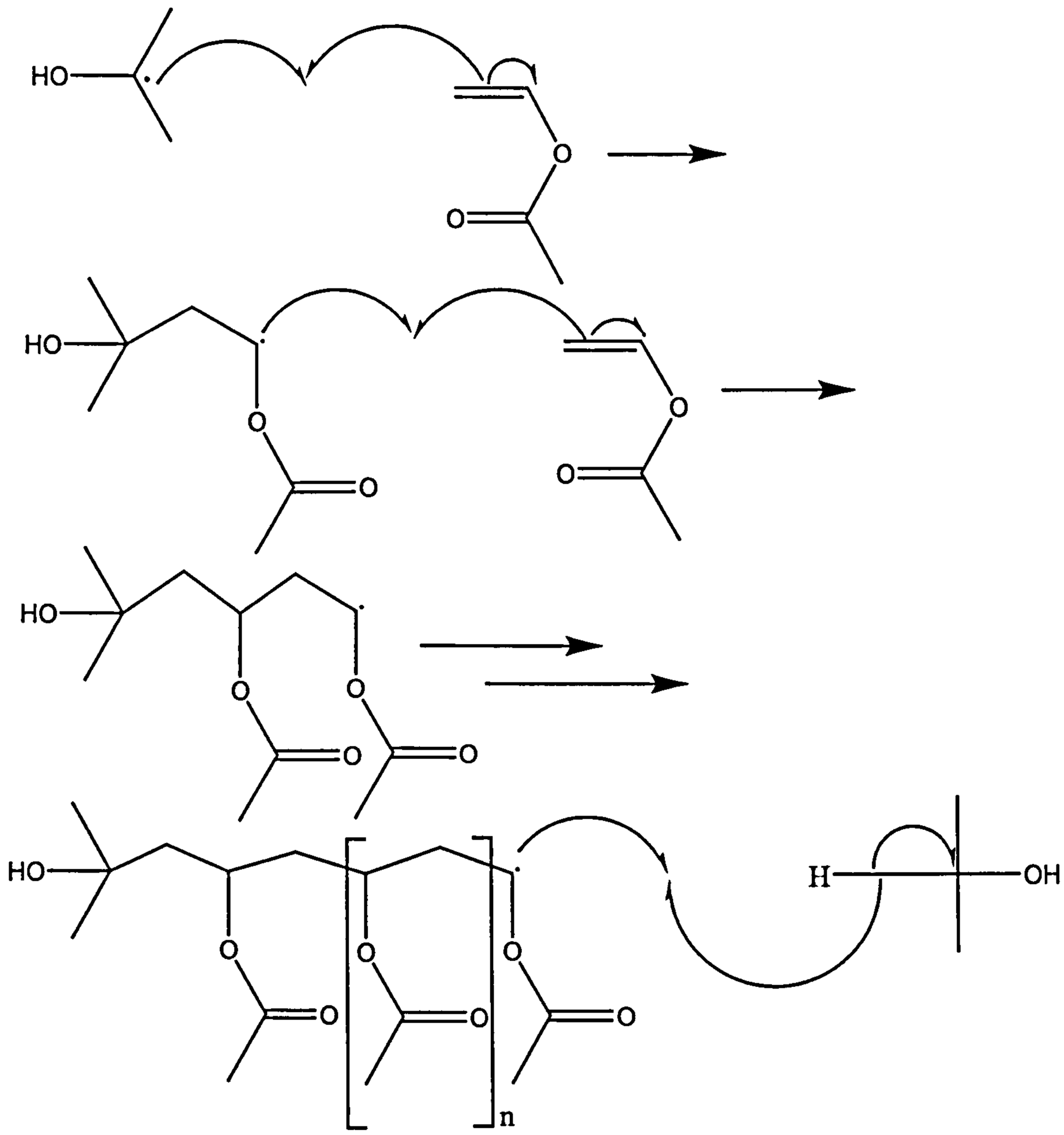


Figure 1-3 Diagram showing reaction pathway during synthesis of PVAc when subject to chain transfer to isopropanol

In the course of the study, the reaction kinetics of a polymerisation which was affected by the phenomenon of chain transfer to solvent were examined.

Other studies have also looked at the transfer of propagating radicals to monomer, Britton *et al*[43] have used ^{13}C NMR as a tool to look at the carbon center at the end of the polymer chain because this group has a signal in the NMR spectra that is not hidden by other peaks, unlike the branch point carbons. In this study we

have attempted to use ^{1}H NMR to justify the transfer to solvent, by looking for solvent endgroup based signals. Primarily these signals are from the methyl groups of isopropanol, which have a lower shift, and lower intensity than that of the methyl group of the acetate. Mass spectrometric methods have also been used in order to elucidate the end-groups of the polymers produced.

The polymerisations discussed in this chapter were performed in solvents that are known to have a tendency for chain transfer with the propagating vinyl acetate radical. The solvents used in this study were isopropanol, and 2-isopropoxy ethanol; methyl butanone was also used but the number of polymerisations was too small to be able to determine any useful kinetic data. It was thought that they would all act as transfer agents, but with different transfer rates. This was found to be the case. The advantage of this method of producing PVAc are that there is no other transfer agent in the reaction mixture, thus ensuring that hydroxy terminated oligomers are produced, and also by adjusting the ratio of monomer to solvent the molecular weight of the oligomer can be selected. Polymers made by this method had number average molecular weights ranging between 1000-23,000 $gmol^{-1}$, and by drawing a graph of molecular weight against solvent concentration, it was possible to select the weight of polymer used approximately to within a few hundred $gmol^{-1}$.

Usually, when studying the chain transfer constant of a polymerization, the concentration of the monomer is kept constant and the amount of the chain transfer agent is varied[44]. The total volume is kept constant with the use of an inert solvent. An inert solvent for the polymerisation of vinyl acetate is butyl acetate. However in the case presented here, the solvent was also acting as the transfer agent, so it is not inert. Thus the problem was how to evaluate the transfer constant, as the ratio of solvent to monomer was changing.

It was decided that a novel approach would be required in order to deal with this problem. The usual method used to evaluate chain transfer is by use of the Mayo equation[44]. However this treatment has the condition of constant monomer concentration. An alternative approach was to differentiate the Mayo equation with respect to monomer concentration, this then removes the need for constant monomer concentration. These differentials can then be used to draw a further graph in order to evaluate the transfer constant. The Mayo equation can be represented as

$$\frac{1}{X_n}=\left(\frac{1}{X_n}\right)_0+C_S\left(\frac{[S]}{[M]}\right)$$

Equation 1 The Mayo equation

where X_n = number average degree of polymerisation

$(1/X_n)_0$ = reciprocal number average degree of polymerisation at [S]=0

C_s = chain transfer constant

[S] = concentration of solvent

[M] = concentration of monomer

and the chain transfer constant can be obtained from the Mayo equation by plotting $1/X_n$ against [S]/[M] for a series of reactions, making the slope of the graph the chain transfer constant. This is true for conditions of constant monomer concentration therefore the reactions are only taken to low conversions. However, this condition cannot hold in these preparations where the solvent is acting as a chain transfer agent. Therefore in order to allow for the change in the solvent to

monomer ratio, the Mayo equation can be differentiated. The treatment of the equation follows.

From the Mayo equation we have

$$\frac{1}{X_n} = \left(\frac{1}{X_n}\right)_0 + C_S\left(\frac{[S]}{[M]}\right)$$

where $C_s = k_{tr}/k_p$

now

$$(X_n)_0 = {k_p[M]}\Big/{k_t[M^\bullet]} \qquad \text{where } [M^\bullet] = \left({2k_d[I]}\Big/{k_t}\right)^{\frac{1}{2}}$$

which can therefore be written as

$$(X_n)_0 = {k_p[M]}\Big/{k_t\left(2k_d[I]/k_t\right)^{\frac{1}{2}}}$$

and following from this

$$(X_n)_0 = {k_p[M]}\Big/{k_t^{\frac{1}{2}}\left(2k_d[I]\right)^{\frac{1}{2}}}$$

so we can write

$${1}\Big/{X_n} = \left({k_t^{\frac{1}{2}}\left(2k_d[I]\right)^{\frac{1}{2}}}\Big/{k_p[M]}\right) + C_s\left({[S]}\Big/{[M]}\right)$$

this can now be written as

$$1/X_n = C'/[M] + C_s([S]/[M]) \qquad \text{where } C' = \left(k_t^{\frac{1}{2}}\left(2k_d[I]^{\frac{1}{2}}\right)\right)/k_p$$

if this is now differentiated with respect to solvent concentration we get

$$\left(\partial(1/X_n)/\partial[S]\right)_{[M]} = 0 + C_s(1/[M])$$

using this equation we can evaluate C_s, simply by plotting

$$\left(\partial(1/X_n)/\partial[S]\right) vs \left(1/[M]\right)$$

this treatment gives the gradient = C_s, with the intercept at zero.

The chain transfer constants quoted within this thesis were evaluated using the graph drawing package *Microcal Origin6*. This was used in order to evaluate the partial differential $\partial(1/X_n)/\partial[S]$. A graph of $1/X_n$ against [S] was then plotted, and then the program was used to differentiate the graph. The resulting differentials, were then re-plotted against 1/[M] in order to obtain C_s.

Work by Heuts *et al*[19] has compared the Mayo treatment for working out the chain transfer constant, with an alternate method called the Chain Length Distribution (CLD) procedure. The procedure takes the high molecular weight slope of the number molecular weight distribution, P(M), plotted as ln(P(M)) vs M. The high molecular weight slope of this plot is denoted as Λ_{high}, it is related to the kinetic parameters by the following equation

$\Lambda_{high} = \lim_{M\to\infty} \frac{d\ln(P(M))}{d[M]} = -\left(\frac{\langle k_t\rangle[R^\bullet]}{\langle k_t\rangle[M]} + C_M + C_S\frac{[S]}{[M]}\right)\frac{1}{M_0}$. Compare this to the Mayo equation $1/X_n = k_t^{\frac{1}{2}}(2k_d[I])^{\frac{1}{2}}/k_p[M] + C_s([S]/[M])$, and the similarity between the two is clear. Moad and Moad[20], have shown that for a chain transfer

dominated system, the Mayo procedure and CLD procedure are in complete equivalence. They used both methods to calculate the chain transfer for the polymerization of methyl methacrylate with n-dodecane thiol as the transfer agent. Their results show that both treatments give good results for the chain transfer constant and the results are consistent. The equations used by the different methods are essentially the same, in fact the only difference between the Mayo treatment and the CLD treatment is that in the latter the termination term of the equation is not dependant on the fraction of termination by disproportionation. This work also highlights the problems of the two methods for the calculation of the chain transfer constant. It is taken that M_n calculated from SEC is the least reliable of the average molecular weights obtained using this technique, and the authors suggest that a slightly more reliable method of determining M_n is to halve the value for M_w. However it is also stated in the paper that this is only valid where the polymerization is dominated by chain transfer, excepting for very low molecular weight polymers.

However the method of differentiating the Mayo equation means that the absolute molecular weight is not needed. The differentiation means that it is the change in molecular weight that is important.

2.Synthesis of hydroxy-terminated poly (vinyl acetate)

2.1. Materials

Vinyl acetate (Aldrich) was purified by passing through an inhibitor removal column (Aldrich) before fractional distillation using a 30x3cm column filled with 5mm glass beads, lagged with glass wool and aluminium foil (the fraction at 73°C collected). Isopropanol (IPA) was dried by reflux over calcium hydride, before distillation. 2-isopropoxy ethanol (2IPE)(Aldrich) was used as received. Azobisisobutyronitrile (AIBN) was recrystallised from diethyl ether. 3-methyl-2-butanone (MB) was used as received.

2.2. Methods

2.2.1. Method 1

To a 100ml ampoule, fitted with a B10 cone, and with a constriction half way down the length of the neck, a solution of vinyl acetate, solvent (either IPA or 2IPE), and initiator (AIBN) was added. The reaction mixture was prepared as follows: using a graduated pipette, solvent was added to a beaker which was placed on a magnetic stirrer; a PTFE follower was added, followed by a known mass of the initiator, AIBN; this was left stirring for 5 minutes, after this time a

known amount of vinyl acetate was added and the stirring continued for another minute. The ampoule was then clamped upright and a syringe and needle were clamped above the ampoule so that the needle passed the constriction in the neck of the ampoule. The contents of the beaker were then poured into the barrel of the syringe and the plunger was inserted in order to force the contents into the ampoule. This was repeated until all of the solution had been added to the ampoule. The contents of the ampoule were then degassed using 4 freeze-pump-thaw cycles, on a vacuum line at 10^{-5}mbar, before the ampoule was flame sealed. The compositions of the reactions are shown in table 1.

The ampoules were then kept in a freezer until a batch of ampoules was ready. Once a batch was ready, they were polymerised in a thermostatically controlled water bath set at 60°C. The polymerisations were left to react for 4 hr 15 mins. Once the ampoules had been left in the water bath to react for the allotted time, the reactions were quenched by placing the ampoules first into a bowl of ice water, and stored in a freezer until they could be worked up. The ampoules were removed from the freezer and allowed to thaw, they were then opened and the contents poured from the ampoule into a round bottomed flask. The ampoule was then rinsed with several small aliquots of THF, to ensure that all of the polymer was removed from the ampoule.

Solvent and excess monomer were removed, firstly on a rotary evaporator, and finally by connection to a high vacuum line. The polymers were isolated in this way in order to avoid fractionation of the polymer. The polymers were isolated as clear, colourless viscous liquids.

Sample	Vol Solvent /ml	Amount solvent /mol	Vol monomer /ml	Amount monomer /mol	Mass Initiator /mg	Amount Initiator /mol	Solvent type
cs1/2/1	55	0.72	5	0.05	53	0.000323	IPA
cs1/2/2	35	0.46	25	0.27	54	0.000329	IPA
cs1/5/1	50	0.65	10	0.11	53	0.000323	IPA
cs1/5/2	45	0.59	15	0.16	55	0.000335	IPA
cs1/5/3	40	0.52	20	0.22	55	0.000335	IPA
cs1/6/2	50	0.43	10	0.11	55	0.000335	2IPE
cs1/6/3	45	0.39	15	0.16	54	0.000329	2IPE
cs1/6/4	40	0.35	20	0.22	55	0.000335	2IPE
cs1/6/5	35	0.30	25	0.27	53	0.000323	2IPE
cs1/6/6	55	0.48	5	0.05	50.3	0.000306	2IPE

Figure 2-1 Table showing composition of reactions

2.2.2. Method 2

A further series of reactions was performed, using the same synthetic methods as described for method 1. This time however, the reactions were quenched after a period of 25 min. The compositions of the reactions are shown table 2.

Sample	Vol Solvent /ml	Amount Solvent /mol	Vol Monomer /ml	Amount Monomer /mol	Mass Initiator /mg	Amount Initiator /mol	Solvent type
cs1/9/1	55	0.72	5	0.05	52.4	0.000319	IPA
cs1/9/2	50	0.65	10	0.11	52.1	0.000317	IPA
cs1/9/3	45	0.59	15	0.16	52.1	0.000317	IPA
cs1/9/4	40	0.52	20	0.22	52.3	0.000319	IPA
cs1/10/5	35	0.46	25	0.27	50.8	0.000309	IPA
cs1/9/6	55	0.48	5	0.05	52.3	0.000319	2IPE
cs1/9/7	50	0.43	10	0.11	52.2	0.000318	2IPE
cs1/9/8	45	0.39	15	0.16	52.4	0.000319	2IPE
cs1/9/9	40	0.35	20	0.22	52.2	0.000318	2IPE
cs1/9/10	35	0.30	25	0.27	52.7	0.000321	2IPE
cs1/18/3	50	0.65	10	0.11	50	0.000305	IPA
cs1/18/4	47.5	0.62	12.5	0.14	50.5	0.000308	IPA
cs1/18/5	45	0.59	15	0.16	50.2	0.000306	IPA
cs1/18/6	42.5	0.56	17.5	0.19	50.3	0.000306	IPA
cs1/18/7	40	0.52	20	0.22	50.2	0.000306	IPA
cs1/18/8	37.5	0.49	22.5	0.24	50	0.000305	IPA
cs1/18/9	35	0.46	25	0.27	50.8	0.000309	IPA
cs1/18/10	55	0.48	5	0.05	50.7	0.000309	2IPE
cs1/18/11	50	0.43	10	0.11	50.4	0.000307	2IPE
cs1/18/12	45	0.39	15	0.16	50.7	0.000309	2IPE
cs1/18/13	40	0.35	20	0.22	50.7	0.000309	2IPE
cs1/18/14	35	0.30	25	0.27	50.4	0.000307	2IPE

Figure 2-2 Table showing composition of reactions

2.2.3. Method 3

A series of reactions were performed in order to evaluate the application of chain transfer to solvent as a means of producing oligomers. The synthetic method used was the same as method 1, except that the reactions were left for a period of 24 hours to react. An additional solvent was used for these reactions, 3-methyl-2-butanone. The compositions of the reactions are shown in table 3.

Sample	Vol solvent /ml	Amount solvent /mol	Vol monomer /ml	Amount monomer /mol	Mass initiator /mg	Amount initiator /mol	Solvent type
cs1/27/1	59.9	0.78	0.1	0.00	52.6	0.00032	IPA
cs1/27/2	59.3	0.77	0.7	0.01	53.1	0.000323	IPA
cs1/27/3	57.5	0.75	2.5	0.03	51.7	0.000315	IPA
cs1/27/4	55.6	0.73	4.4	0.05	53.1	0.000323	IPA
cs1/27/5	56.1	0.49	3.9	0.04	52.5	0.00032	2IPE
cs1/27/6	55.7	0.48	4.3	0.05	51.2	0.000312	2IPE
cs1/27/7	54.9	0.48	5.1	0.06	52.9	0.000322	2IPE
cs1/27/8	54.3	0.47	5.7	0.06	53.1	0.000323	2IPE
cs1/27/9	59	0.55	1	0.01	52.9	0.000322	MB
cs1/27/10	58	0.54	2	0.02	53.1	0.000323	MB
cs1/27/11	57	0.53	3	0.03	52.8	0.000322	MB
cs1/27/12	56	0.52	4	0.04	51.7	0.000315	MB

Figure 2-3 Table showing composition of reactions

2.2.4. Method 4

A series of polymerisation reactions were performed in order to test the suitability of a parallel synthesis robot (Chemspeed ASW2000) for the production of polymeric materials. Reagent bottles were filled with isopropanol, vinyl acetate, and a stock solution of AIBN dissolved in isopropanol (0.1089g in 100ml, 0.007mol dm^{-3}). Before the robot began the synthesis, the reagents were sparged with nitrogen for a period of 20 min. The reaction vessels which are jacketed to allow heating and cooling of its contents were purged with nitrogen before the reagents were added. The polymerisations were performed at 70°C for 2 hours with stirring. Once the allotted reaction time had passed, the reaction vessels were cooled to –20°C in order to quench the reaction. The reaction vessels were then removed from the robot so the polymeric products could be recovered. This was achieved by dissolving the polymer in THF to remove it from the reaction vessel. The polymer solution was then concentrated on a rotary evaporator in order to remove the solvent and any excess monomer. The samples were analysed by SEC. The compositions of the reactions are shown in table 4.

Sample	Vol solvent /ml	Vol initiator solution /ml	Vol monomer /ml	Amount monomer /mol
cs1/61/1	7	4	5	0.05
cs1/61/2	6	4	6	0.07
cs1/61/3	5	4	7	0.08
cs1/61/4	4	4	8	0.09
cs1/61/5	3	4	9	0.10
cs1/61/6	2	4	10	0.11
cs1/61/7	1	4	11	0.12
cs1/61/8	0	4	12	0.13

Figure 2-4 Table showing composition of reactions

3.Results and discussion for the synthesis of hydroxy terminated poly (vinyl acetate)

3.1. Method 1

The polymers produced using method 1 were isolated as clear colourless viscous liquids through the use of rotary evaporation of the solvent and excess monomer. This process worked well, but left polymers that on the whole were sticky amorphous masses, this made them extremely hard to remove from the round bottom flasks in which they were isolated with out losing some of the polymer produced. However, cooling in liquid nitrogen can be used to produce a more easily handled product. The polymer being of an amorphous nature now formed a clear colourless glass, which could be chipped out of the flask and placed into a sample vial. In many cases this operation had to be performed as quickly as possible as the lower molecular weight polymers tended to soften very quickly. One method of getting round the problem of the lower molecular weight polymers was to scrape the frozen polymer onto a watch glass, or petri dish which had a small amount of liquid nitrogen contained on it, the polymer then remained vitrified until it was scraped from the dish into the sample vial.

3.1.1. SEC results

The polymers thus isolated were dissolved in THF (2mg ml^{-1}) and subjected to analysis by size exclusion chromatography. The results are shown in table 1.

Table 3-1 Table showing SEC results

Sample	Mn /$gmol^{-1}$	Mw /$gmol^{-1}$	Pd	Solvent type
cs1/2/1	2100	3570	1.7	IPA
cs1/5/1	3590	7010	2.0	IPA
cs1/5/2	5150	10750	2.1	IPA
cs1/5/3	7020	15240	2.2	IPA
cs1/2/2	7640	17460	2.3	IPA
cs1/6/6	3190	6280	2.0	2IPE
cs1/6/2	5360	11200	2.1	2IPE
cs1/6/3	7900	17100	2.2	2IPE
cs1/6/4	9670	22400	2.3	2IPE
cs1/6/5	12200	28200	2.3	2IPE

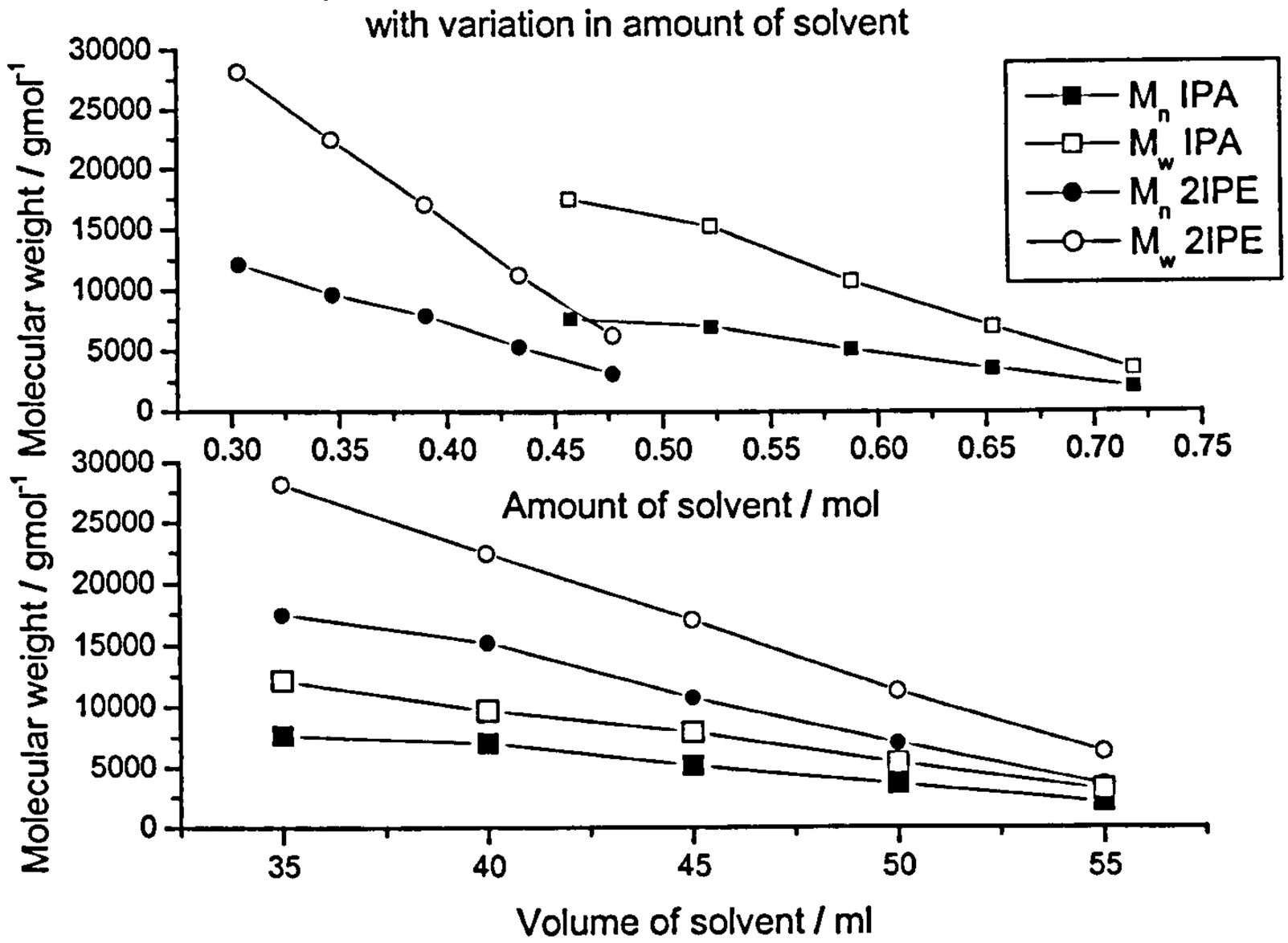


Figure 3-1 Graph showing the variation in molecular weight with variation in amount of solvent

The relationship between the amount of solvent and the molecular weight that is produced is shown in figure 1 quite clearly. The explanation for this trend is that as the amount of solvent is increased, the potential number of chain transfer events increases. Thus the molecular weight achieved decreases. Shown in figure 2 are some representative SEC chromatograms, showing a high molecular weight trace, medium molecular weight trace and a low molecular weight trace. On the low molecular weight trace, smaller peaks, attributable to oligomer species can be seen.

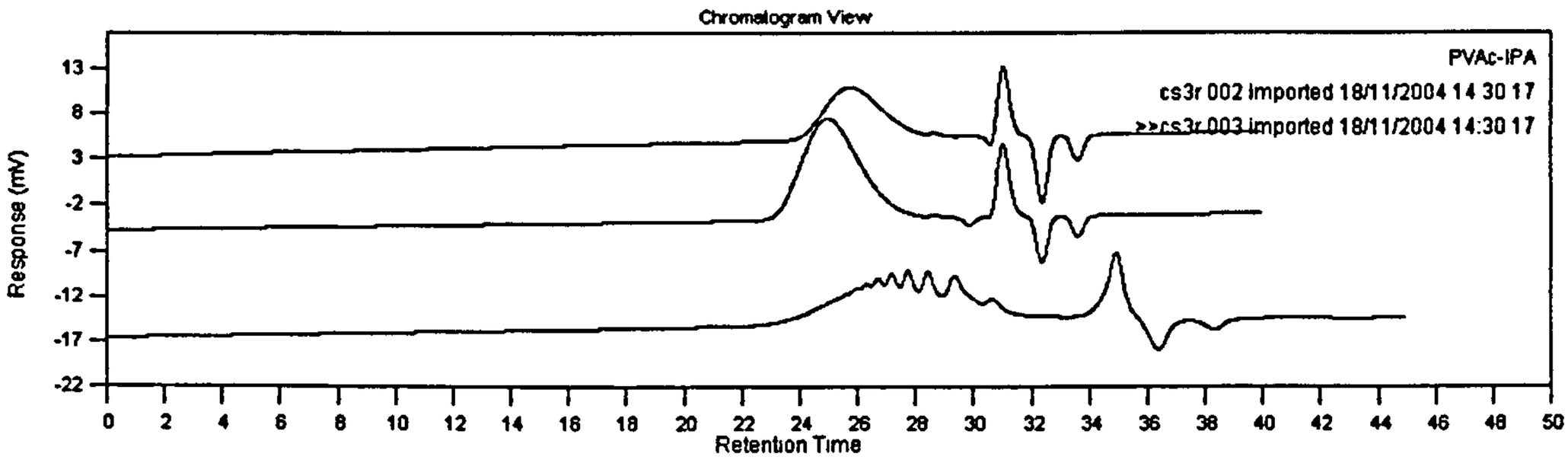


Figure 3-2 SEC chromatograms

3.2. Method 2

The polymers synthesised using this method were isolated using the same techniques as used for the polymers synthesised in method 1.

3.2.1. SEC results

The polymers thus isolated were dissolved in THF (2mg ml^{-1}) and were analysed by size exclusion chromatography. The SEC data was calibrated using polystyrene standards, the results were also corrected for poly (vinyl acetate)

using published Mark Houwink constants inputed into the SEC software. In table 2 are the SEC results, with the standard polystyrene calibration applied.

Table 3-2 Table showing SEC results

Sample	Mn /gmol^{-1}	Mw /gmol^{-1}	Pd	Solvent type
cs1/9/1	3030	5790	1.9	IPA
cs1/9/2	5320	11000	2.1	IPA
cs1/9/3	9270	17800	1.9	IPA
cs1/9/4	14900	27800	1.9	IPA
cs1/10//5	18400	33300	1.8	IPA
cs1/9/6	5080	10800	2.1	2IPE
cs1/9/7	10500	19600	1.9	2IPE
cs1/9/8	9640	20900	2.2	2IPE
cs1/9/9	20900	38500	1.8	2IPE
cs1/9/10	26900	46000	1.7	2IPE
cs1/18/3	6770	10200	1.5	IPA
cs1/18/4	6520	11400	1.8	IPA
cs1/18/5	9370	15100	1.6	IPA
cs1/18/6	11200	17700	1.6	IPA
cs1/18/7	12300	20000	1.6	IPA
cs1/18/8	13000	22400	1.7	IPA
cs1/18/9	14600	25100	1.7	IPA
cs1/18/10	3410	6220	1.8	2IPE
cs1/18/11	7990	13500	1.7	2IPE
cs1/18/12	13400	22800	1.7	2IPE
cs1/18/13	24400	40100	1.6	2IPE
cs1/18/14	31100	49300	1.6	2IPE

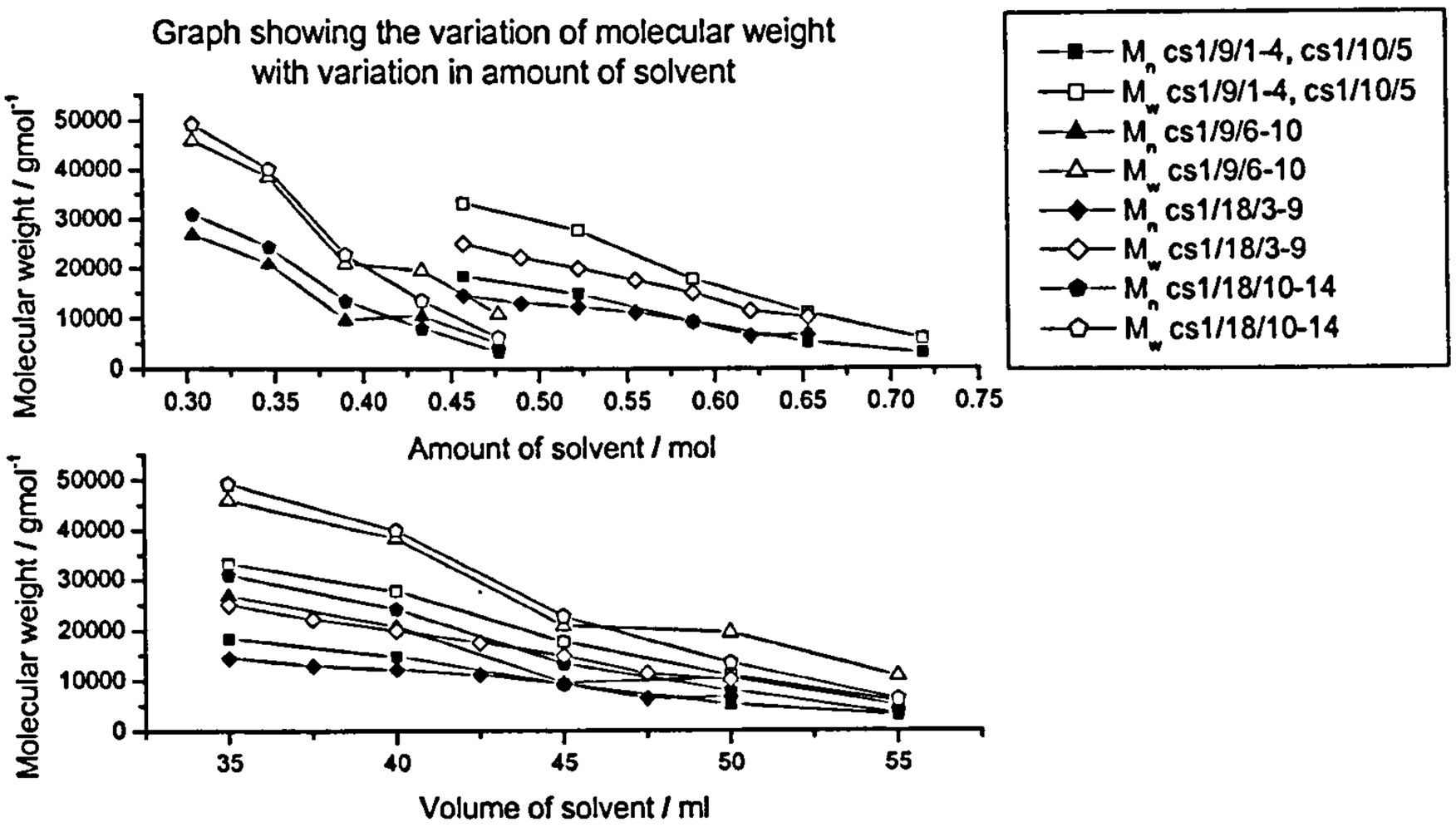


Figure 3-3 Graph showing the dependence of molecular weight on the amount of solvent

The results obtained from the SEC analysis of the polymers has been used in combination with a differentiated form of the Mayo equation to evaluate the chain transfer constant to solvent for the polymerisation of vinyl acetate. As explained previously it was necessary to differentiate the Mayo equation in order to remove the monomer concentration dependency of the equation. This monomer concentration dependency needed to be removed as the amount of monomer is usually kept constant when analysing the Mayo equation in order to obtain a transfer constant. In this case, however, the reaction conditions meant that the concentration of the monomer was changing, as was the ratio of solvent to monomer. This ratio is normally kept constant by the addition of a cosolvent, however the unstablised vinyl acetate radical has appreciable transfer constants to most solvents.

As discussed within the introduction to this section the Mayo equation is often written in the form

$$\frac{1}{X_n} = \left(\frac{1}{X_n}\right)_0 + C_s\left(\frac{[S]}{[M]}\right)$$

Equation 2 The mayo equation

where X_n = number average degree of polymerisation

$(1/X_n)_0$ = reciprocal number average degree of polymerisation at [S]=0

C_s = chain transfer constant

[S] = concentration of solvent

[M] = concentration of monomer

if this is now differentiated with respect to solvent concentration we get

$$\partial(1/X_n)/\partial[S] = 0 + C_s(1/[M])$$

Equation 3 Differentiated Mayo equation

using this equation we can evaluate C_s, simply by plotting

$$\partial(1/X_n)/\partial[S] \text{ vs } 1/[M]$$

this treatment gives the gradient = C_s, with the intercept at zero.

The chain transfer constants quoted within this thesis were evaluated using the graph drawing package *Microcal Origin6*. This was used in order to evaluate the partial differential $\partial(1/X_n)/\partial[S]$.

Here a graph of $1/X_n$ against [S] was plotted, and then the program was used to calculate the slope of the graph at points along the line. The resulting data, was then plotted against 1/[M] in order to obtain C_s. The graphs used in this work to evaluate C_s are shown below.

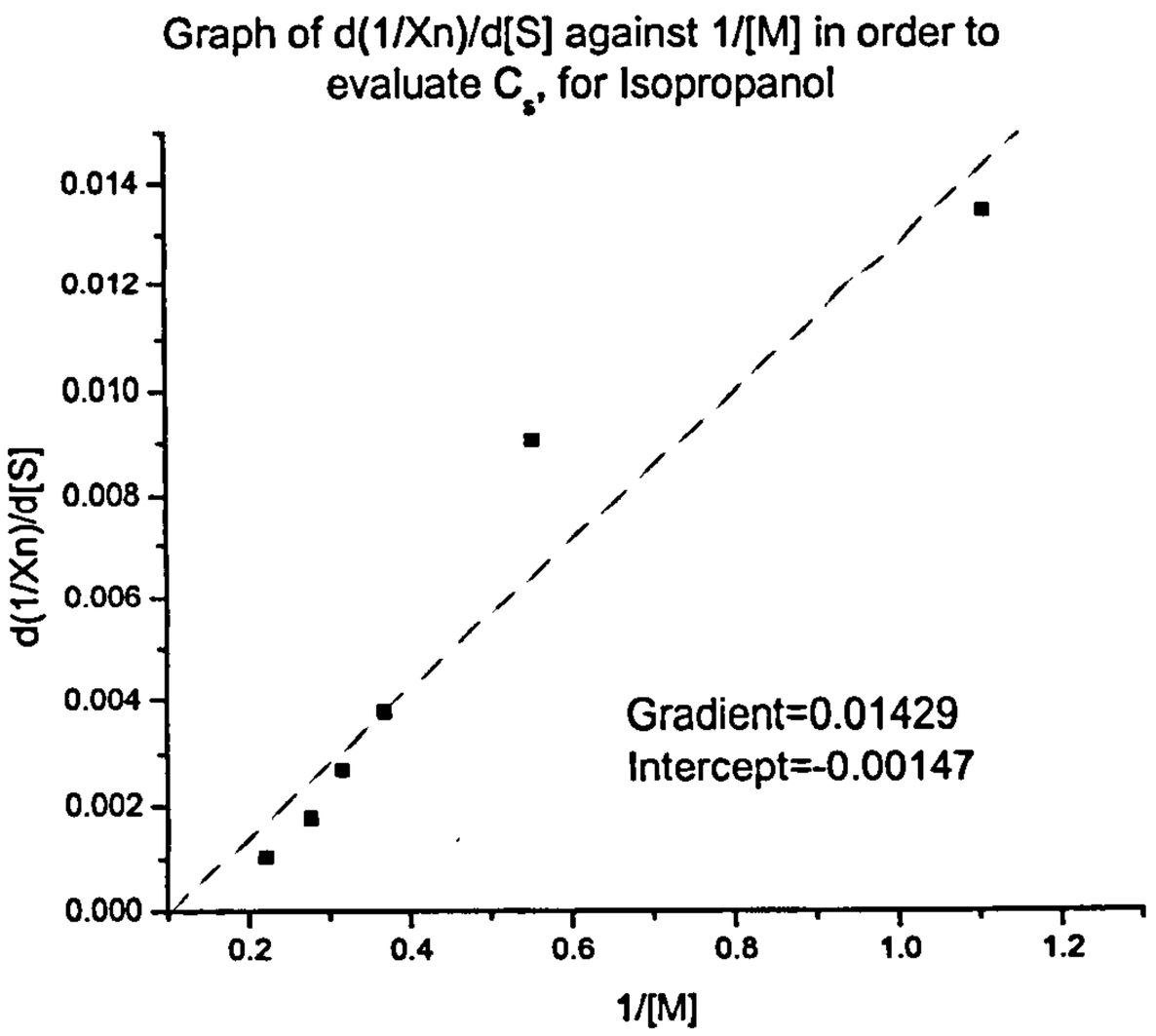


Figure 3-4 Graph used to determine C_s for isopropanol

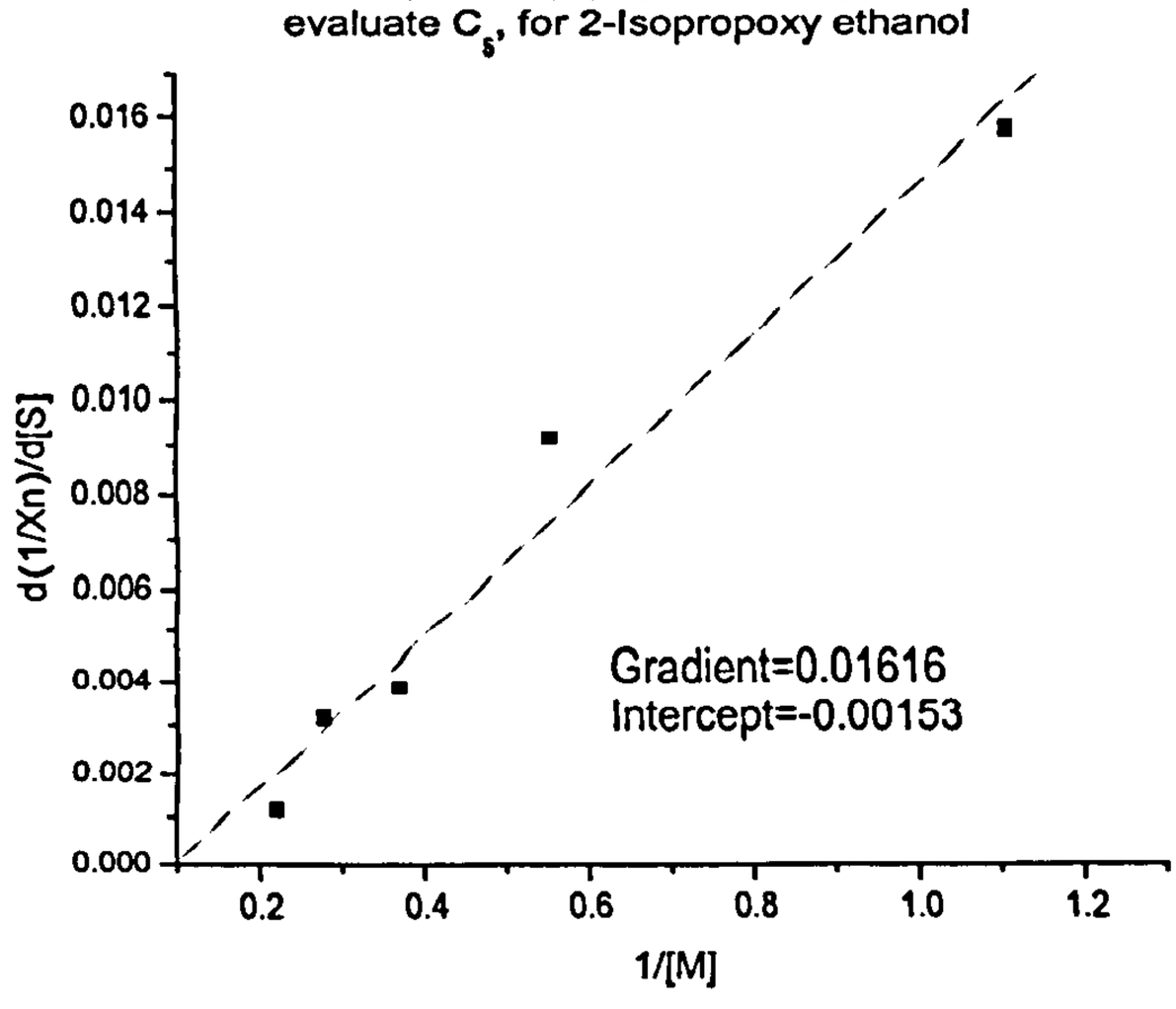


Figure 3-5 Graph used to determine C_s for 2-isopropoxy ethanol

The results of these graphs are interesting, both graphs are straight lines, and both have a similar but distinctly different gradient, from which the chain transfer constant is determined. The line of best fit was plotted by the graph package, and

it was noted that although the line did not go exactly through the origin, the lines for both graphs went through the same point, which was very close to the origin.

The value of the chain transfer constant is quite low for the two solvents investigated being 0.014 for isopropanol and 0.016 for 2-isopropoxy ethanol. Many commonly used chain transfer agents have transfer constants an order of magnitude or two orders of magnitude higher than the transfer constants for the solvents examined.

It is of course for this reason that this method of transfer was investigated, as conventional chain transfer agents have transfer constants far too large and are of little use for the control of vinyl acetate polymerisation, due to their extremely rapid transfer.

For a conventional transfer agent with Cs=1 then a 10:1 ratio of monomer to transfer agent will result in a polymer with an Mn=1000. However, for a similar result using the solvent as the only chain transfer agent, a much larger ratio of monomer:transfer agent (solvent) would be required for a similar result, this was found to be the case.

The results from the VPO experiments, are discussed in the following section. These would normally be used for the Mayo determination of the chain transfer constant, although because the method used here depends on the change in molecular weight, the absolute number average molecular weights obtained from these experiments are not necessary.

3.2.2. VPO results

The results from the VPO experiments, are shown in table 3. These would normally be used for the Mayo determination of the chain transfer constant, although because the method used here depends on the change in molecular weight, the absolute number average molecular weights obtained from these experiments are not necessary. It was found that results from the VPO experiments performed had poor reproducibility. Some of the polymers were examined more than once in an attempt to gain some consistency of reading, and although the values given by the osmometer gave a straight line with good values of R^2, the values for Mn were not consistent if the polymer was reanalysed. Also, after an attempt was made to recalibrate the machine, it was noticed that there appeared to be a problem with the solvent, and two sets of calibration data gave different answers for the calibration constant. The apparatus was recalibrated again this time with a different solvent, and when repeated, a reproducible calibration constant was achieved. The original solvent of choice was SEC grade THF, and it was thought that inconsistencies in the batches, and problems with the stabilizing agents might have caused the problems with the results, the second solvent used was HPLC grade Toluene, and this appeared to give much more consistent results. Much of the samples had been used up by the analysis process by this point, and so it was not possible to re-analyse some of the polymers via VPO, approximately 0.15g being required per set of measurements. Due to the low conversions of the VAc polymerisations, as little as 0.5g product yield were routinely obtained. Although the results in table 3 have not been used in the determination of the chain transfer constant, all the results obtained are presented in order to highlight the variation in the results.

Table 3-3 Table showing the results from VPO analysis

Sample	Solvent	Mn /gmol^{-1}
cs1/18/04	THF	4420
cs1/18/05	THF	5450
cs1/18/06	THF	5940
cs1/18/06	Toluene	6160
cs1/18/07	Toluene	4350
cs1/18/07	Toluene	5330
cs1/18/07	THF	7960
cs1/18/08	Toluene	5630
cs1/18/08	THF	7440
cs1/18/09	Toluene	7210
cs1/18/09	THF	10780
cs1/18/13	THF	3260
cs1/18/13	Toluene	6960
cs1/18/14	THF	3850
cs1/18/14	Toluene	9840
cs1/27/01	THF	300
cs1/27/02	THF	550
cs1/27/03	Toluene	1030
cs1/27/03	THF	1110
cs1/27/03	THF	1370
cs1/27/04	Toluene	1140
cs1/27/04	THF	1440
cs1/27/04	THF	2750
cs1/27/05	Toluene	1350
cs1/27/05	THF	1650
cs1/27/05	THF	1700
cs1/27/06	Toluene	1460
cs1/27/06	THF	1500
cs1/27/06	THF	1760
cs1/27/07	THF	1320
cs1/27/07	THF	1770
cs1/27/07	Toluene	1830
cs1/27/08	THF	1080
cs1/27/08	THF	1820
cs1/27/08	Toluene	1880
cs1/27/09	THF	430
cs1/27/10	THF	570
cs1/27/11	THF	570
cs1/27/12	THF	630

Data from SEC analysis was used due to problems with the consistency of the VPO data. VPO measurements were repeated up to 3 times for some samples but

it was found that between 3-61% variation in results for individual samples resulted; hence, SEC data was believed to be more reliable, and was certainly more reproducible.

3.2.3. NMR results

The polymers produced using the chain transfer to solvent method were further analysed through the use of NMR spectroscopy. In the NMR spectra shown, an attempt to assign the peaks present has been made in order to elucidate the structure of the polymers. The work by Ohnaga and Sato[41] has proved useful in assigning the NMR spectra presented here. As a comparison, a 250MHz ^{1}H spectrum of 45kgmol^{-1} commercial poly (vinyl acetate) has been included (fig 6). The lack of solvent endgroups for this polymer is apparent. The NMR spectra shown are those of polymers made in isopropanol (fig 7), and those made in 2-isopropoxy ethanol (fig 8). There are clear differences between the spectra, which can be attributed to the solvent. The structural differences between the solvents leads to additional peaks in the spectrum of the polymer synthesised in 2-isopropoxy ethanol. The peaks are due to the additional CH_2's that are present in that solvent. All the samples were run on a 400MHz NMR spectrometer, unless stated otherwise; the ^{13}C spectra were run overnight.

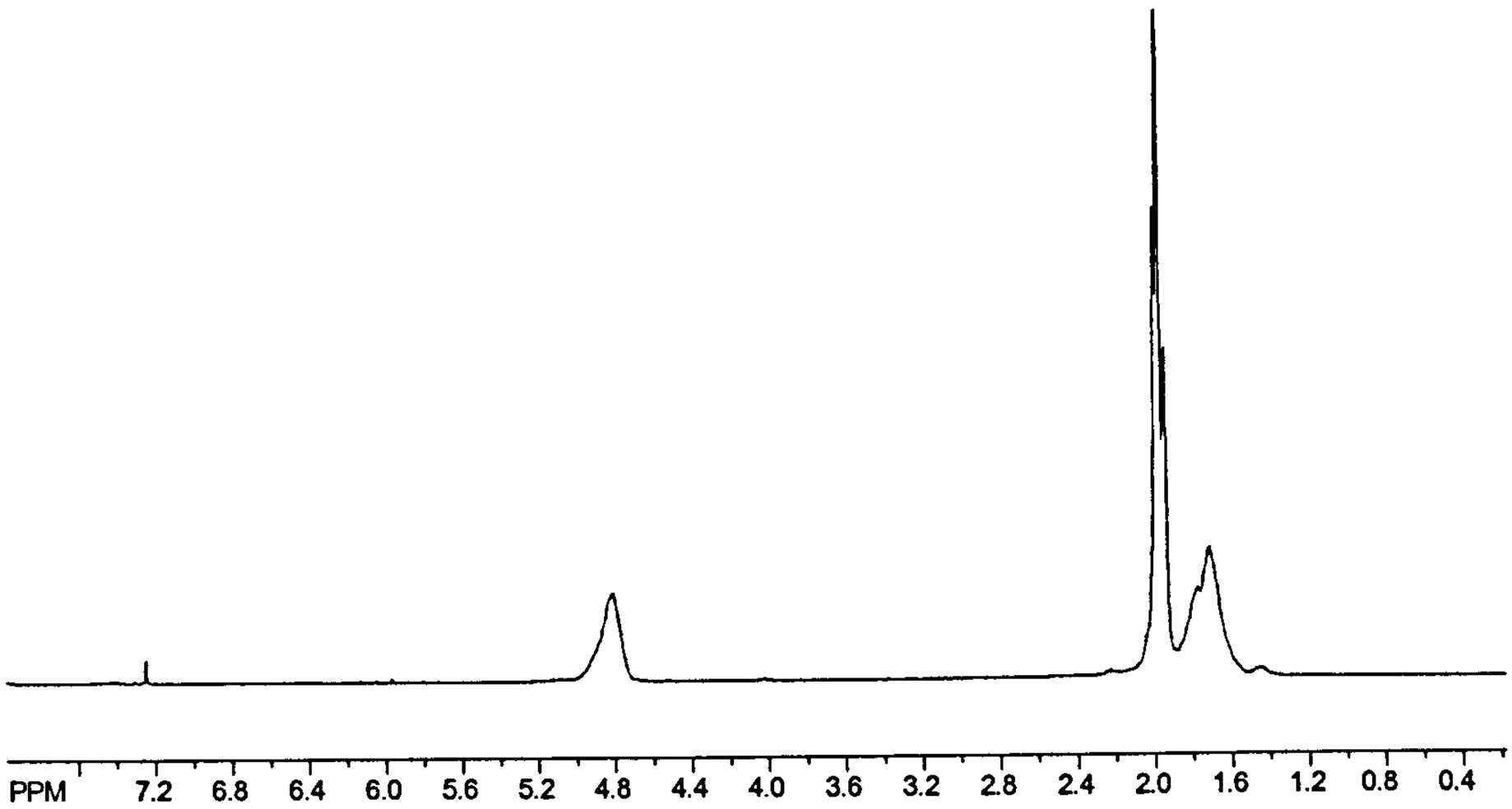


Figure 3-6 ^{1}H NMR spectrum of commercial PVAc

The NMR spectrum shown in figure 6 is of commercially available poly (vinyl acetate) of 45,000 gmol^{-1}, here the peaks are assigned as: backbone C*H* δ≈4.8; backbone CH_2 δ≈1.7; ultimate CH_2 δ≈4.0; pendant methoxy CH_3 δ≈2.0; $CDCl_3$ δ≈7.25.

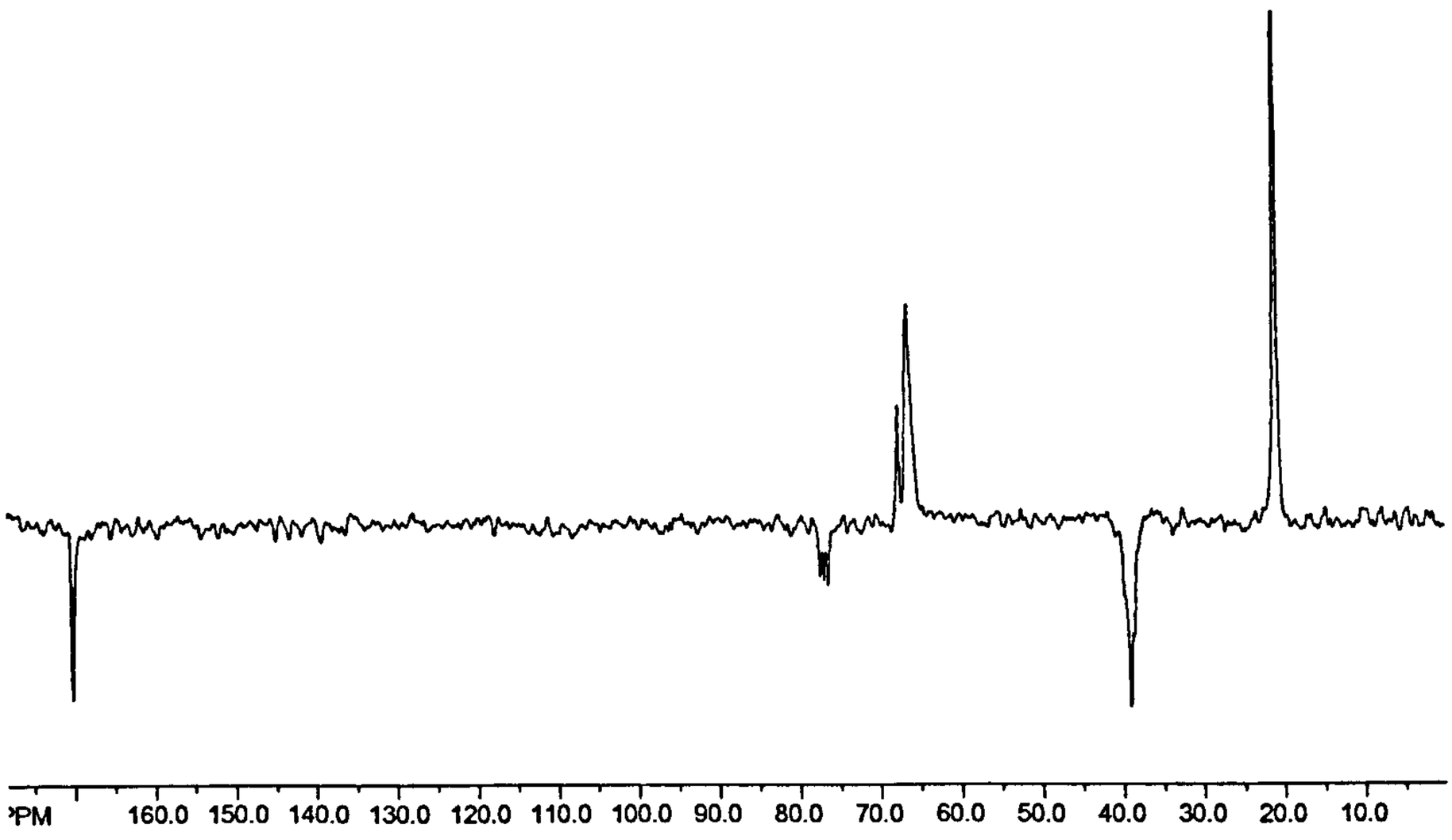


Figure 3-7 ^{13}C PENDANT NMR spectrum of commercial PVAc

The NMR spectrum shown in figure 7 is of commercially available poly (vinyl acetate) of 45,000 $gmol^{-1}$, here the peaks are assigned as: backbone C*H* δ≈66; backbone CH_2 δ≈39; pendant methoxy CH_3 δ≈21; carbonyl δ≈170; $CDCl_3$ δ≈77.

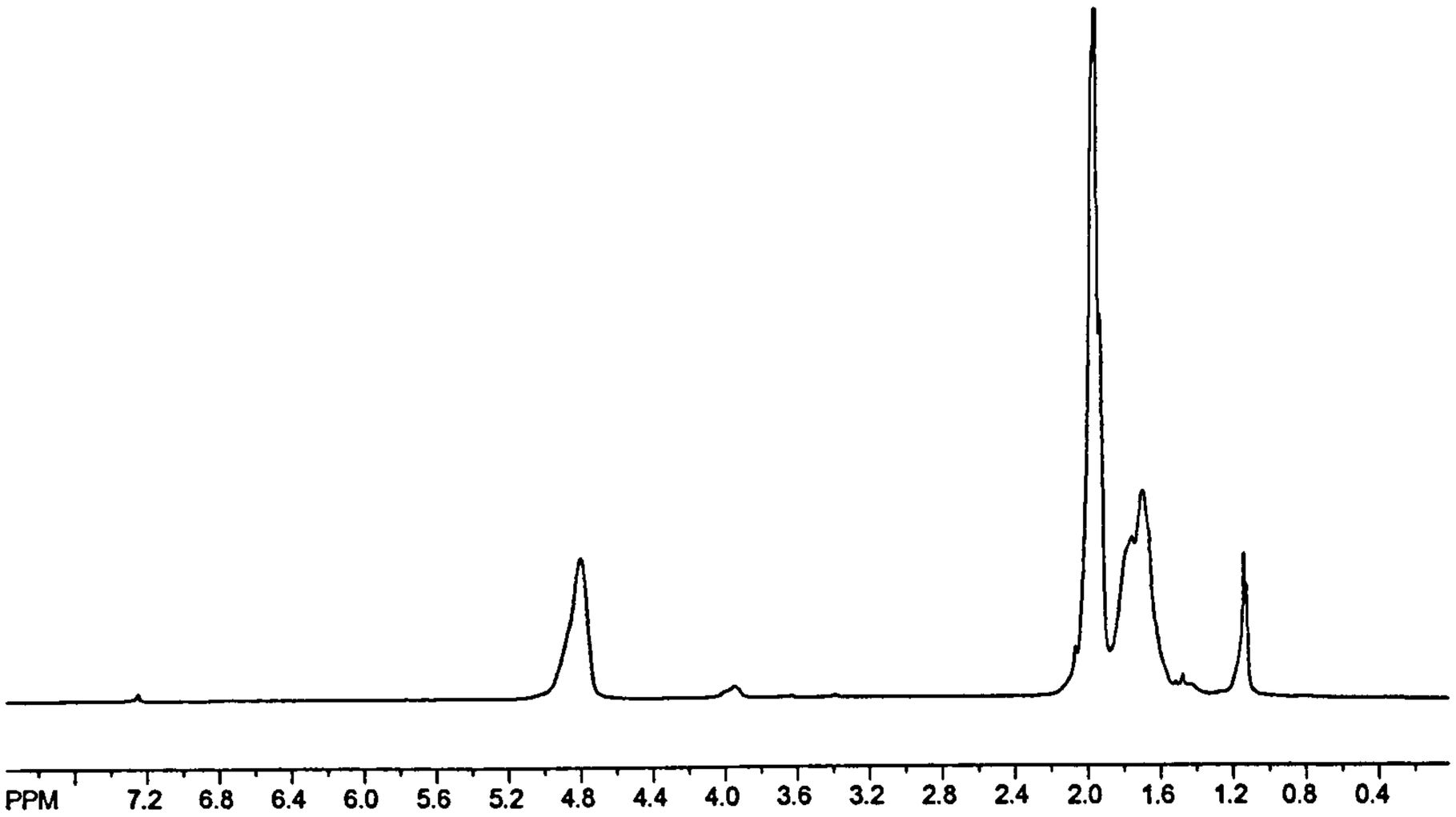


Figure 3-8 ^{1}H NMR spectrum of PVAc synthesised in isopropanol

The NMR spectrum shown in figure 8 is of poly (vinyl acetate) synthesized in isopropanol, the assignments are: backbone C*H* δ≈4.8; backbone CH_2 δ≈1.7; pendant methoxy CH_3 δ≈2.0; endgroup methyl δ≈1.1.

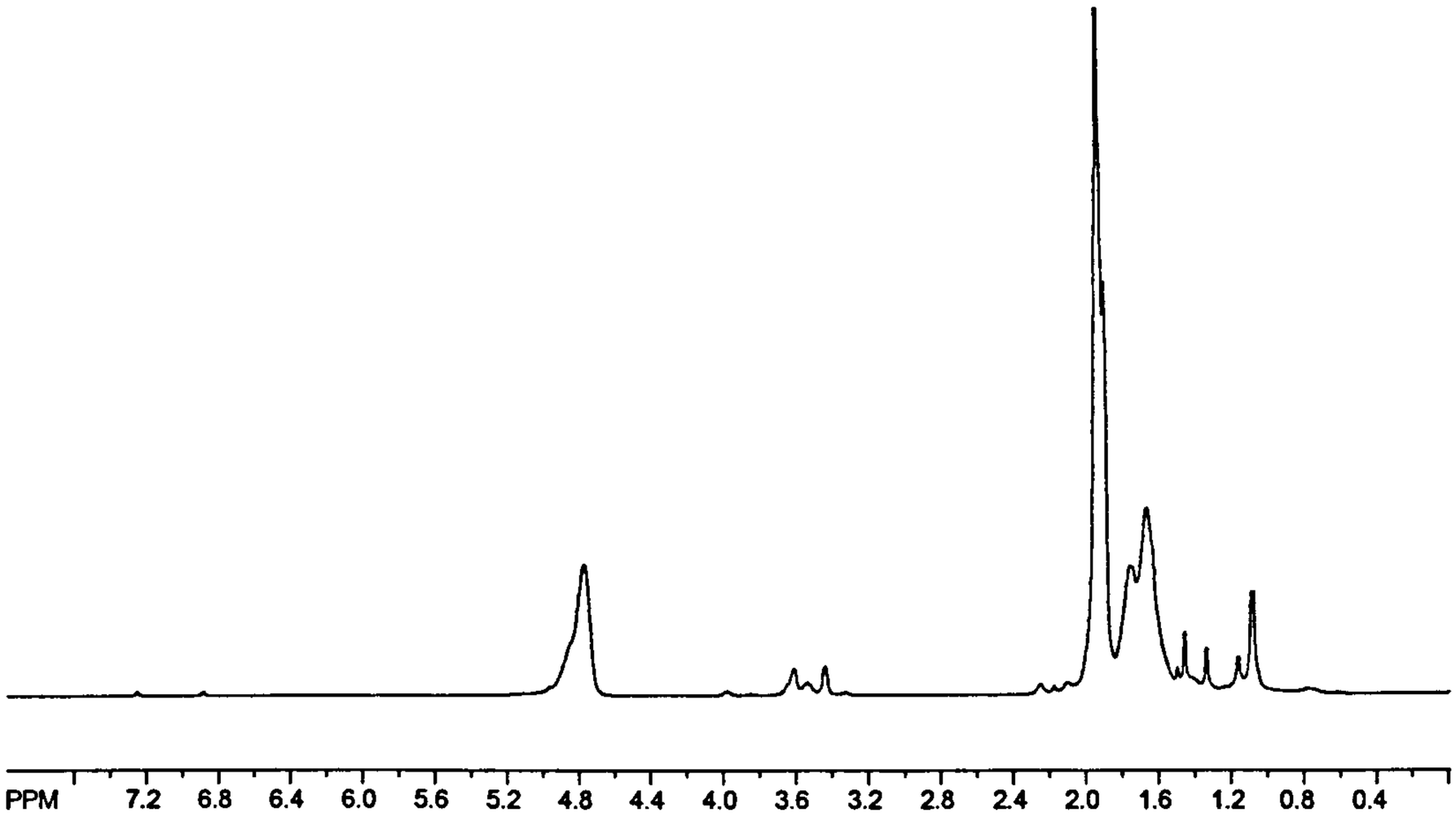


Figure 3-9 ^{1}H NMR spectrum of PVAc synthesised in 2-isopropoxy ethanol

The NMR spectrum shown in figure 9 is of poly (vinyl acetate) synthesized in 2-isopropoxy ethanol, the assignments are: backbone C*H* δ≈4.8; backbone CH_2 δ≈1.7; ultimate CH_2 δ≈4.0; pendant methoxy CH_3 δ≈1.9; endgroup methyl δ≈1.1; endgroup CH_2's δ≈3.4, δ≈3.6.

It is also possible to determine the number average molecular weight from NMR spectra. By integrating the peak arising from the endgroup protons and comparing it to the integral of a peak arising from a repeat unit, the degree of polymerisation can be calculated. However this procedure can only be used for low molecular weight species as the number of endgroups present in the sample is decreased with increasing molecular weight. The polymers were not precipitated in order to keep all the fractions produced, because of this some residual solvent was still present and the peaks from this residual solvent swamps the end group signals.

3.2.4. Mass spectra

The polymers were further examined through the use of mass spectrometry. Two methods were used; these were ElectroSpray Ionisation Mass Spectrometry (ESI-MS) and Matrix Assisted Laser Desorption/Ionisation Mass Spectrometry (MALDI-MS).

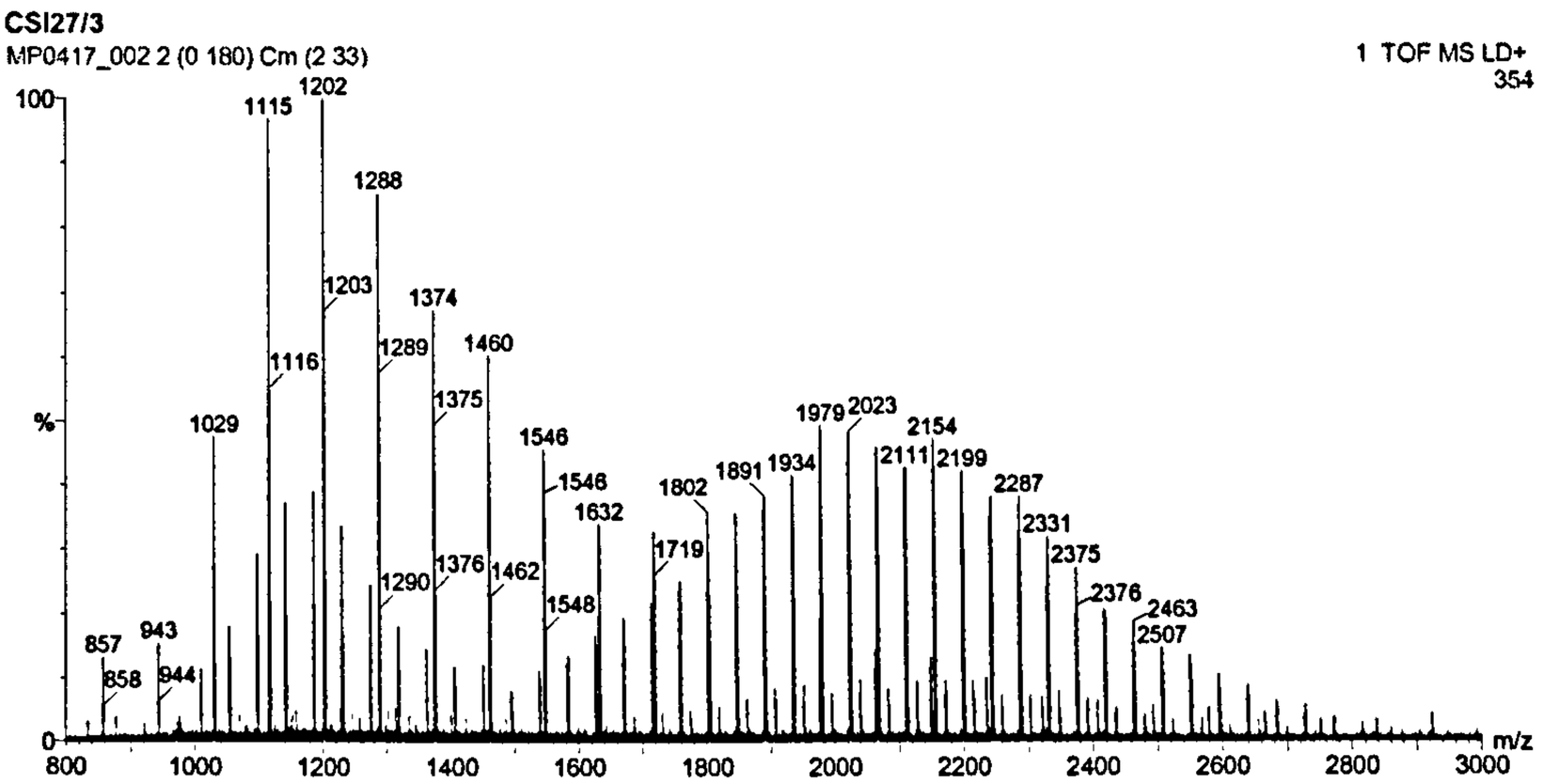


Figure 3-10 MALDI-TOF MS of PVAc sample cs1/27/3

The above spectra are of the same sample, a poly (vinyl acetate) synthesised in the presence of isopropanol. The main peaks in the above spectra are spaced at a distence of m/z = 86, this is the because vinyl acetate has a relative molecular mass of 86 $gmol^{-1}$, and each peak is therfore due to an individual polymer with a defined number of repeat units, the peaks on either side having either one more or one less repeat unit present. An analysis of the peaks reveals that the polymers do indeed have solvent derived endgroups, for example, the peak m/z = 1115, (1115-23-60)/86 = 12. Thus, it can be determined that we have a polymer of 12 repeat units, and an isopropyl endgroup of mass 60 Da. The value of 23 Da is deducted in order to allow for the catenisation agent, sodium iodide, of which the sodium cation has a mass of 23 Da.

The endgroups can also be determined by plotting $M_n = nM + r$, where M_n = number average molecular weight, n = number of repeat units, M = monomer mass, r = residual.

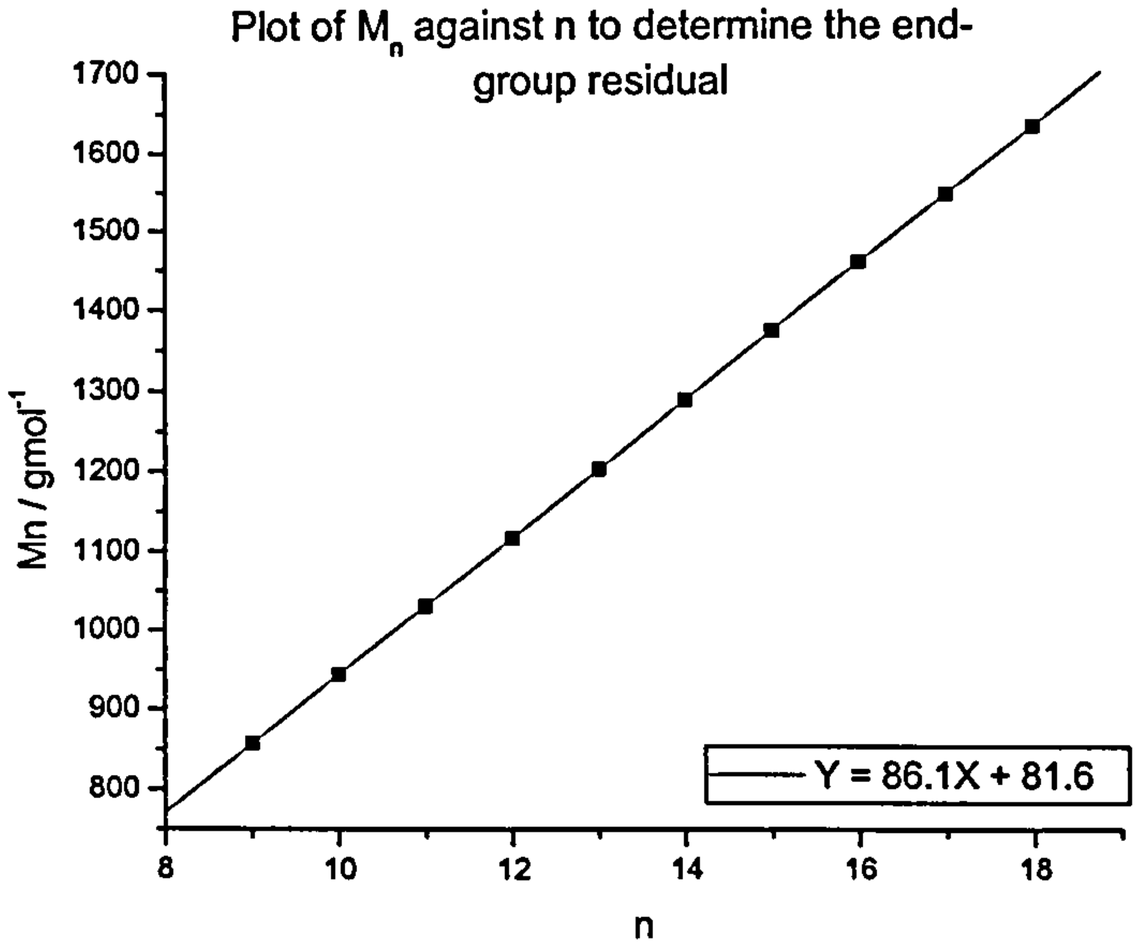


Figure 3-11 Graph to determine the end-group residual

The residual of 81.6 Da can be justified as the solvent endgroup of 60 Da, plus the cation mass of approximately 22 Da.

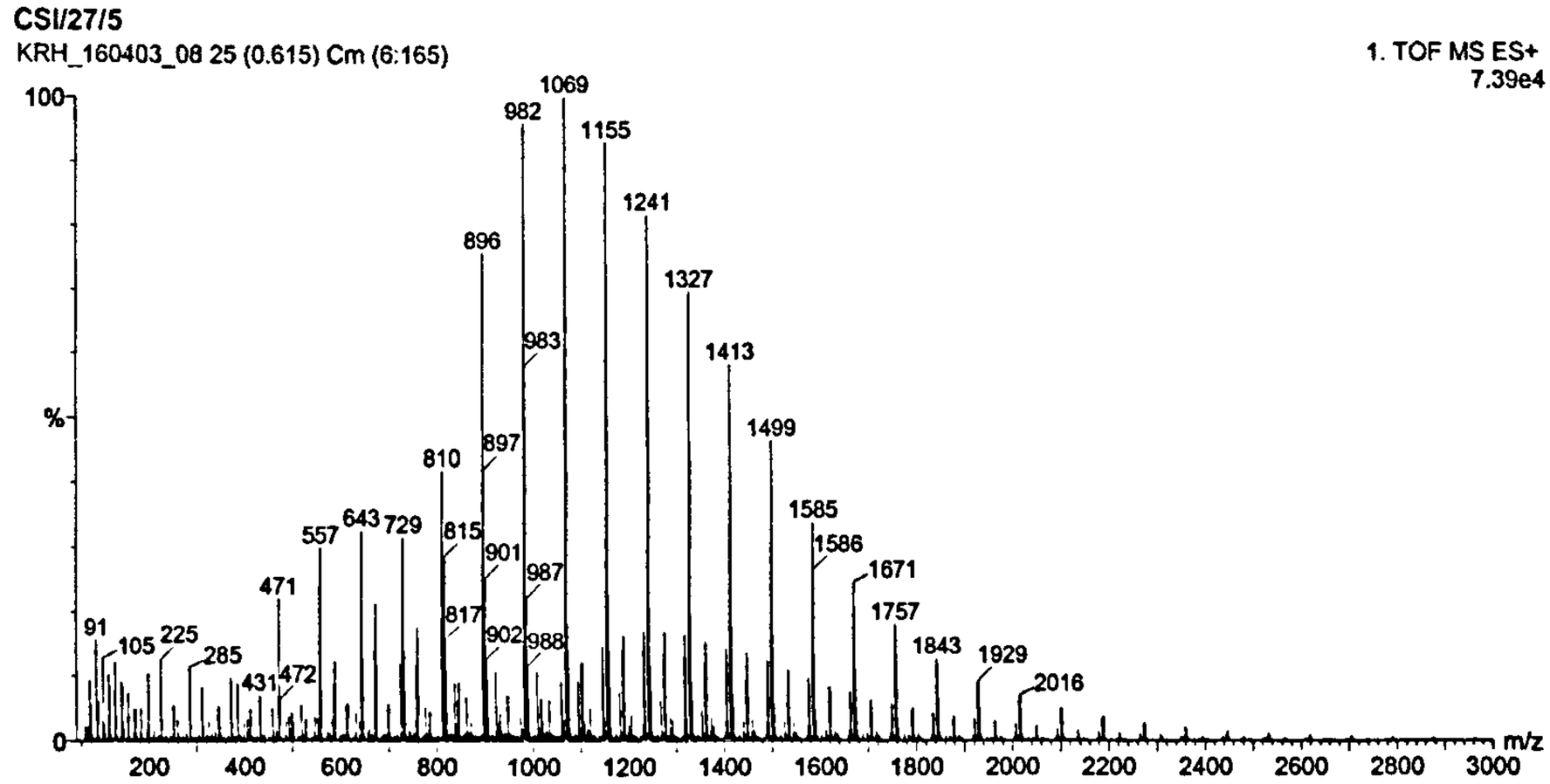


Figure 3-12 ESI-MS of PVAc sample cs1/27/5

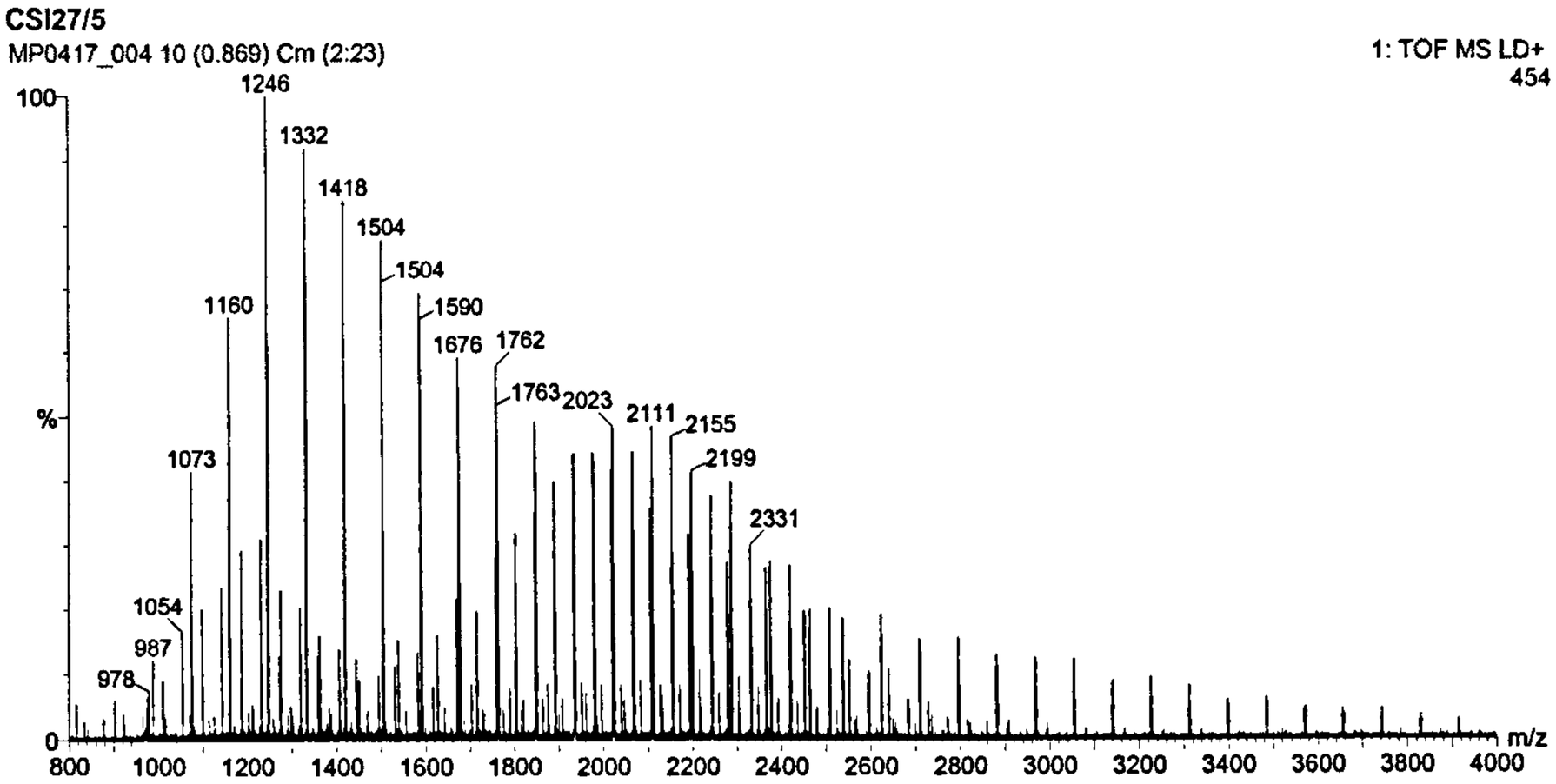


Figure 3-13 MALDI-TOF MS of PVAc sample cs1/27/5

The differences in the above spectra are due to the ionisation method used. In the first spectrum the spectrometer was run in electrospray mode, in the second it was run in MALDI mode. In both of these cases, signals spaced by the vinyl acetate repeat unit, 86, are clearly seen. The peaks have been analysed and the endgroups have been assigned as follows. Taking a random peak from the ESI spectum, m/z = 810, the calculation is, (810-18-104)/86 = 8, thus the peak at m/z = 810 is due to a poly (vinyl acetate) polymer, with 8 repeat units, having an endgroup derived from the solvent in which the polymer was synthesised, namely, 2-isopropoxy ethanol, which has a relative molecular mass of 104 Da. The catenisation agent used was ammonium acetate, giving rise to an increase in detected mass of 18 Da due to the ammonium cation. All of the above spectra were obtained with the spectrometer runing in a positive ion mode. The same graphical method can be applied to these spectra.

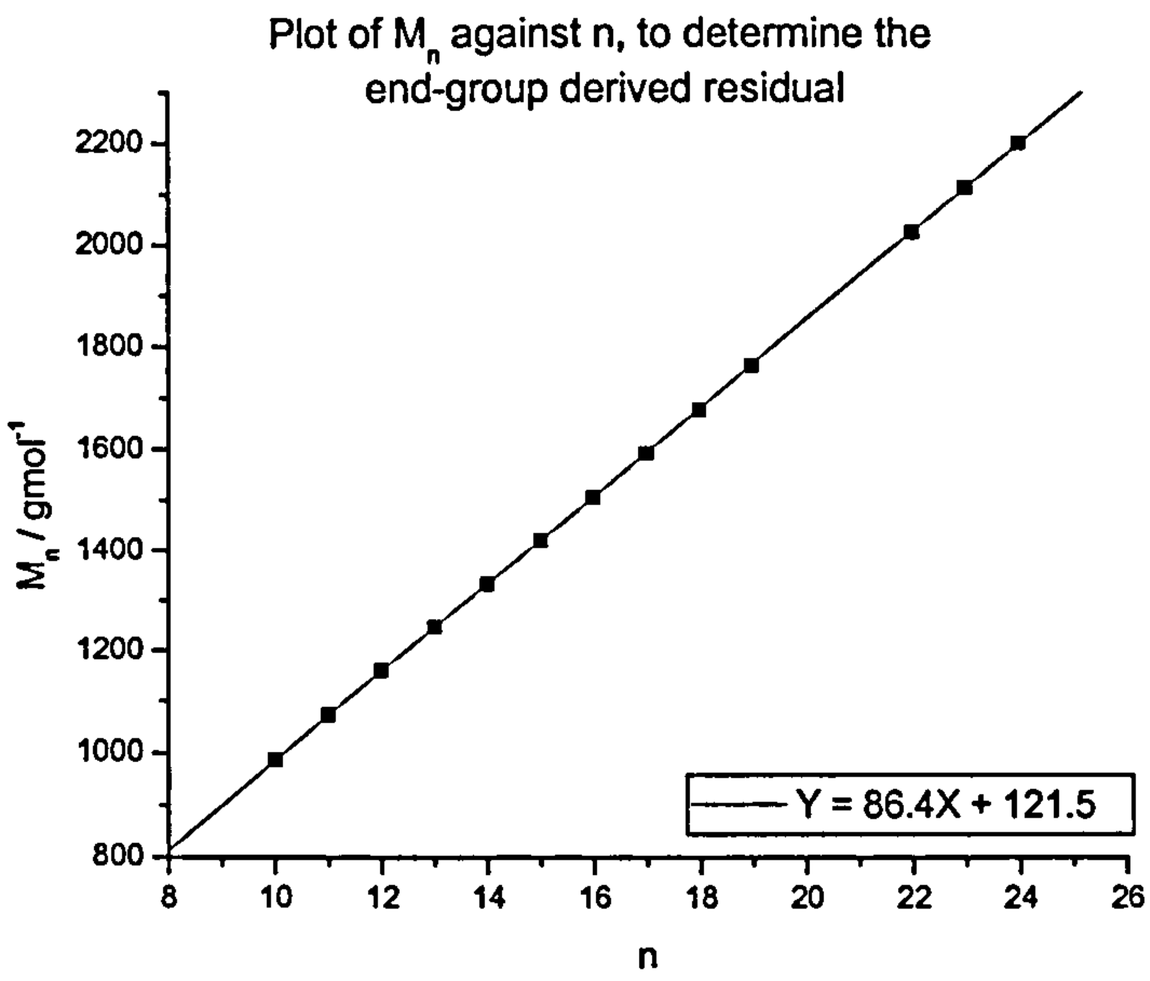


Figure 3-14 Graph to determine the end-group residual

The residual can be justified as the solvent end-group having mass of 104 Da, and ammonium cation, with mass of 18 Da. The different cation mass is due to the different ionisation methods employed.

3.3. Method 3

Other vinyl acetate polymers were synthesised during the course of this work, however they were of little use when it came to the determination of the chain transfer constants. However, they do serve to demonstrate the ability of the method of chain transfer to solvent, and also in the synthesis of lower molecular weight species at close to 100% conversions.

Through the use of large amounts of solvent, low molecular weight polymers, oligomers, can be formed. However, in these polymerisations, conversion was taken close to 100% in order to yield as much polymer as possible. For this

reason the results obtained were not applicable in the determination of the chain transfer constants. Also four of the polymers were synthesised using 3-methyl-2-butanone, this number of reactions is too few to accurately determine the chain transfer constant (even if low conversions were to be obtained). The polydispersity of these polymers is artificially low due to the low molecular weight of the polymers.

The low molecular weight oligomers synthesised using method 3 were isolated in the same way as method 1 and method 2. The polymer solutions were concentrated on a rotary evaporator, in order to remove solvent and excess monomer. The polymers produced were clear colourless viscous liquids.

3.3.1. SEC results

The isolated polymers were dissolved in THF (2mg ml^{-1}) and analysed by size exclusion chromatography, the results are shown in table 4.

Table 3-4 Table showing SEC results

sample	Mn	Mw	Pd	Solvent type
cs1/27/1	310	360	1.2	IPA
cs1/27/2	460	640	1.4	IPA
cs1/27/3	950	1500	1.6	IPA
cs1/27/4	1390	2520	1.8	IPA
cs1/27/5	1580	3320	2.1	2IPE
cs1/27/6	1640	3600	2.2	2IPE
cs1/27/7	2740	4680	1.7	2IPE
cs1/27/8	3270	5580	1.7	2IPE
cs1/27/9	410	490	1.2	MB
cs1/27/10	470	600	1.3	MB
cs1/27/11	810	930	1.2	MB
cs1/27/12	950	1150	1.2	MB

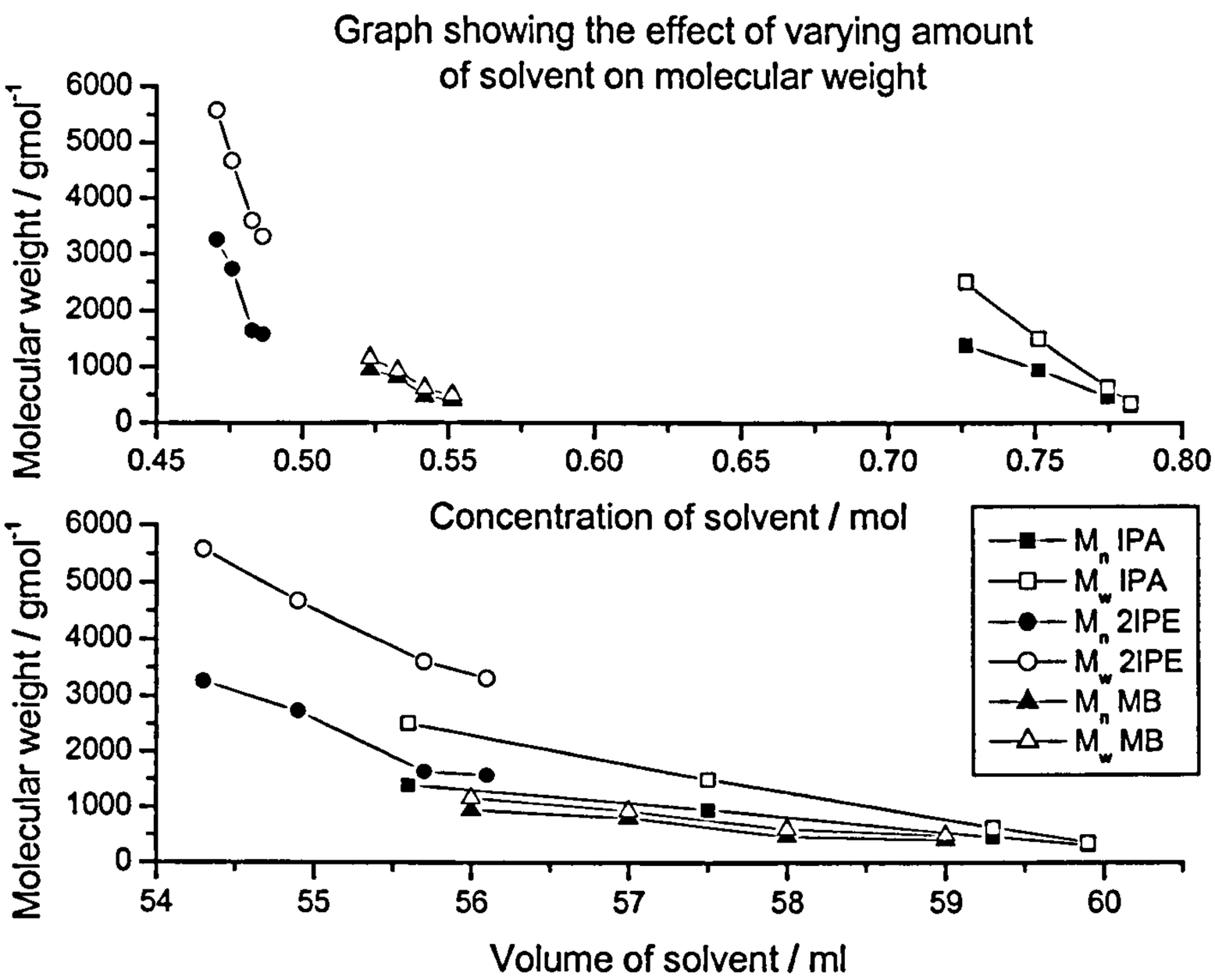


Figure 3-15 Graph showing the effect varying amount of solvent on molecular weight

3.4. Method 4

A robotic synthesis machine was evaluated during the course of this work, with regards to its applicability to the synthesis of polymers. A series of eight polymers were synthesised using the robot, and the results whilst of no use for determining the chain transfer constant, give another insight to the ease at which it is able to approximately select the molecular weight of polymer that is desired. The solvent used in these reactions was isopropanol.

3.4.1. SEC results

The polymers were dissolved in THF (2mg ml^{-1}), and were subjected to analysis by size exclusion chromatography. The results are entirely similar to the results for methods 1, 2 and 3.

Table 3-5 Table showing SEC results

Sample	Mn	Mw	Pd
cs1/61/1	5580	11500	2.1
cs1/61/2	6950	13900	2.1
cs1/61/3	7850	16400	2.1
cs1/61/4	9500	19900	2.1
cs1/61/5	12700	25300	2.0
cs1/61/6	11800	23700	2.0
cs1/61/7	19300	37300	1.9
cs1/61/8	24900	46700	1.9

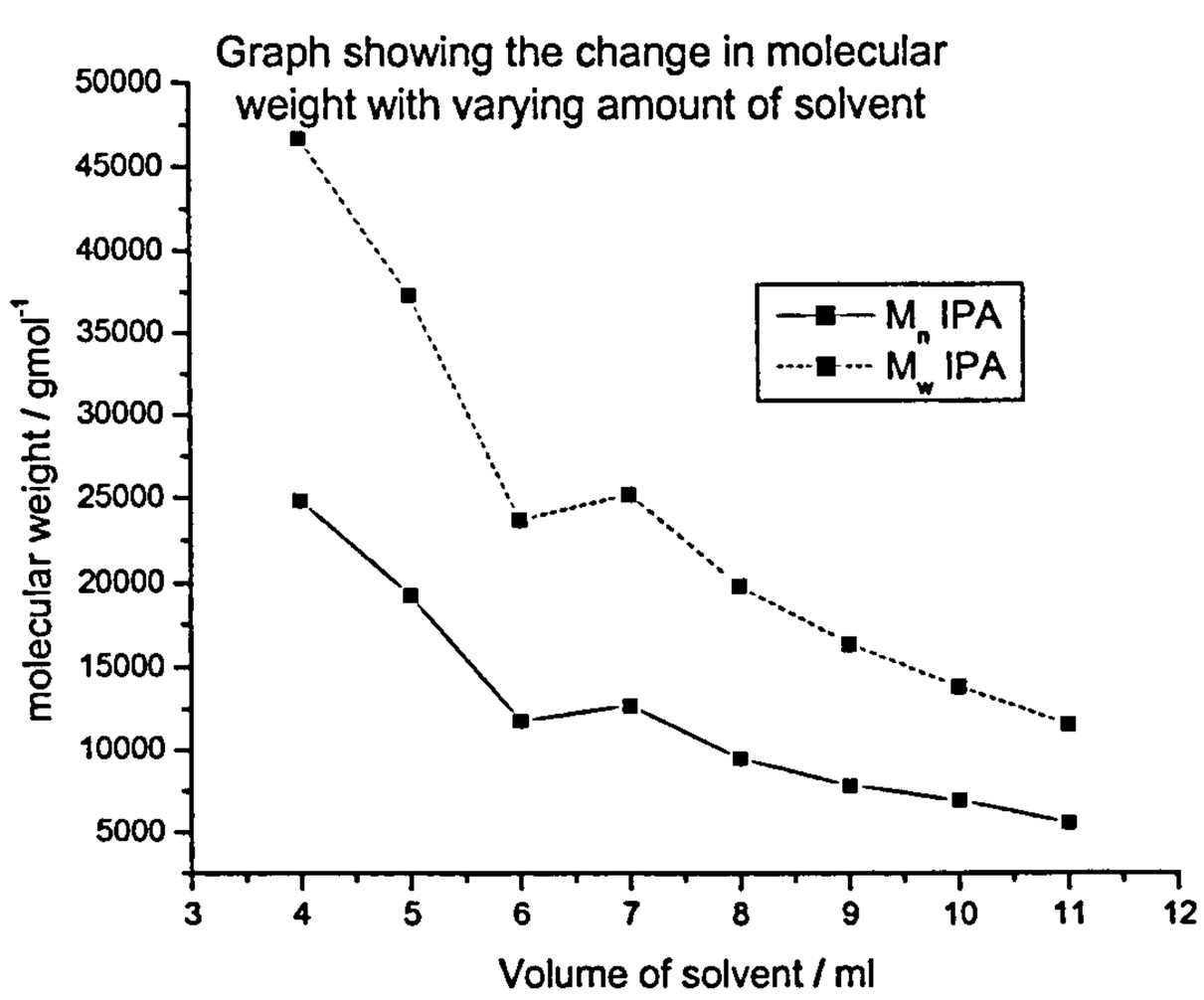


Figure 3-16 Graph showing the change in molecular weight with varying amount of solvent

It must be noted that the total reaction volume used with the robot was limited to 16ml, the previous reactions had been performed with a reaction volume of 60ml. Although the polymers could be synthesised easily enough using the parallel

synthesis robot, it must be noted that due to the construction of the machine, recovery of the polymers once synthesised was not a trivial operation.

4.Tandem mass spectrometry

4.1. Introduction

The use of tandem mass spectrometry (MS:MS) has yet to gain general use among the polymer community. It is however an extremely useful technique in the analysis of polymers. The outstanding feature of this technique is that it allows the user to perform mass spectrometry on a single species. For small molecules, where only one species is present this is of limited use, however small molecules can still be fractionated through the use of Fast Atom Bombardment (FAB). With polymers, however, there is a distribution of species, and therefore a corresponding distribution of peaks. It would be useful, therefore, to be able to analyse individual peaks, in order to investigate the chemical components that make up that particular species.

There are several different methods of MS:MS available, one method uses an ion trap mass spectrometer in order to select the weight of choice, before fragmentation and further mass spectrometry. A second method is also known as Time of Flight –Time of Flight (TOF-TOF) mass spectrometry; here a TOF instrument is used as the selector prior to fragmentation, and analysis of the fragments by TOF mass spectrometry. Another method is known as Q-TOF, here

the initial mass selection is performed by a quadrapole mass spectrometer, before fragmentation and subsequent analysis by TOF-MS once more.

Because of the unique potential of MS:MS for the elucidation of polymer structures, it was decided to analyse some of the polymers synthesised in the course of this work by this method. However, the necessary equipment was not directly available and so the samples could not be analysed in-house. The samples were analysed with the help and cooperation of Micromass UK Ltd. The samples were analysed using their Ultima Global Q-TOF mass spectrometer. With this machine it is possible to take a mass spectrum of a compound, after a spectrum has been recorded from TOF analysis. A quadrapole can then be used to select a particular mass ion, which is then fragmented through bombardment of the ions with noble gas atoms accelerated through an electric field. The mass spectrum of the resulting fragmented ion is then recorded on the TOF analyser. Adjusting the voltage differential over which the noble gas atoms are accelerated can vary the collision energy. If the energy is still insufficient, the gas can be changed for one of higher molecular weight.

Work performed by Rizzarelli et al[45], used online HPLC/ESI-MS-MS in order to determine the products resulting from enzymatic hydrolysis of poly(butylene succinate-co-butylene sebacate) and poly(butylene succinate-co-butylene adipate). In this case an Ion Trap tandem mass spectrometer was used to differentiate between oligomers of the same monomer composition and molar mass, but having different monomer sequences. Giguère and Mayer[46] have used collision-induced fragmentation to cleave successive acetate groups from the backbone of a poly(vinyl acetate) chain. To this end it was decided to use Q-TOF MS:MS to analyse some of the polymers produced within this report.

4.2. Method

The samples were analysed using two different methods of ionisation. For the first method used, electrospray ionisation, the samples were dissolved in THF at a concentration of 2mg ml^{-1}. Ammonium acetate at a concentration of 10mmol/dm^3 was used to supply the counter ion. The samples were then directly infused into the mass spectrometer, through the use of a syringe pump. The second method used was MALDI. Here dithranol (the matrix) was dissolved in chloroform at a concentration of 10mg ml^{-1}, the polymer was dissolved in chloroform at a concentration of 6mg ml^{-1}, and sodium iodide (ionisation agent) was dissolved in methanol at a concentration of 2mg ml^{-1}. A solution was made up consisting of 20μl of polymer solution, 20μl matrix solution and 10μl of ionisation agent solution. 1μl of this was then spotted onto a MALDI target plate and the solvents allowed to evaporate before the target plate was inserted into the mass spectrometer and the samples analysed.

4.3. Results and Discussion

It was the third method of analysis, Q-TOF, that the vinyl acetate polymers were subjected to, using both electrospray, and MALDI as ionisation sources. In each case, when a particular molecule had been chosen and fragmented, the resulting spectrum, had a "repeat unit" of 60, with the highest peak being that of the chosen species. This "repeat unit" is quite clearly the acetate group of the polymer chain being stripped off the backbone.

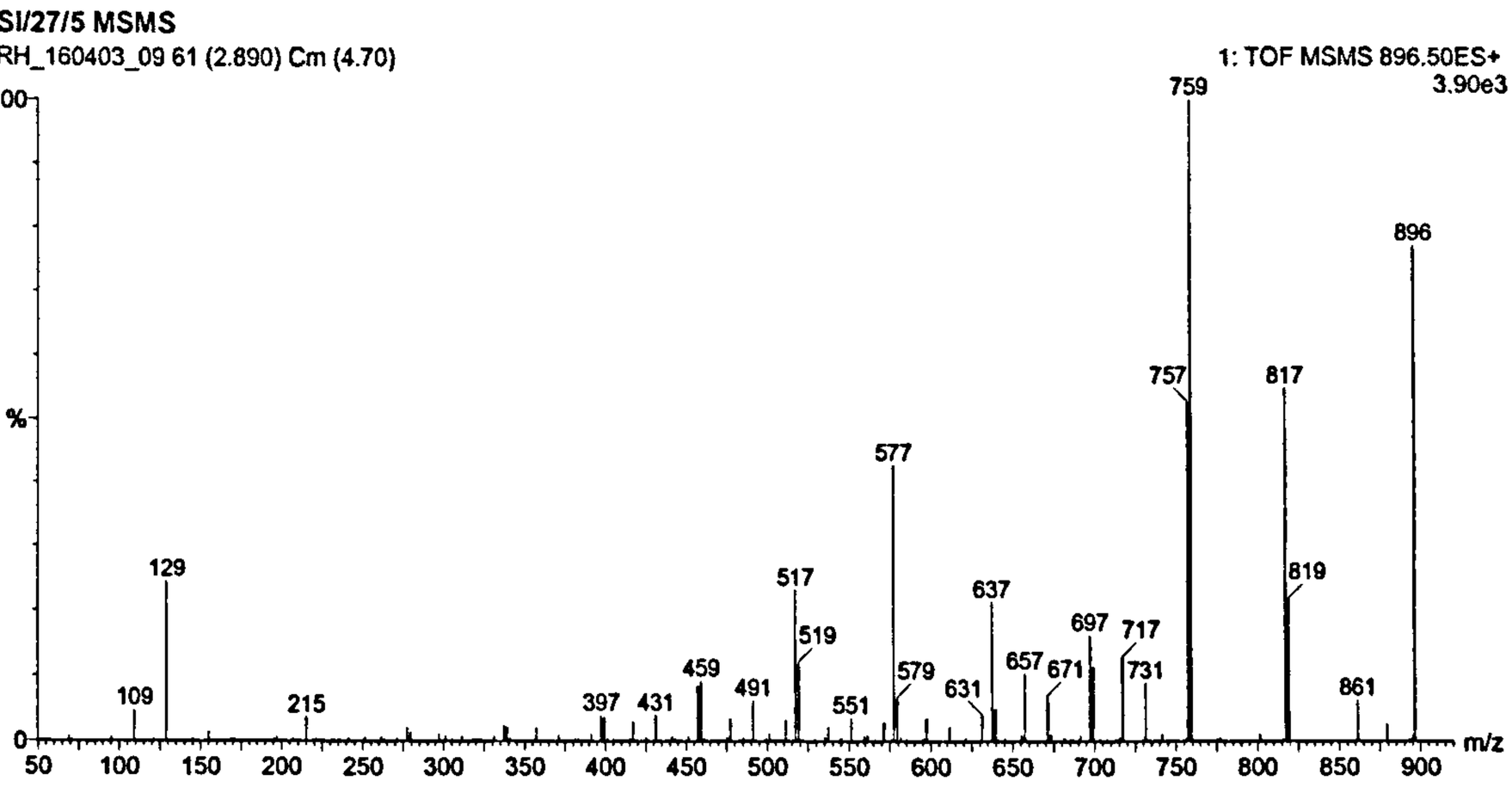


Figure 4-1 ESI-MS-MS of peak m/z = 896, for sample CS1/27/5

In the mass spectrum in figure 1, the parent mass ion is quite clearly seen at m/z = 896, this peak can be assigned to a poly (vinyl acetate) having 9 repeat units and bearing a 2-isopropoxy ethanol end-group and an ammonium counter-ion,. Starting at m/z = 819 or 917, it is possible to count 7 clear losses of 60Da, 2 further losses can been seen at m/z = 337 and then m/z = 277. This then adds up to the loss of 9 acetic acid residues from the molecule, from this we can count back (9*86)+104+18 = 896.

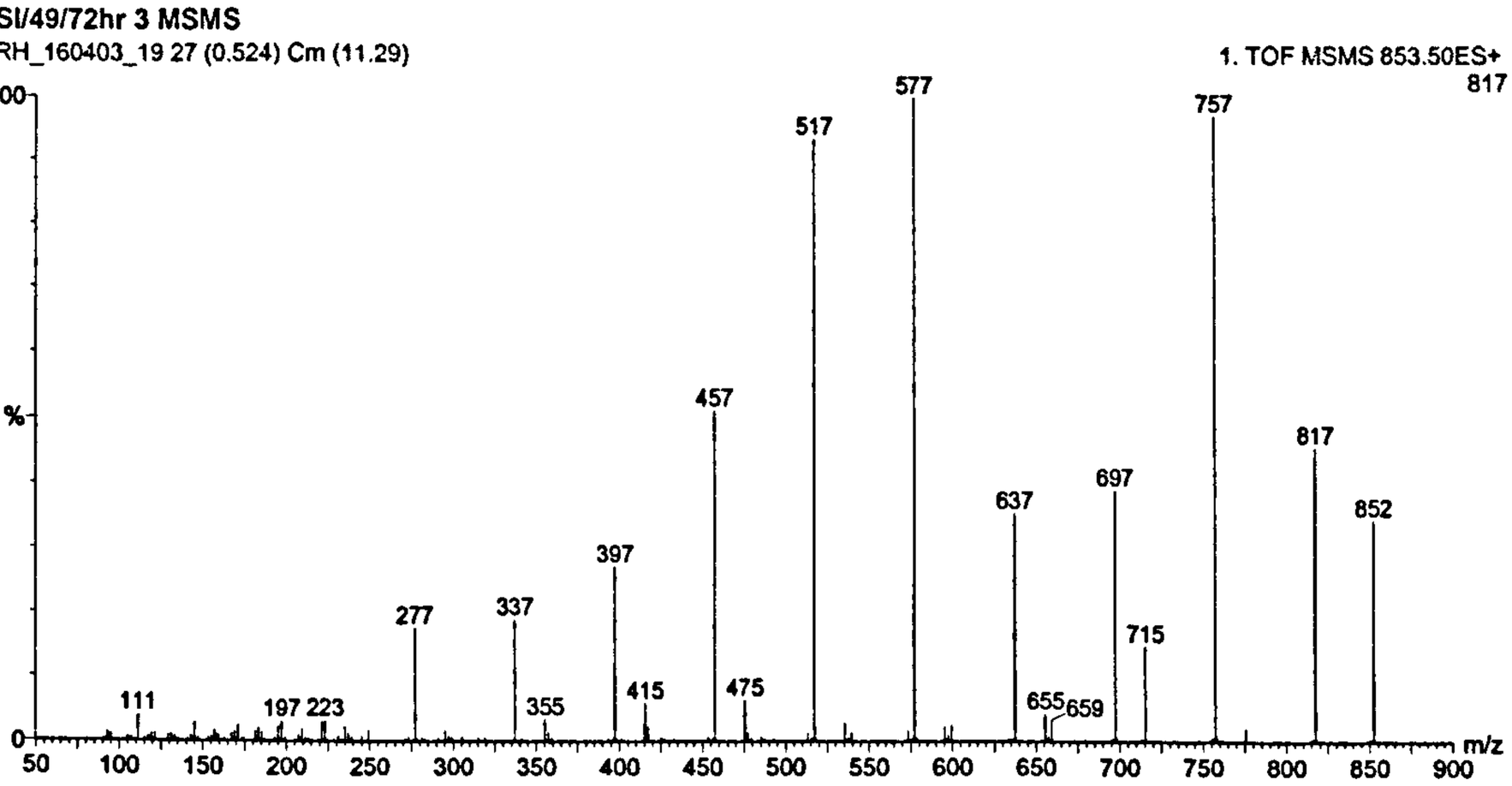


Figure 4-2 ESI-MS-MS of peak m/z = 853, for sample CS1/49/72hr3, with collision voltage set at 20v

The parent spectrum for the mass spectrum in figure 2 is of a copolymer of vinyl acetate and ε-caprolactone. The peak chosen for MS:MS however was of poly (vinyl acetate) homopolymer. The parent ion is at m/z = 862, counting from m/z = 817, it is possible to find 9 clear losses of 60Da, once again it is possible to count back, (9*86)+60+18 = 852. Here although the number of repeats is the same, the solvent end-group is now due to isopropanol.

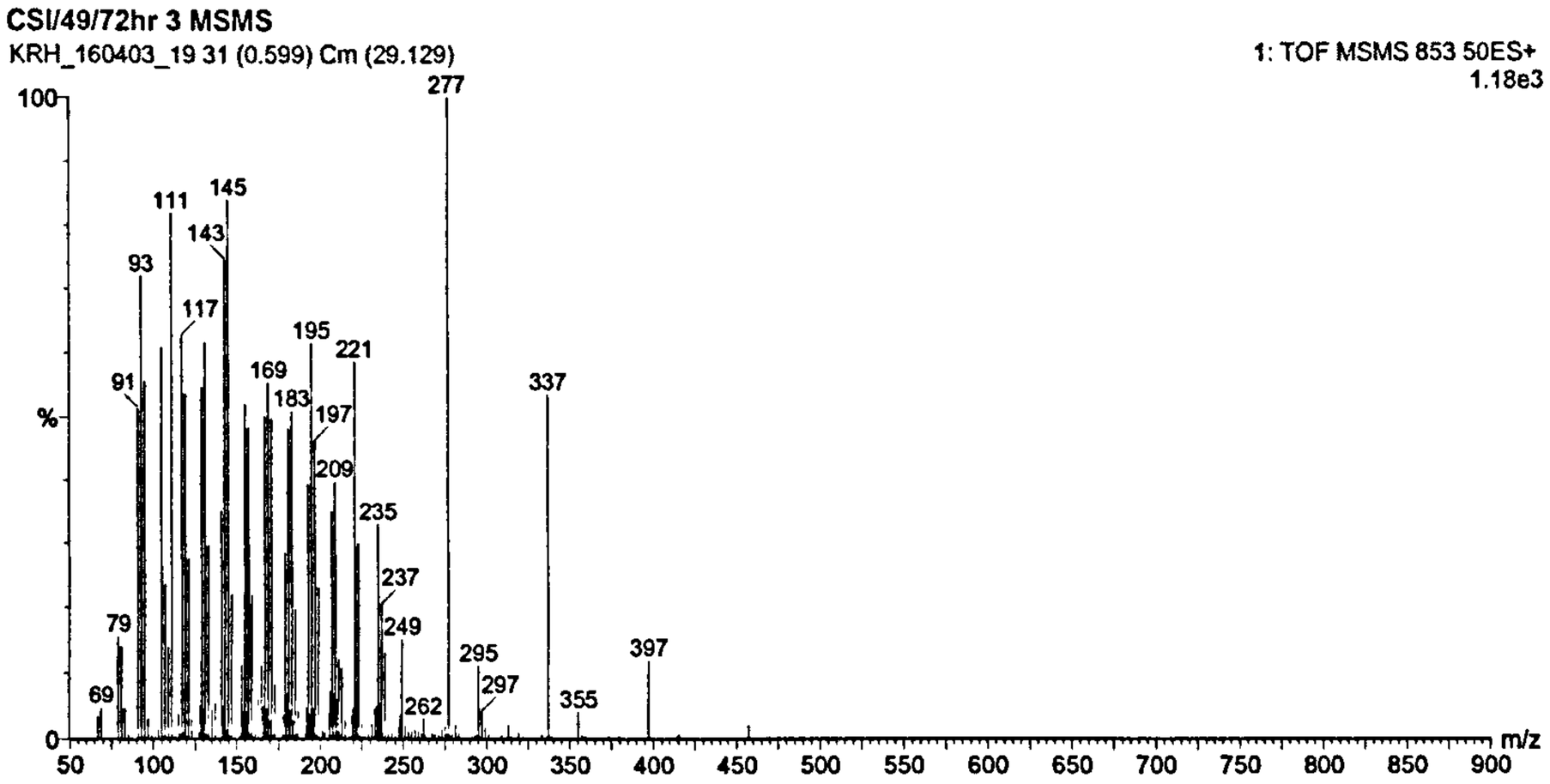


Figure 4-3 ESI-MS-MS of peak m/z = 853, for sample CS1/49/72hr3, with collision voltage set at 40v

The mass spectrum in figure 3 is taken from the same parent mass ion as the previous spectrum. The change in the spectrum is due to the acceleration voltage of the noble gas atoms being increased from 20v to 40v. This change increases the impact energy of the noble gas atoms and because of this the polymer being analysed is fragmented further and more quickly than when the impact energy was lower.

5.Conclusion to synthesis of hydroxy terminated poly (vinyl acetate)

The control of vinyl acetate polymerisation has been achieved insofar as the molecular weight of the product can be controlled with some degree of accuracy. In addition to this, the end-group functionality of the polymers can be set by the choice of solvent. A range of polymers has been synthesised, with molecular weights ranging between 400 and 35,000gmol^{-1} with 3 different solvent derived end-groups. Of the solvents used, 2 have similar chemical motifs i.e. an isopropyl group.

Through the use of this synthetic route polymers or oligomers with chosen end-groups can be synthesised with ease. Chain transfer constants for two of the solvents used were evaluated, and the data presented within this thesis. As expected, the rate of chain transfer for these solvents is significantly lower than the rates of transfer seen for other commonly used transfer agents such as DDT. It is this feature that makes the solvents used particularly suitable for use in a system where the propagation is from an unstabilised radical species. Monomers of this type can include vinyl acetate, as studied in this work, n-vinyl pyrrolidinone.

A novel method for the evaluation of the Mayo equation to determine the chain transfer constant for a polymerisation was used, and the results presented within this thesis. This method is of use where it is not possible to keep the monomer

concentration constant within a polymerisation. This is of particular interest where the monomer in question is of similar nature to vinyl acetate or n-vinyl pyrrolidinone, that is: it has an appreciable transfer constant with many common solvents.

Also presented within this work are some interesting results obtained from the use of tandem mass spectrometry, a method that as yet has not seen extensive use amongst the polymer community. Here the results obtained for this technique show the pendant acetate groups being cleaved one at a time from the backbone of the polymer. By adding the number of acetate losses together and multiplying this by the vinyl acetate repeat mass, it is possible to calculate the mass of the mass ion that was being studied.

Part 2: The synthesis of poly (vinyl acetate-*block*-ε-caprolactone)

6.Introduction to the synthesis of poly (vinyl acetate-*block*-ε-caprolactone)

6.1. Synthesis of block copolymers

The production of block copolymers can be performed in a variety of different ways. Anionic polymerisation, where the growing chain always has an active chain end, allows production of block copolymers that are near-monodisperse. Controlled radical, or living radical polymerisations, such as ATRP (atom transfer radical polymerisation) can also offer similar results. Cationic polymerisation can also be used to produce well defined blocks.

The technique of anionic polymerisation has been much used in the synthesis of block copolymers. A review of living polymerisation techniques, including the application of anionic polymerisation to the formation of defined block copolymers was published by Webster[2]. Some of the methods of copolymer synthesis discussed include the formation of AB diblocks and ABA triblocks. For example, the initiation of styrene by butyl lithium, gives rise to polystyrene with one reactive end, whereas the initiation of styrene by sodium naphthalenide gives rise to polystyrene with two reactive ends, these are shown in scheme 1. These could then be used to initiate the polymerisation of another monomer, leading to a block copolymer.

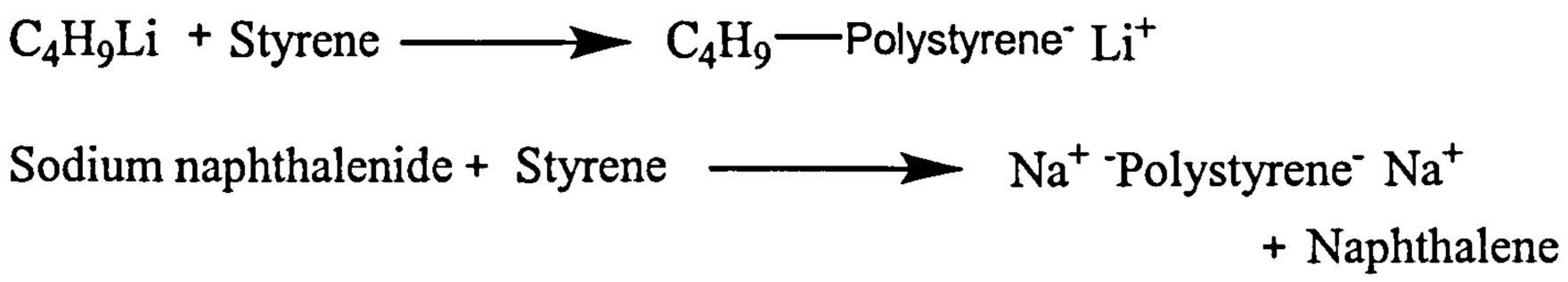


Figure 6-1 Scheme 1

Conventional radical polymerisation can produce block copolymers but these are not as well-defined as those made by other methods and usually require that all the materials are added at the start of the reaction. The block composition then relies on the reactivity ratios of the different monomers. The reactivity ratios of many monomers are published in the academic press or in reference books such as the Polymer Handbook [47]. The choice of monomers determines the structure of the final copolymer. For example if the two monomers have similar reactivity ratios, then the polymer formed will have a statistical composition. However, if two monomers are used that have widely differing reactivity ratios then one of the monomers will polymerise before the other giving rise to a block type structure.[44, 48]

An alternative method of producing block copolymers with a relatively defined composition is starve-fed emulsion polymerisation. Here, monomer is fed into the reaction at a controlled rate, and by addition of other monomers after the initial polymerisation has taken place, a block can be formed provided the radical is confined within the particle. In emulsion polymerisations, the growing chain is kept inside a micelle-like particle formed by monomer on the inside and water on the outside, with a surfactant at the interface. The result of this is a low active radical to monomer ratio, so the termination rate is low. In starve-fed emulsions, the feed rate matches the rate of propagation as soon as it reaches the reaction locus. Using this method it is possible to start a polymerisation using one

monomer and then switch monomers at some point in the reaction. A proportion of these polymers will have block structures.

6.2. The use of enzymes in polymer science

In nature enzymes are used to catalyse the synthesis and the degradation of different biological compounds. In many cases the targeted molecules are either large single molecules or biological polymers such as proteins or DNA for example. With this in mind some research groups have investigated the action of enzymes on synthetic polymers.

However in the literature there is a lot of potentially conflicting information about the use of enzymes in relation to polymers. Some groups such as Gross's[49-58] use enzymes mainly as catalysts to produce polymers, however some other groups are using enzymes as agents to degrade polymers, in an attempt to measure the polymers' potential for organic degradation.

6.2.1. Enzymatic synthesis of monomers and polymers

In the main, the work of Gross and co-workers has been extensive in the field of using enzymes to synthesise monomers and polymers. A review[52] of most of the currently available techniques was published by his group in 2001, and contains many examples of the uses of enzymes such as enzymes in the synthesis of monomers, particularly ones that are hard to synthesise by conventional chemical methods. Specifically, these include enantiomericly enriched monomers, macromonomers and polymers.

6.2.2. Supported enzymes

As well as their use in the synthesis of monomers and polymers, it has also been noticed by several groups [50, 59, 60] that some enzymes can have their activity enhanced with respect to certain reactions by the immobilization of the enzyme within, or on, a polymer substrate. There is some debate as to the method of this enhancement of activity, one possibility is that the base substrate causes a structural rearrangement in the enzyme and/or the chemical reactant. Supported enzyme catalysts have been widely employed as they are relatively easy to remove from the reaction mixture after a reaction is complete, due to the relatively large size of the immobilizing beads, or substrate.

Further to the work on the synthesis of monomers and polymers using enzymes as catalysts, Gross *et al* have also performed a study to check the activity of *candida antarctica* lipase B (CALB) immobilized on a solid support (Novozym 435) in a variety of different organic solvents, using a range of solvents, each having a different dielectric constant[54]. When the resulting polymerisations were analysed, it was found that the results grouped into two statistically different regions. When the solvents were of a polar nature the polymerisation that occurred only went to low conversion and gave a low molecular weight. However when the solvent used was less polar, the conversion of the reaction was much higher (x2-x4) and the products were of a higher molecular weight. It was noticed that the dielectric constant of the solvent was not the only factor in the conversion of monomer to polymer in the reaction studied and it is thought that the geometrical arrangement of the solvent, along with dipole moments and the solubilisation of substrates affects the catalytic activity of the enzyme. In addition, the authors also studied the effects of varying the ratio of solvent to monomer and also varying the temperature at which the polymerisation took

place. The polymerisation had the highest conversion and largest molecular weight when the ratio of solvent to monomer was 2:1. When the reaction was scaled up the conversion stayed the same but the molecular weight of the product was also increased. This was thought to be associated with heat transfer rates and the susceptibility to water uptake during the reaction. By increasing the amount of solvent, the polydispersity of the reaction was reduced. The effect of temperature on the reaction was also studied *in situ* by NMR spectroscopy. It was discovered that the polymerisation carried out at 90°C had the fastest conversion of monomer to polymer and that the apparent rate of propagation increased with increasing temperature from 60°C up to 90°C where the rate started to fall. It was conjectured that this was due to protein denaturation and deactivation. However it was also observed that although the rate of polymerisation was the greatest at 90°C the products had the lowest molecular weight, whereas the reaction performed at 60°C had the lowest rate and the products had the highest molecular weight.

6.3. Degradable polymers

The subject of biodegradable polymers is one of great relevance and importance. The landfill sites in our own country are overwhelmed with plastic consumables, the same is also true for most industrial economies. A product that would break down into its non-toxic constituent parts would be the goal of many governments.

Polymers that degrade also have applications in the medical industry. For example resorbable sutures have existed for quite some time. These are of enormous use in cases in which a patient receives internal stitches which could be difficult to remove. Biodegradable polymers are being tested as scaffolds for

regeneration of cartilage, or bone[61-63]. In these applications, sometimes it is preferred that the polymer scaffold remains, and sometimes it is preferential for the polymer scaffold to be absorbed into the body and excreted.

Poly lactic acid (PLA) is a well-known biodegradable[62-67]and bio-acceptable polymer and studies have been made by polymer chemists as to its degradation, whilst biologists have looked at the histology of implanted PLA scaffolds[68, 69]. However, there is a problem with species such as poly lactic acid in that they break down into lactic acid, giving a rise in local pH, and although this is not such a drawback for items such as disposable carrier bags or nappies, it precludes PLA's use *in vivo* because of the detrimental effect of lactic acid on cell growth. It is now one of the aims of the polymer chemists to provide polymers that are acceptable to the body but do not have an adverse effect on the environment around them when degrading.

The thermal degradation of poly (caprolactone) (PCl) has been studied by coupling a Thermal Gravimetric Analyser with Mass Spectrometry and also with FTIR. Dubois *et al.* [70] noted two forms of breakdown, the first at temperatures between approximately 300-390°C, the second at temperatures higher than 390°C. In the first temperature range, a range of products are produced, including water, carbon dioxide and 5-hexenoic acid, the latter arising from the random chain scission at the ester groups. Above 390°C, the polymer undergoes an unzipping reaction where the polymer is returned to its monomer units, however this only occurs when the polymer is of the unsubstituted hydroxyl derivative.

6.3.1. Enzymatic degradation of polymers

The breakdown of polymers such as poly ε-caprolatone is an area of active research; Albertsson *et al*[71] have performed a study on the biodegradation of film blown poly ε-caprolatone. It was discovered that the samples subjected to biodegradation displayed cracks or grooves in the surface of the substrate, where as the control samples subjected to an abiotic, chemical degradation showed no such features. It was concluded that the cracks were due to the amorphous regions of the polymer being degraded in preference to the crystalline regions in biotic media. The morphology of the blown films consists of parallel rows of crystalline and amorphous lamellae, with their normals parallel to the direction of extrusion. The degradation was performed in different media: garden compost; anaerobic sewage sludge; a pure microbial culture of *A. fumigatus*; and chemical hydrolysis with basic solution. Chen *et al*[72] produced poly (ε-caprolatone) microparticles, and then studied their degradation in phosphate buffered saline, with and without the presence of a lipase. The study was prompted by the potential for poly (ε-caprolactone) to encapsulate drugs, which can often be hydrophobic, and then deliver them to the site where the drugs are needed, as if often the case with cancer drugs[73]. Clinicians often want to have a high level of anti-cancer drug in the tumour site but wish the level of the drug to be kept to a minimum at other locations in the body. One of the variables of interest is the rate of degradation of the polymer particle; it must degrade and release the drug within a period suitable to the required drug release rate. In this study, poly (ε-caprolactone) was dissolved in dichloromethane, this non-aqueous phase was then added to an aqueous phase consisting of 1% gelatin solution containing 0.05% Tween-60. This was then stirred at 1200 rpm for one minute, before stirring for a further 2-3

hours, (the rate of stirring was not defined). The microparticles thus produced were separated by centrifugation, washed with distilled water and freeze-dried, to obtain free flowing powder like PCL microparticles. These particles were then degraded in phosphate buffered saline (PBS), and the results were studied by SEC and Scanning Electron Microscopy as well as X-ray diffraction. The x-ray diffraction was used to measure the change in the proportion of crystalline material relative to the amount of amorphous material, the amorphous regions being degraded in preference to the crystalline regions. When the degradation is performed in PBS, at pH7.4, the degradation occurs more slowly than in the presence of lipase. By studying the particles with SEM, the morphology of the particle is shown not to have changed, even though the molecular weight of the polymers making up the particle has fallen. However when the degradation is performed with lipase present, not only does the degradation progress more quickly, but the particles have a substantially different morphology after degradation. Here, when the SEM micrographs are studied channels and pores can be seen quite clearly. Whilst performing this study, the group compared the difference in the degradation of films and the microparticles, and found no significant difference in the rate of degradation, even though the specific area of the particles was 67 times larger than that of the film. However the main oversight of this paper is that it does not mention which lipases are used in the degradation studies.

The group of Tsuji, has looked at the environmental degradation of aliphatic polyesters. This work was performed on, poly (ε-caprolactone), poly [(R)-3-hydroxybutyrate] (PHB) and poly (L-lactide) (PLLA). The studies[74, 75] were performed first in static sea water, at a set temperature. The second study was performed in natural dynamic sea water, which also had variations in temperature. In the first study, it was PCL that showed the largest amount of degradation

followed by PHB and PLLA. Both amorphous and crystalline forms of PLLA were studied but there was no observable difference between the degradation behaviour of the two. However when the study was moved into dynamic seawater conditions, it was the PLLA that showed the largest amount of degradation. It was hypothesised that this larger amount of degradation was due to the high Tg of PLLA, relative to the other polymers under test, and because of this it was more susceptible to the mechanical stresses caused by the flow of the water, which led to the physical destruction of the sample.

Following this work, Aoyagi *et al*[64] looked at the thermal degradation of three aliphatic polyesters, PCL, PHB, and poly s-lactide. The study was performed using two methods, isothermal and non-isothermal. They used TGA, and pyrolysis GC-MS methods to probe the degradation path of the different polymers. They concluded that the degradation of PHB had a random chain scission mechanism, PCL progressed by an unzipping reaction, where as the route for poly s-lactide was not fully resolved due to several procedures occurring concurrently.

An interesting paper recently published by Gao *et al*[76], has looked into the synthesis of water soluble, degradable hyper-branched polymers, with respect to their use as a drug delivery system. In this work they take an AB type monomer and react it with a CD_n type monomer to form an AD_n monomer which can then be reacted via a self condensation reaction in the presence of a catalyst to give a hyper-branched polymer. The materials used in this study were methyl acrylate, diethanolamine (DEOA), and N-methyl-D-glucamine (NMGA). One of the two amine compounds was reacted with the methyl acrylate via a Michael type addition reaction. The resulting monomer was then heated with zinc acetate, whilst under vacuum, to yield the final product. In the second step, the methyloxy

carbonyl unit reacted with the hydroxyl group of another monomer unit to form an ester linkage. These linkages impart degradability to the final polymer product. In this way the group uses a novel "one pot-two step" reaction, the polymerisations were performed in round bottomed flasks and used attached to rotary evaporation equipment, for the application of heat, vacuum and stirring. The study made a particular note of the temperature at which the reaction was to be performed; below 135°C the polycondensation reaction did not give hyper-branched polymers with high molecular weight but above 165°C cross linking was observed. High molecular weight hyperbranched polymers were therefore formed only in the region 135-150°C. An alternative catalyst was used, tetrabutyl titanate, in the place of zinc acetate and it was found that the molecular weights increased, indicating that tetrabutyl titanate was the superior catalyst for the polycondensation reaction.

Sivalingam, has published a number of papers on the degradation of different polymers including the degradation of poly (vinyl acetate) and poly (ε-caprolactone), with different enzymes[77-79]. The effect of enzyme type on the degradation of PVAc has been studied. Here it was noticed that different enzymes degraded the polymer in different ways. One enzyme acts to hydrolyse the short branches in preference to long branches, but with another enzyme the long branches are hydrolysed in preference to the short branches. In the study in question the enzymes used were Hog Pancreas (HP), *Candida Rugosa* (CR), Lipolase-100T (LL) and Novozym 435 (NV). All the reactions were performed at 60°C, and the different rates at which the different length side chains were hydrolysed were measured. The rate for long chains was in the order HP>NV>LL>CR, this order being reversed for the rate of hydrolysis of the short chains. After the polymer had been reacted with an enzyme, the products were passed through a SEC column for separation. The chromatogram was divided into

three sections, the first corresponded to the bulk high molecular weight polymer, the second to the oligomeric species resulting from long chain branched species being hydrolysed, and the third was from the solvent reference peak (toluene) and other low molecular weight species. This third fraction was collected and analysed by gas chromatography and mass spectrometry. In a second study ref the same group studied the effect of enzymes on the degradation of poly (ε-caprolactone), and blends of poly (ε-caprolactone) and PVAc as it was thought that blends of the two polymers would have superior mechanical properties to the homopolymers on their own. In this study two lipases were used, Novozym 435 and *Candida Rugosa*.

One of the differences between the two polymers is the method of degradation. PVAc degrades by side chain hydrolysis, where as poly (ε-caprolactone), having heteroatoms in the main chain, degrades by hydrolysis of the main chain. It was discovered that on blending PCL with PVAc the rate of degradation of PCL dropped rapidly. This effect has been noted before [80] where poly lactic acid has been blended with PVAc, and a similar effect noticed. Here the degradation of films was studied, in comparison to the solution degradation studied by Sivalingam. The reduction in degradation rate in the case of the films was put down to changes in surface tension, whereas it was thought that conformational changes in the PCL molecules caused by the presence of the PVAc molecules affected the rate.

Sivalingam *et al* have also studied the affects of different solvents on the degradation of PCL. The study looked at the effects of viscosity and polarity of the solvents on the rate of degradation. It is known that the amount of water present in these reactions affects the rate of reaction. This effect was studied by using acetone as a solvent and then changing the amount of water. It was found

that while the rate of degradation decreased with increasing viscosity, it increased with increasing polarity for the solvents used. These observations were rationalized as follows: decreasing the viscosity allows for greater fluid transport properties, allowing the polymers to reach the enzyme, and its active site more readily. Increasing the polarity allows the solvent to disrupt the tightly bound polymer molecules more readily and therefore increases the degradation rate.

6.4. Enzymatic modification of polymers

A study by Jarvie *et al*[81], looked at the enzyme modification of polybutadiene. The polymer chain is made up of three species, cis-but-2-enyl double bonds, trans-but-2-enyl double bonds and pendant ethan(1-vinyl)yl groups. When this polymer is reacted with acetic acid and hydrogen peroxide with Novozym 435 in dichloromethane, the backbone double bonds are epoxidated, however the pendant vinyl groups do not react. Previous work has shown that epoxidation occurs in the following order: cis-but-2-eny l> trans-but-2-enyl >> ethan(1-vinyl)yl when the double bonds are epoxidated chemically. However it was noted that in these systems the vinyl double bond starts to epoxidise before all of the backbone double bonds are reacted and in some systems small amounts of ring-opened products were observed along with a 1:2 mixture of acetic acid : 60wt% hydrogen peroxide.

A study was conducted into the activities of lipases[40], with a view to using them to selectively cleave a single acetate group from the end of the polymer, this was performed in an attempt to synthesise an α,ω-telechelic oligomer or polymer, with a view to them being used in the synthesis of a polyurethane. One of the interesting pieces of information that was gleaned from this work was that the

lipases that could cleave acetate groups from a poly (vinyl acetate) chain were not active in the polymerisation of (ε-caprolactone), and conversely the lipases that were active in the polymerisation of (ε-caprolactone) were not active with regard to cleaving acetate groups from a PVAc chain. This fact would allow us to make a block copolymer of vinyl acetate and (ε-caprolactone), and then after removing the first lipase, addition of the second would allow the cleavage of one or two acetate groups from the vinyl acetate backbone.

In this study, a different method to those described above for the synthesis of block copolymers has been used. It was thought that since previous work had indicated that the polymerisation of (ε-caprolactone) could be controlled by aromatic alcohols and catalysed by enzymes [14, 40, 55, 82-85], it would be interesting to see if the same procedures could be applied to control the polymerisation of ε-CL with hydroxyl-group terminated poly (vinyl acetate)s. Usually the polymerisation requires the use of metal catalysts such as dibutyl tin oxide (DBTO), however this tends to also catalyse other trans-esterification reactions as well. Kavros *et al*[40] detailed the use of enzymes as the catalyst, and compared the results to that of DBTO.

In the work performed here, an hydroxyl terminated poly (vinyl acetate) was used in conjunction with a suitable enzyme to control the polymerisation of (ε-caprolactone). The reaction scheme for a polymerisation of (ε-caprolactone) and PVAc synthesised in isopropanol is shown in figure 2, a similar scheme could be drawn for the reaction of PVAc synthesised in 2-isopropoxy ethanol and ε-caprolactone. The polymers thus synthesised were subjected to analysis by SEC, NMR and mass spectrometry.

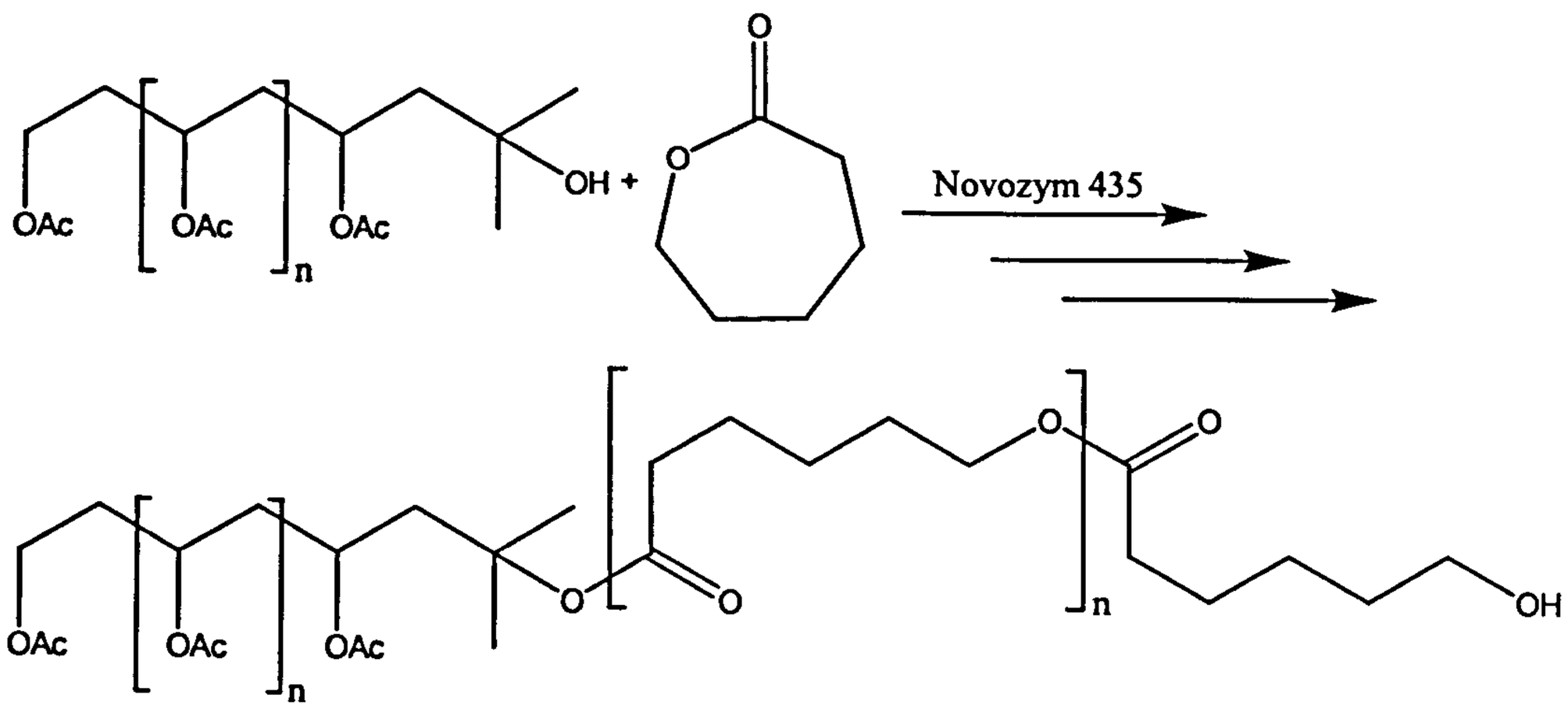


Figure 6-2 Reaction scheme for the synthesis of block copolymers

7.Synthesis of Poly (vinyl acetate-*block*-ε-caprolactone)

7.1. Synthesis of hydroxy-terminated poly (vinyl acetate)

Hydroxy-terminated poly (vinyl acetate)s were prepared on a large scale, the amount of product being sufficient for several further reactions. Two polymers were produced, the first used isopropanol (IPA) as the chain transfer agent/solvent the second used 2-isopropoxy ethanol (2IPE) as the chain transfer agent/solvent.

7.1.1. Materials

The IPA (general purpose reagent grade) was dried by refluxing over CaH_2 followed by distillation. 2-Isopropoxy ethanol was used as received. Vinyl acetate monomer was passed through an inhibitor removal column (Aldrich) before fractional distillation (fraction collected at 73°C). AIBN was recrystallised from diethyl ether.

7.1.2. Method

A 2 litre resin kettle, with a 5 neck lid was set up in a constant temperature water bath set at 60°C. An overhead stirrer (IKA RW20.n) was set up, along with a nitrogen inlet, two pressure equalised addition funnels and a coil reflux condenser.

The vessel was purged with nitrogen for 20 mins. IPA (950 ml) was added to the reaction vessel. This was heated to 60°C and sparged with nitrogen for 1hour. Vinyl acetate (71.5ml, 0.78mol) was charged to an addition funnel and sparged with nitrogen for 30mins. AIBN (0.9g, $5.5x10^{-3}$mol) was dissolved in IPA (50ml) before being charged to the second addition funnel. This was sparged with nitrogen for 15mins.

After the sparging of the reactants was complete, the vinyl acetate was added into the reaction kettle and left stirring for 5mins in order to reach the reaction temperature. The mixture of AIBN and IPA was added quickly to initiate the reaction. The reaction was left to run for 5 hours and 20 mins. It was then removed from the water bath and cooled in an ice bath. The reaction mixture was poured into a round bottomed flask and the excess solvent and unreacted monomer removed on a rotary evaporator. The concentrated mixture was then dissolved in THF (200 ml) and precipitated into 40-60 petroleum ether (2500 ml). The resultant clear polymer liquid was then dried *in vacuo*.

The same method was used when producing hydroxy terminated poly vinyl acetate with 2-isopropoxy ethanol as the solvent/chain transfer agent.

After precipitation the isolated yield was 15g of polymer for the synthesis in IPA and 10g of polymer for the synthesis in 2-IPE.

7.2. Synthesis of block copolymers

7.2.1. Materials

ε-caprolactone (Aldrich) was used as received. THF (GPR grade) was used as received. Hydroxy-terminated poly (vinyl acetate) (PVAc-OH) was prepared as detailed above. Lipase from porcine pancreas and lipase from *candida antarctica* (Fluka), were used in their lyophilised powder (PPL and CA respectively), and immobilised forms (Sup PPL and NV respectively).

7.2.2. Method

A series of ten reactions were carried out using a Radley's multi reaction carousel (see appendix A figure 1) in order to check which enzyme had the greatest potential for catalysing the reaction of ε-CL and PVAc-OH. The molar ratio of ε-caprolactone to poly (vinyl acetate) used was 1:0.07. Radley's reaction tubes, equipped with stirrer bars, were filled with the previously prepared PVAc-OH (ca. 0.95mmol, 1.5g for polymer produced in IPA, 1.9g for polymer produced in 2-IPE), ε-CL (1.5g 13.2mmol), and THF (10ml). The lipase (ca. 50mg) was then added to each tube. The compositions of the tubes are shown in table 1. The tubes were then capped and flushed with nitrogen. After flushing, stirring commenced and the reaction tubes were heated to 70°C. 2ml aliquots of the reaction mixture were removed after 6, 24, 48 and 72 hours. The samples were placed in a freezer to quench the reaction prior to the removal of lipase from the mixture by filtration.

The filtered solution was concentrated on a rotary evaporator and the polymeric products were precipitated into 40-60 petroleum ether (25 ml) the products were

then dried *in vacuo*. The products were characterised by SEC, NMR and mass spectrometry.

Table 7-1 Composition of reactions

Reference	Type PVAc	Amount PVAc/g	Lipase	Amount lipase/mg	Comment
CS1/49/1	IPA	1.51	CA	50.8	No rxn
CS1/49/2	IPA	1.56	PPL	51.1	No rxn
CS1/49/3	IPA	1.52	NV	55.1	White solid
CS1/49/4	IPA	1.59	Sup PPL	48.9	No rxn
CS1/49/5	IPA	1.55	Blank	-	No rxn
CS1/49/6	2IPE	1.88	CA	50.4	No rxn
CS1/49/7	2IPE	1.92	PPL	51.5	No rxn
CS1/49/8	2IPE	1.79	NV	56	White solid
CS1/49/9	2IPE	1.81	Sup PPL	49.5	No rxn
CS1/49/10	2IPE	0.3	Blank	-	No rxn

7.3. Enzymatic degradation of hydroxy terminated poly (vinyl acetate)

7.3.1. Materials

THF (GPR grade) was used as received. Hydroxy-terminated poly (vinyl acetate) (PVAc-OH) was prepared as detailed above. Lipase from porcine pancreas and lipase from *candida antarctica* (Fluka), were used in their lyophilised powder (PPL and CA respectively) and immobilised forms (Sup PPL and NV respectively).

7.3.2. Method 1

In order to check the activity of each enzyme with respect to the degradation of the poly (vinyl acetate) used, a further study was performed using similar reaction

conditions as for the synthesis of the block copolymers. However this time no ε-caprolactone was added and the reactions were left for 96 hours. The products of these reactions were analysed by SEC.

Table 7-2 Table showing composition of reactions

Sample	Polymer used	Mass polymer / g	Lipase	Mass lipase / mg	Vol THF / ml
cs1/95/1	cs1/45/1	0.48	CA	6.4	10
cs1/95/2	cs1/45/1	0.49	PPL	31	10
cs1/95/3	cs1/45/1	0.57	NV	53	10
cs1/95/4	cs1/45/1	0.52	Sup PPL	0	10
cs1/95/5	cs1/45/1	0.43	blank	0	10

7.3.3. Materials

THF (GPR grade) was used as received. Hydroxy-terminated poly (vinyl acetate) (PVAc-OH) was synthesised using a parallel synthesis robot as described in synthesis section 1. Lipase from *candida antarctica* (Fluka), was used in its immobilised form (Novozym 435).

7.3.4. Method 2

A further study into the degradation activity of Novozym 435 (NV) with respect to the molecular weight of the polymer being degraded was performed using the same reaction conditions as method 1 above. The products of these reactions were then analysed by SEC.

Table 7-3 Table showing composition of reactions

Sample	Polymer used	Mass polymer / g	Lipase	Mass lipase / mg	Vol THF / ml
cs1/95/6	cs1/61/1	0.21	NV	29.5	10
cs1/95/7	cs1/61/2	0.29	NV	28.7	10
cs1/95/8	cs1/61/3	0.2	NV	30	10
cs1/95/9	cs1/61/4	0.27	NV	29.5	10
cs1/95/10	cs1/61/5	0.22	NV	26.2	10

8.Results and discussion for the synthesis of poly (vinyl acetate-*block*-ε-caprolactone)

8.1. Synthesis of hydroxy terminated poly (vinyl acetate)

Poly (vinyl acetate) was synthesized in both isopropanol and 2-isopropoxy ethanol, in both cases the volume ratio of solvent to monomer was 14:1. The polymers thus synthesised were isolated by the use of rotary evaporation to remove solvent and excess monomer. The resulting polymers were clear colourless viscous fluids. The polymers were dissolved in THF (2mg ml^{-1}) and subjected to size exclusion chromatography. This gave molecular weights of 1600gmol^{-1} and 2000gmol^{-1} for the polymers produced in IPA and 2-isopropoxy ethanol respectively.

8.1.1. NMR analysis

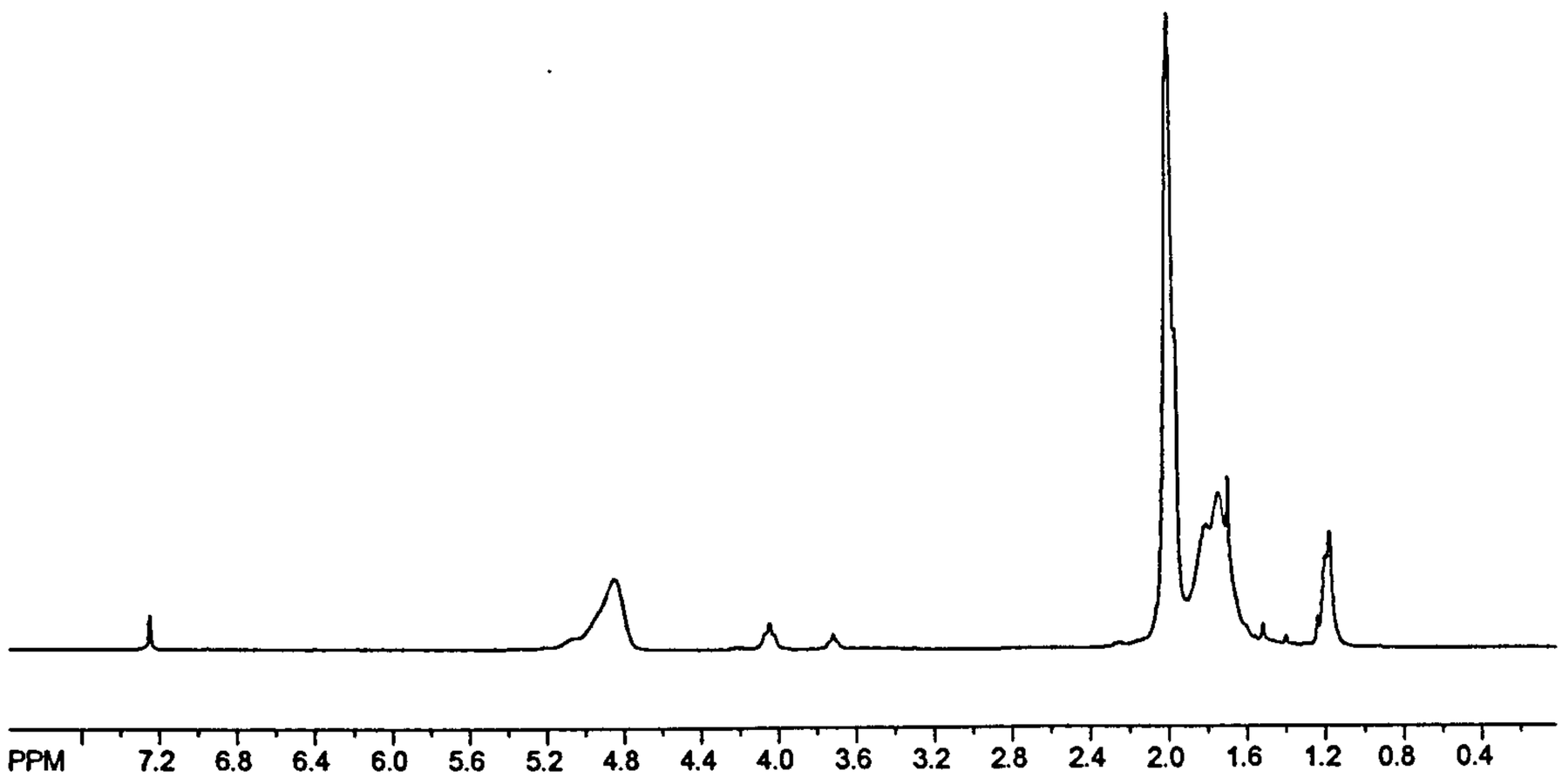


Figure 8-1 1H NMR spectrum of PVAc synthesised in isopropanol

The above NMR spectrum is of poly (vinyl acetate) synthesized in isopropanol, on a large scale. The assignments are: backbone C*H* δ≈4.8; backbone CH_2 δ≈1.7; ultimate CH_2 δ≈4.0; pendant methoxy CH_3 δ≈2.0. The peaks at δ≈3.6 and δ≈1.2 are due to excess solvent not removed on isolation of the product. The end-group methyl signal is at δ≈1.2 and is hidden by the excess solvent signal.

8.2. Synthesis of Poly(vinyl acetate-*block*-ε-caprolactone)

8.2.1. SEC results

During the course of the lipase-catalysed reactions of the pre-synthesised PVAc with ε-CL, 2 ml aliquots of the reaction mixture were removed at various time intervals, worked up, and subsequently analysed by SEC. The SEC chromatograms are shown in figures 2 and 3. Plotting the change in molecular weight (Mp, Mn, and Mw) for the different fractions lead to an interesting observation. At early reaction times, although CA, PPL, supported PPL, show little effect, Novozym 435 shows an initial decrease in mass, possibly indicating the degradation of PVAc as can be seen in figures 4 and 5. However, at longer reaction times, the molecular weight becomes significantly higher than that of the starting material. This would indicate that a polymerisation process is occurring, this is likely to be the homopolymerisation of ε-caprolactone, initiated by water in the reaction medium, it is also possible that block copolymer has formed, initiated by the hydroxy terminated PVAc.

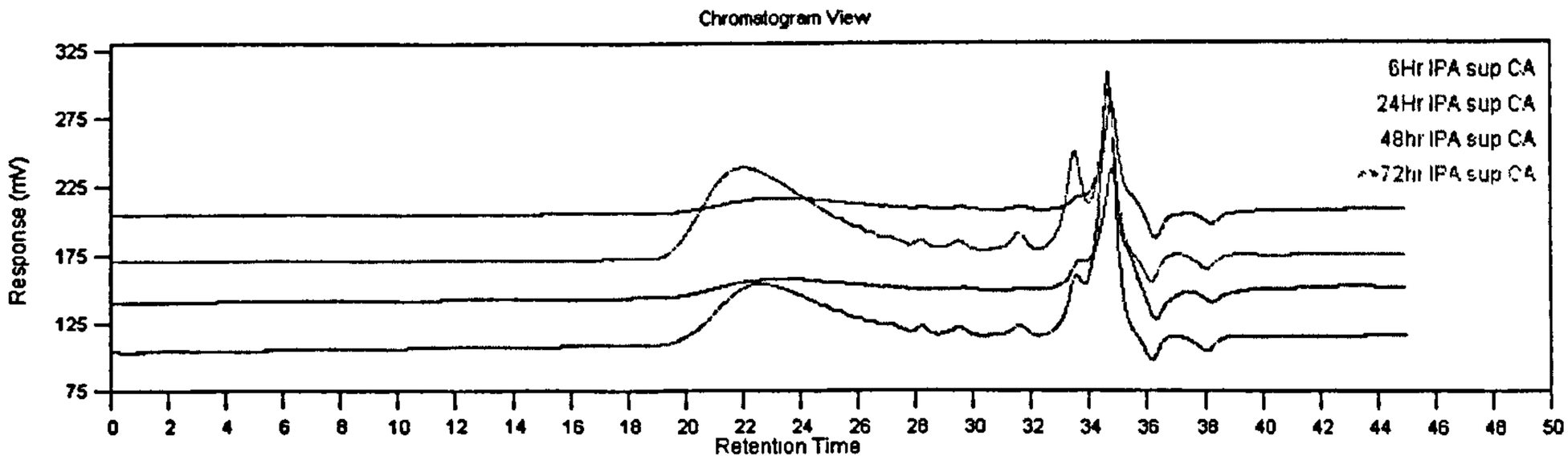


Figure 8-2 SEC chromatogram for the reactions using PVAc synthesised in IPA

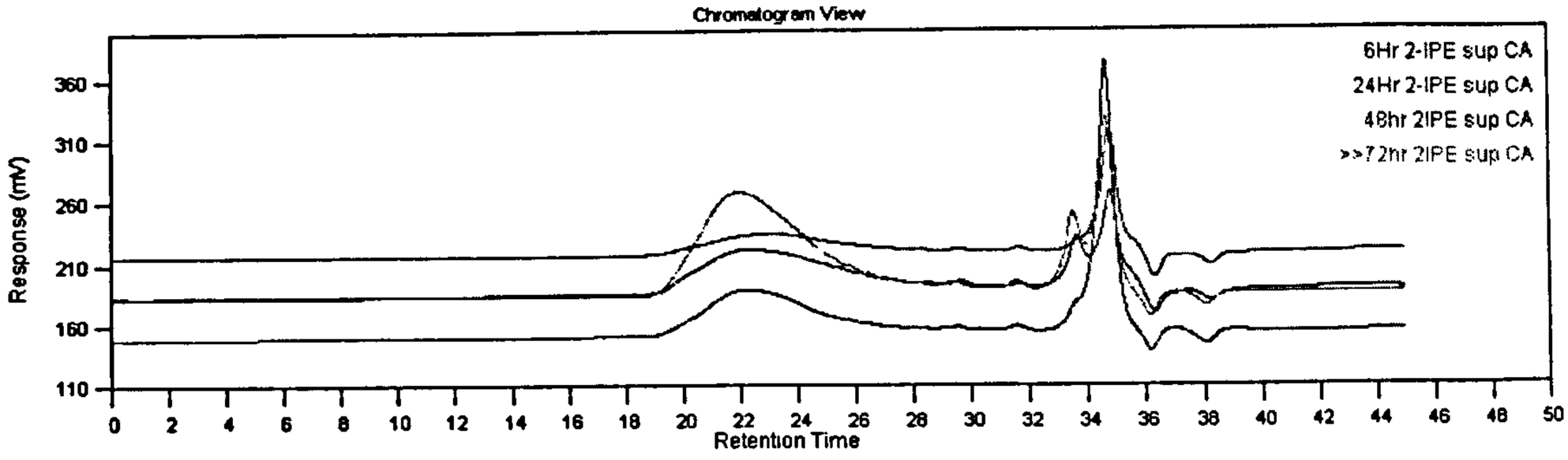


Figure 8-3 SEC chromatogram for the reactions using PVAc synthesised in 2-IPE

Sample	Mp	Mn	Mw	PD
6hr IPA CA	2680	1760	2510	1.4
6hr IPA PPL	2660	1760	2510	1.4
6hr IPA Sup CA	2140	1470	2160	1.5
6hr IPA Sup PPL	2460	1430	2220	1.6
6hr IPA Blank	2560	1530	2290	1.5
24hr IPA CA	2550	1510	2280	1.5
24hr IPA PPL	2610	1640	2390	1.5
24hr IPA Sup CA	2080	1440	2080	1.4
24hr IPA Sup PPL	2590	1550	2320	1.5
24hr IPA Blank	2670	1550	2320	1.5
48hr IPA CA	2530	1410	2220	1.6
48hr IPA PPL	2520	1420	2250	1.6
48hr IPA Sup CA	2640	1410	2190	1.6
48hr IPA Sup PPL	2540	1420	2240	1.6
48hr IPA Blank	2560	1430	2250	1.6
72hr IPA CA	2570	1410	2240	1.6
72hr IPA PPL	2570	1420	2260	1.6
72hr IPA Sup CA	3380	1580	2650	1.7
72hr IPA Sup PPL	2580	1430	2260	1.6
72hr IPA Blank	2700	1460	2330	1.6
6hr 2IPE CA	3700	1770	3070	1.7
6hr 2IPE PPL	3870	2020	3320	1.6
6hr 2IPE Sup CA	3160	1670	2810	1.7
6hr 2IPE Sup PPL	3800	1780	3090	1.7
6hr 2IPE Blank	3940	2480	3770	1.5
24hr 2IPE CA	3810	2030	3310	1.6
24hr 2IPE PPL	4080	2230	3560	1.6
24hr 2IPE Sup CA	2230	1760	2670	1.5
24hr 2IPE Sup PPL	3850	2000	3310	1.7
24hr 2IPE Blank	-	-	-	-
48hr 2IPE CA	3840	1720	3090	1.8
48hr 2IPE PPL	3920	1740	3120	1.8
48hr 2IPE Sup CA	3020	1690	2740	1.6
48hr 2IPE Sup PPL	3920	1780	3130	1.8
48hr 2IPE Blank	3910	1790	3150	1.8
72hr 2IPE CA	3910	1760	3160	1.8
72hr 2IPE PPL	3920	1770	3160	1.8
72hr 2IPE Sup CA	3420	1870	3010	1.6
72hr 2IPE Sup PPL	3870	1770	3140	1.8
72hr 2IPE Blank	3910	2380	3650	1.5

Table 8-1 Table showing SEC results

The following graphs plot the data tabulated in table 1. Fig 4 shows the data for the polymer synthesized in isopropanol, whilst fig 5 shows the data for the polymer synthesized in 2-isopropoxy ethanol. It is clear from these plots that the enzyme with the greatest efficacy is the Novozym 435, the supported *candida antarctica*.

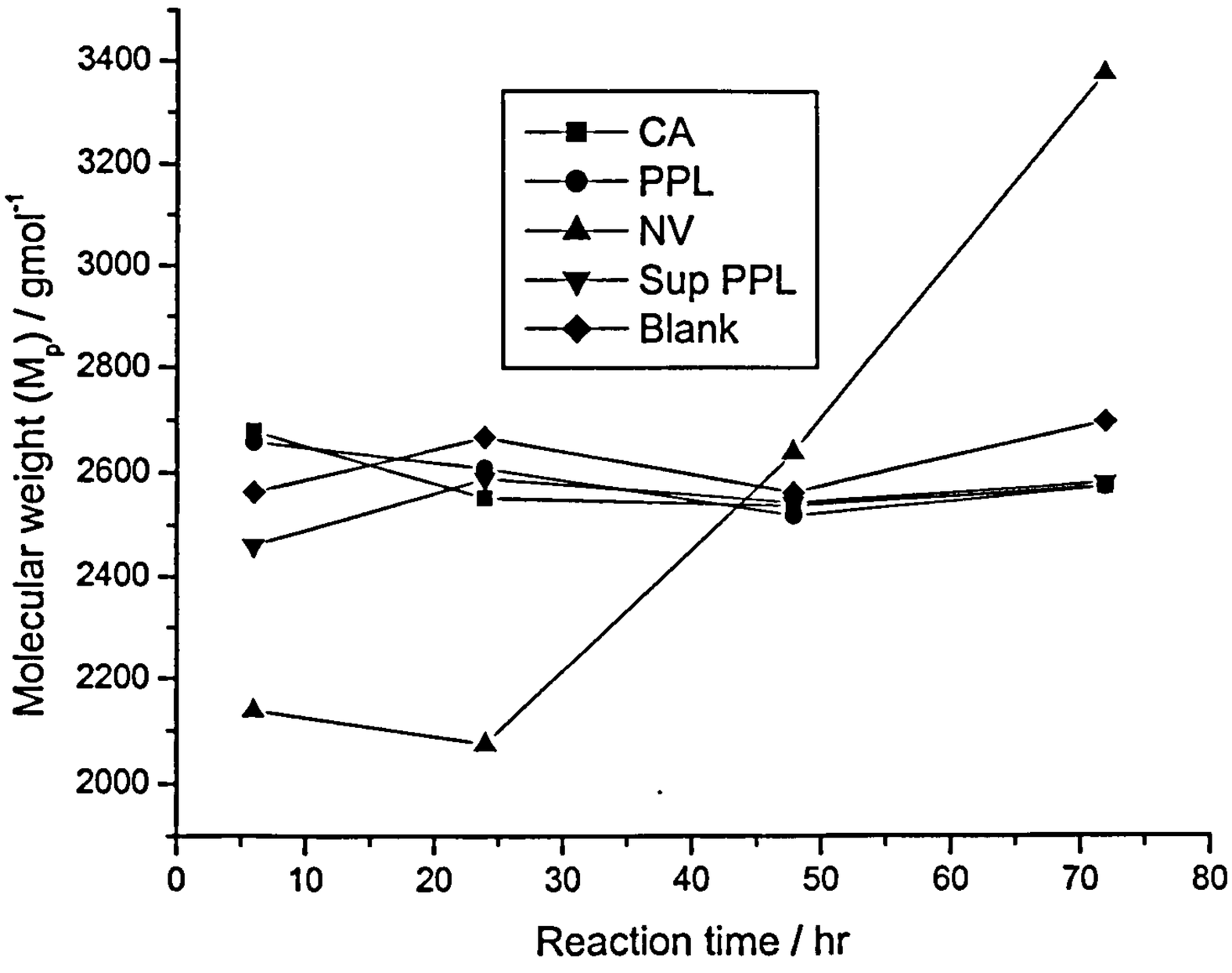


Figure 8-4 Graph showing change in molecular weight against time for the polymers synthesised in the presence of different enzymes, where the PVAc-OH was synthesised in IPA

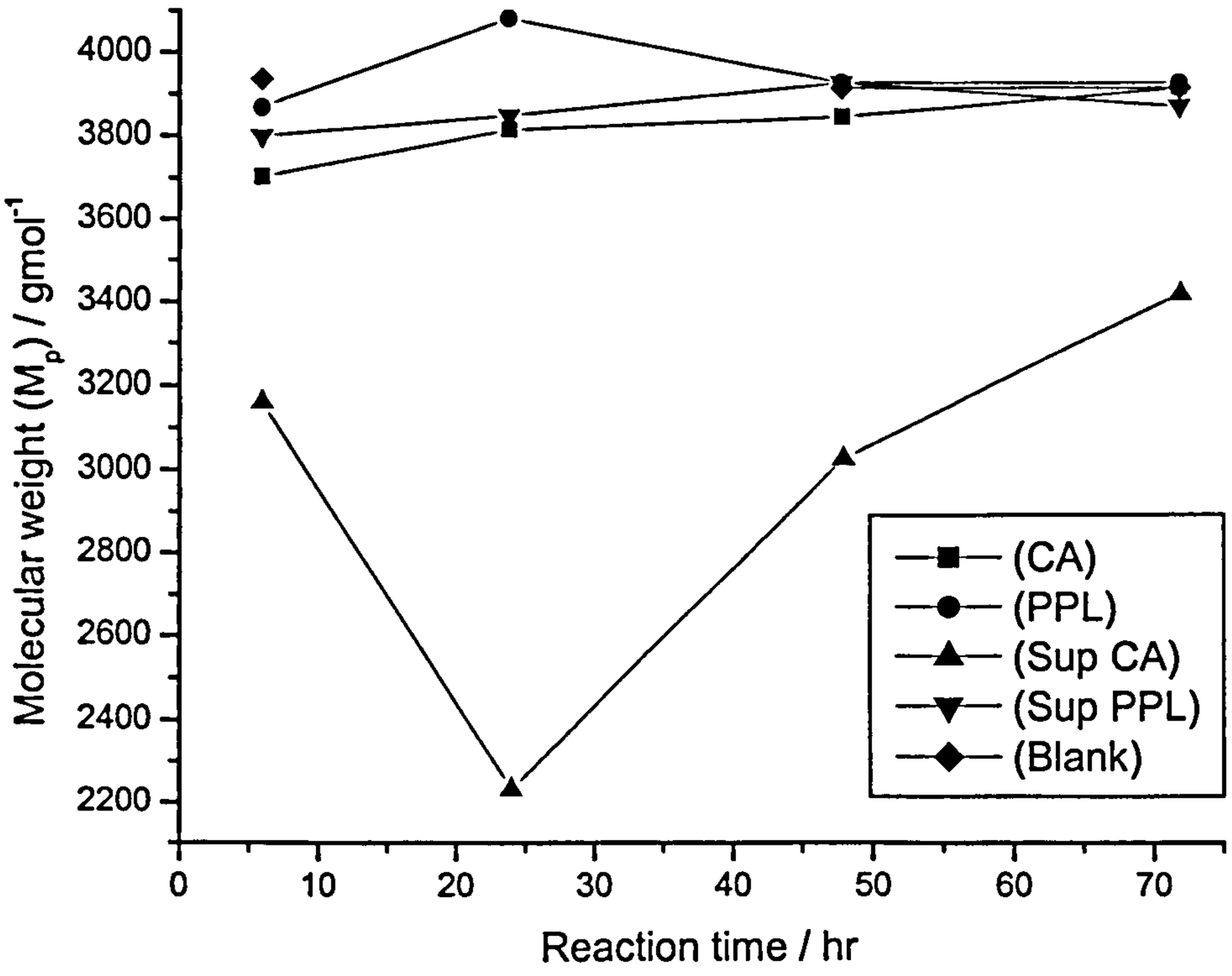


Figure 8-5 Graph showing change of molecular weight against time, for polymers synthesised in the presence of different enzymes, where the PVAc-OH was synthesised in 2-isopropoxy ethanol

When the SEC results are plotted with the molecular weight against time for the different enzyme types, it can be seen that the only one exhibiting any change in mass is the sample catalysed with novozym 435; this result was not unexpected given that the polymers present were now waxy solids, rather than the liquid ε-caprolactone and the viscous liquid of the PVAcs. However, it is the types of changes exhibited that are of interest. At first the molecular weight of the polymers present drops, then after a period the molecular weight starts to increase. This would indicate that two processes were occurring.

The first process occurring in the early stage of the reaction is degradation of the poly (vinyl acetate). After a period however the formation of poly (ε-caprolactone) starts to show in the SEC results, by shifting the molecular weight

of the sample to higher average values. There could be more than one explanation for this observed behaviour. One explanation could be that the enzyme starts to break down the PVAc, and starts the polymerisation of ε-caprolactone at the same time. However, the observed molecular weight by SEC goes down initially until the amount of poly (ε-caprolactone) produced starts to have a higher molecular weight than that of the degraded PVAc. Another explanation could be that the enzyme starts by breaking down the PVAc into smaller pieces before it initiates a polymerisation reaction with ε-caprolactone.

8.2.2. NMR results

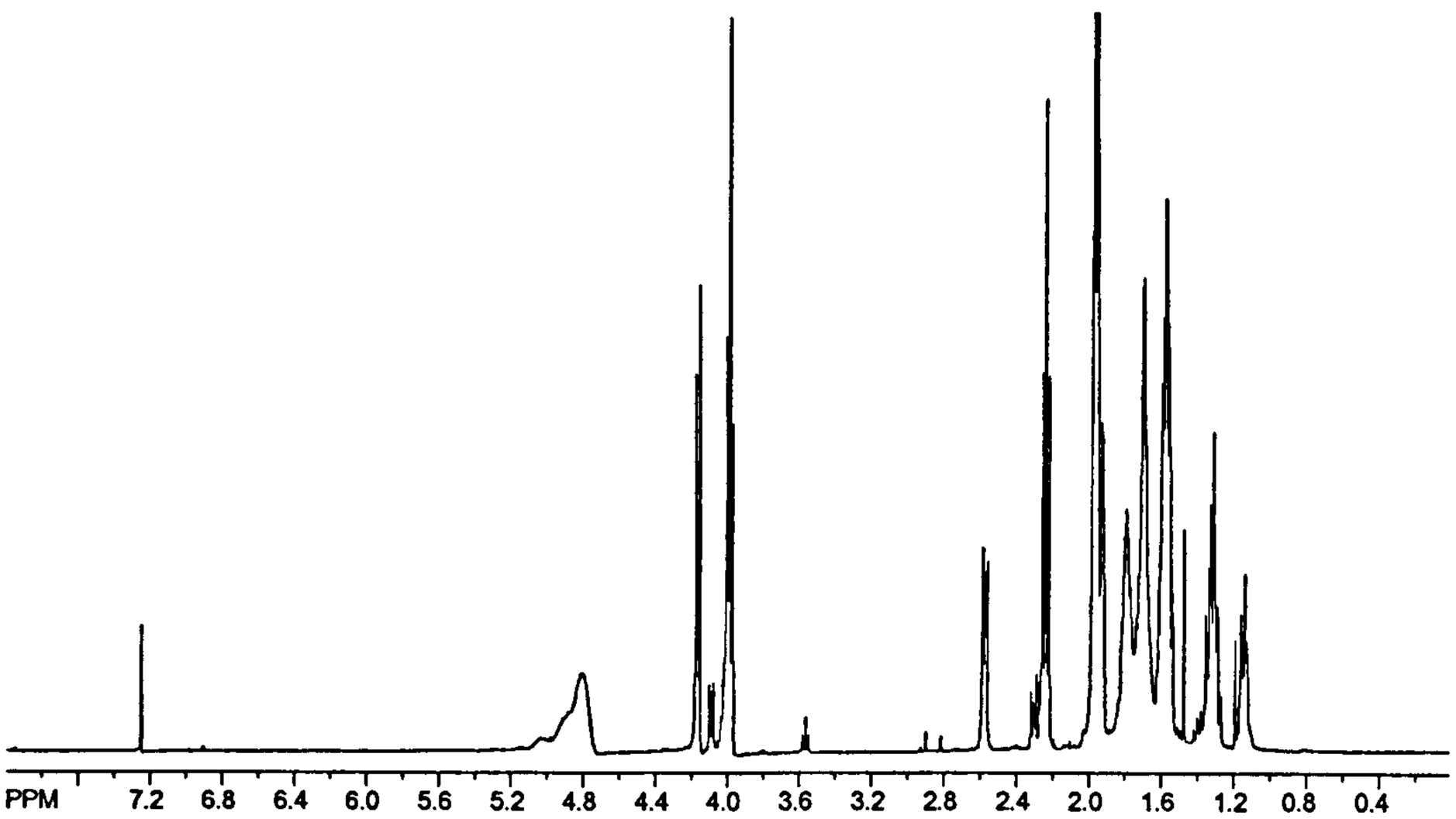


Figure 8-6 ^{1}H NMR spectrum of poly (VAc-e-CL) copolymer

The NMR spectrum in figure 6 is of sample cs1/49/3, present in the spectrum are peaks corresponding to PVAc and poly ε–caprolactone. The reaction time was 72 hours. The assignments are: VAc backbone C*H* δ≈4.9; VAc backbone CH_2 δ≈1.7; VAc pendant methoxy CH_3 δ≈2.0; εCL monomer δ≈4.3, δ≈2.6, δ≈1.8, δ≈1.6(these overlap with other peaks from PVAc); εCL -CH_2-O- δ≈4.0; εCL

COCH_2 δ≈2.3; εCL backbone CH_2 δ≈1.3, δ≈1.6, δ≈1.7(some of these peaks overlap other monomer and polymer peaks already assigned).

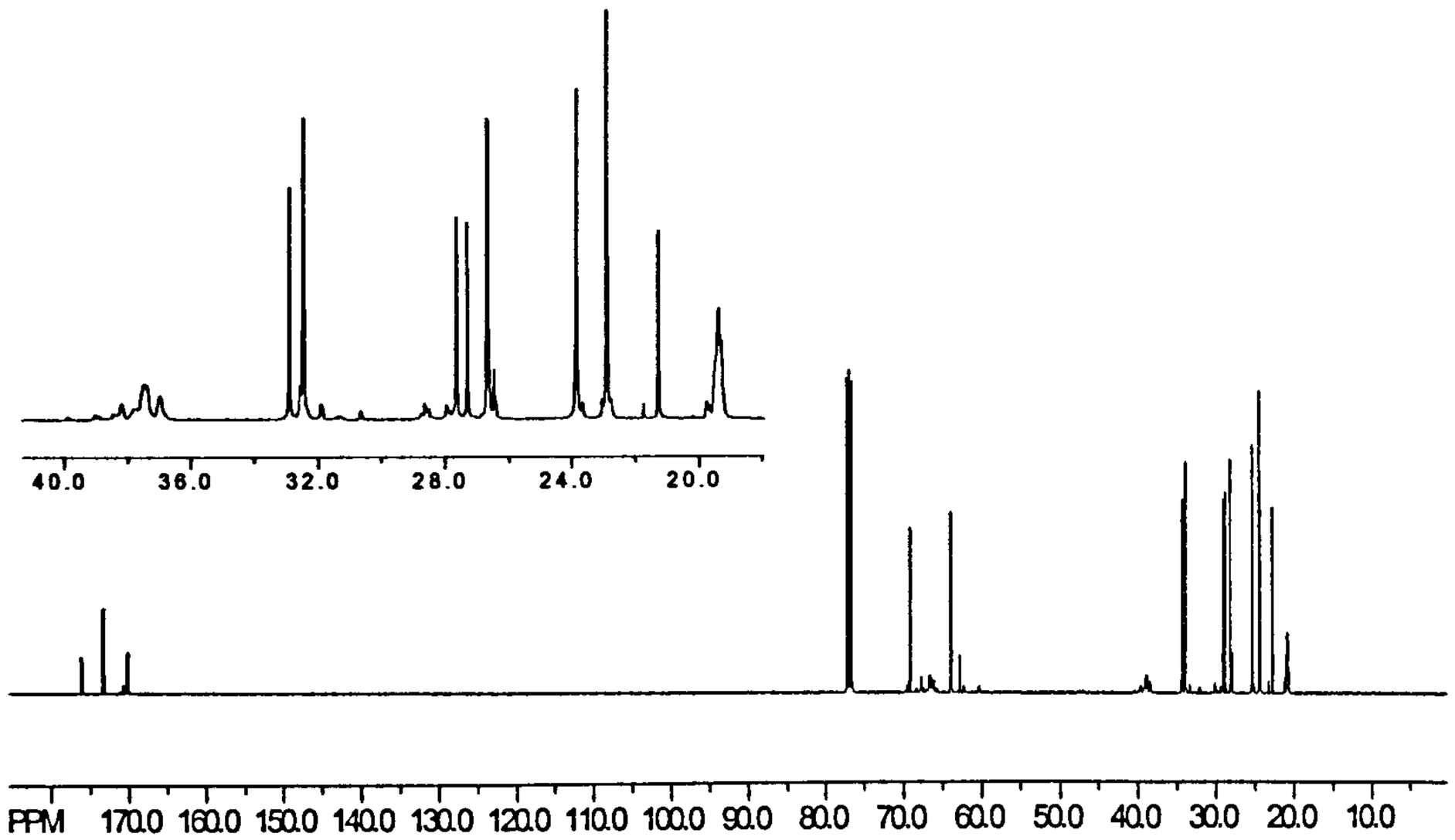


Figure 8-7 ^{13}C NMR spectrum of poly (VAc-e-CL) copolymer

The ^{13}C NMR spectrum shown in figure 7 is of sample cs1/49/3, and corresponds to the ^{1}H spectrum shown in figure 3. The assignments are: VAc backbone *C*H δ≈65; VAc backbone *C*H_2 δ≈38; VAc pendant methoxy *C*H_3 δ≈19; VAc carbonyl δ≈170; eCL monomer δ≈175, δ≈68, δ≈32.5, δ≈27.5, δ≈21; εCL -*C*H_2-O- δ≈62; εCL *C*O*C*H_2 δ≈172; εCL backbone *C*H_2 δ≈33, δ≈27, δ≈24, δ≈23.

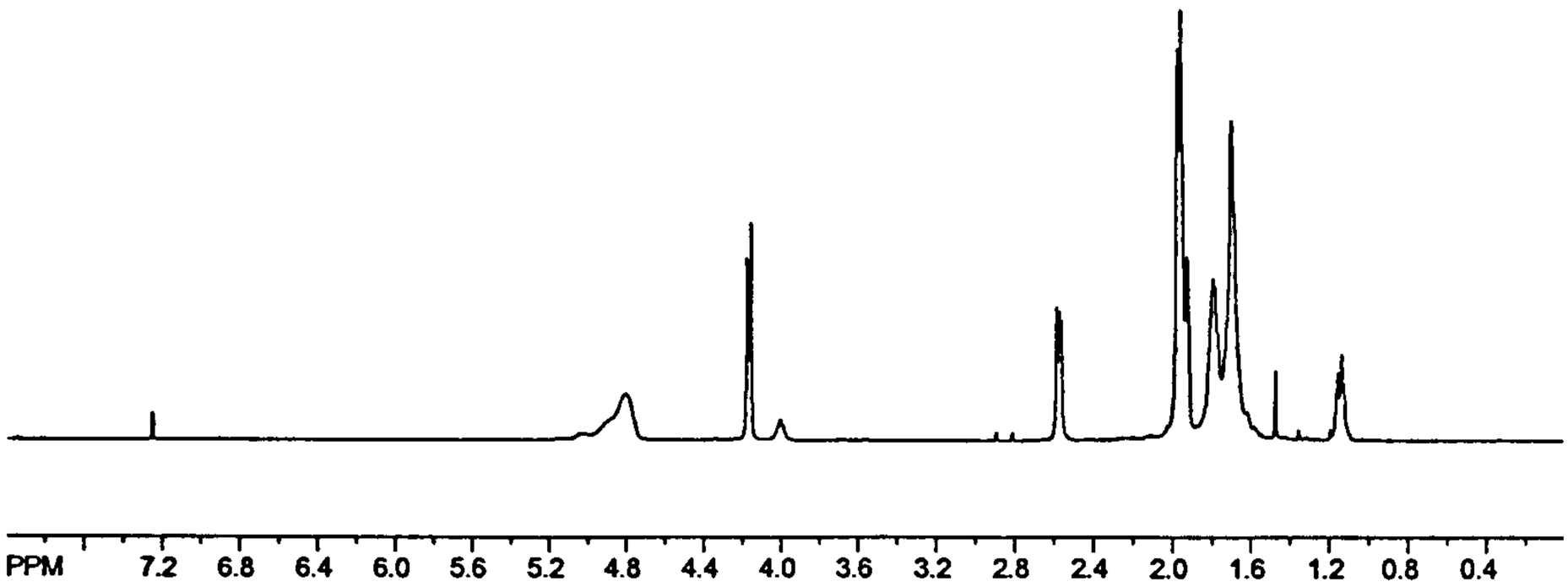


Figure 8-8 ^{1}H NMR spectrum of the blank test sample

The NMR spectrum in figure 8 is of the blank test performed. Hydroxy-terminated poly (vinyl acetate) was added to a reaction vessel with ε-caprolatone monomer, and heated, but without any enzyme to act as catalyst. The assignments are: VAc backbone C*H* δ≈4.8; VAc backbone CH_2 δ≈1.8; VAc ultimate CH_2 δ≈4.0; VAc pendant methoxy CH_3 δ≈2.0; endgroup CH_3 δ≈1.1; eCL monomer δ≈4.3, δ≈2.6, δ≈1.8, δ≈1.6; there are no peaks assignable to εCL polymer. The peak at δ≈7.25 is from $CDCl_3$.

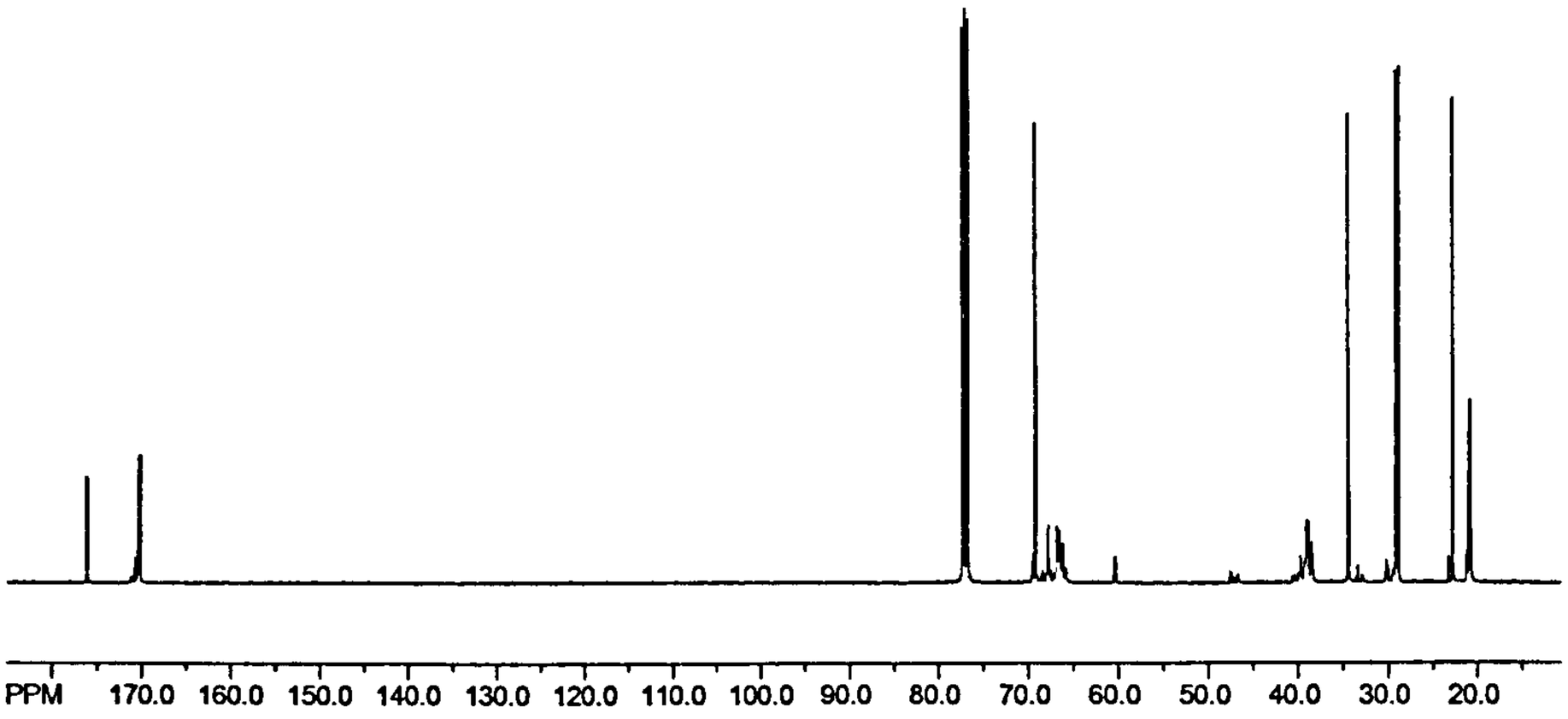


Figure 8-9 ^{13}C NMR spectrum of the blank test sample

The ^{13}C NMR spectrum in figure 9 is of the blank test performed. The assignments are: VAc backbone C*H* δ≈65; VAc backbone CH_2 δ≈38; VAc pendant methoxy CH_3 δ≈20; VAc carbonyl δ≈170; εCL monomer δ≈176, δ≈70, δ≈33, δ≈30, δ≈23; again, there are no peaks assignable to poly (ε-caprolactone). The peaks at δ≈77 are from $CDCl_3$.

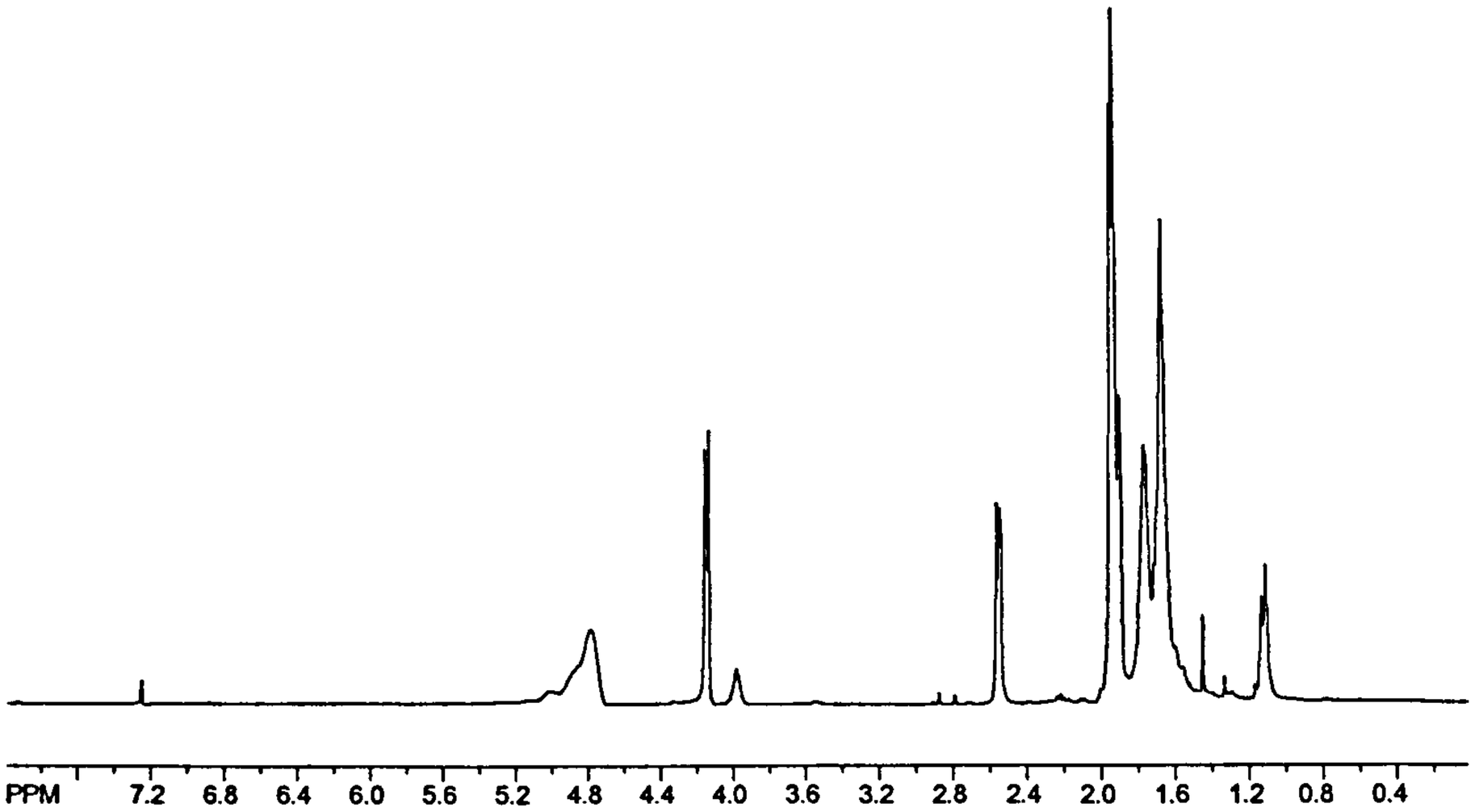


Figure 8-10 ^{1}H NMR spectrum of sample synthesised with CA as catalyst

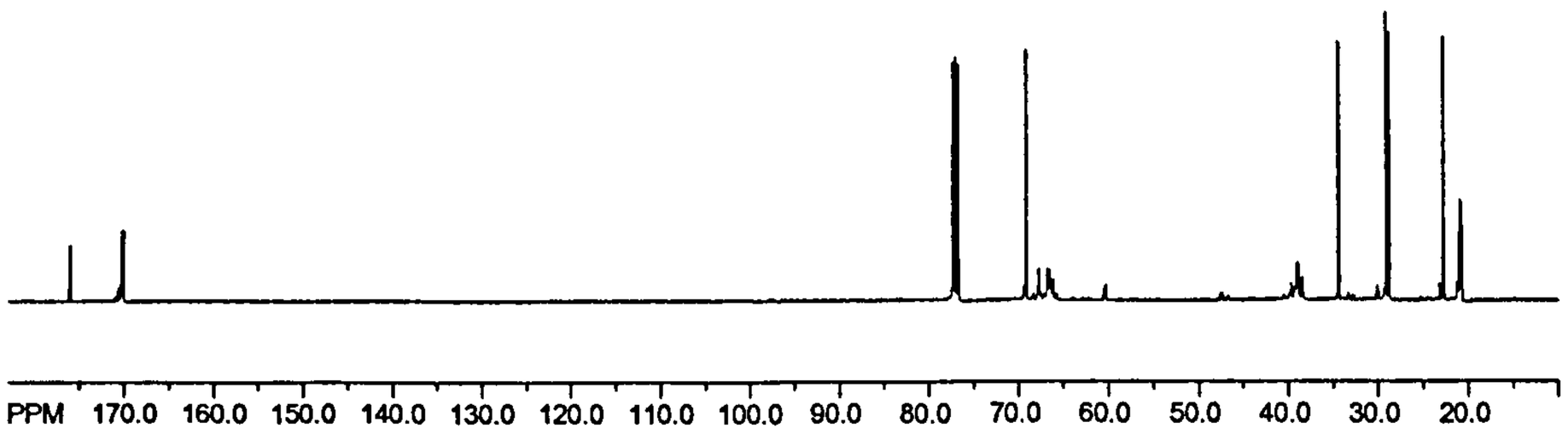


Figure 8-11 ^{13}C NMR spectrum of sample synthesised with CA as catalyst

The NMR spectra in figures 10 and 11 are of the reaction products of hydroxy-terminated poly (vinyl acetate) with ε-caprolactone, using lipase from *candida antarctica*. It must be remembered that Novozym 435 is supported lipase from *candida antarctica*, with this in mind, the similarity between this spectrum and

that of the blank test indicates that no reaction has taken place, even with the similarity of the enzyme employed.

8.2.3. Mass spectrometry results

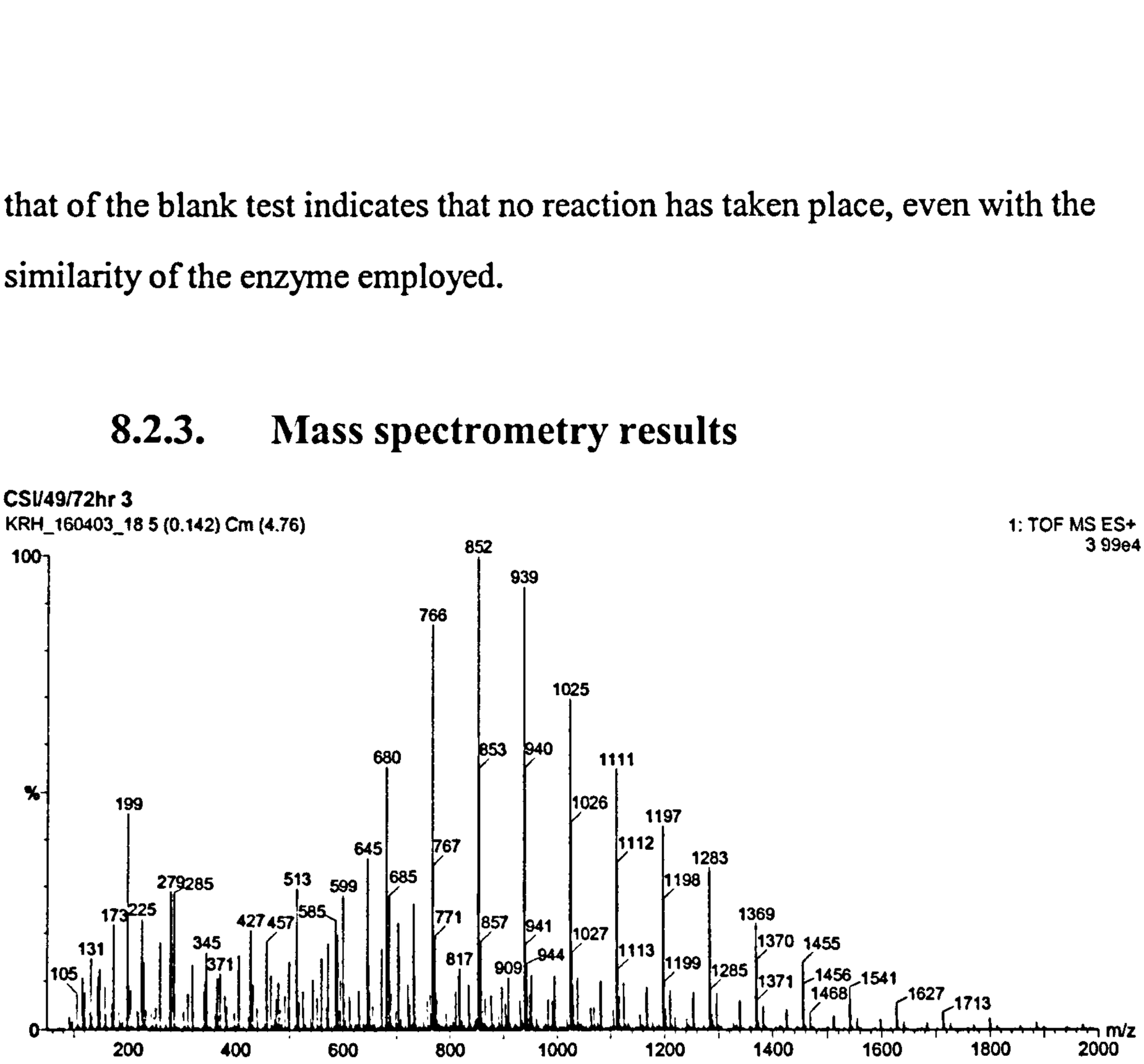


Figure 8-12 ESI-MS of poly (VAc-e-CL) sample CS1/49/72hr3

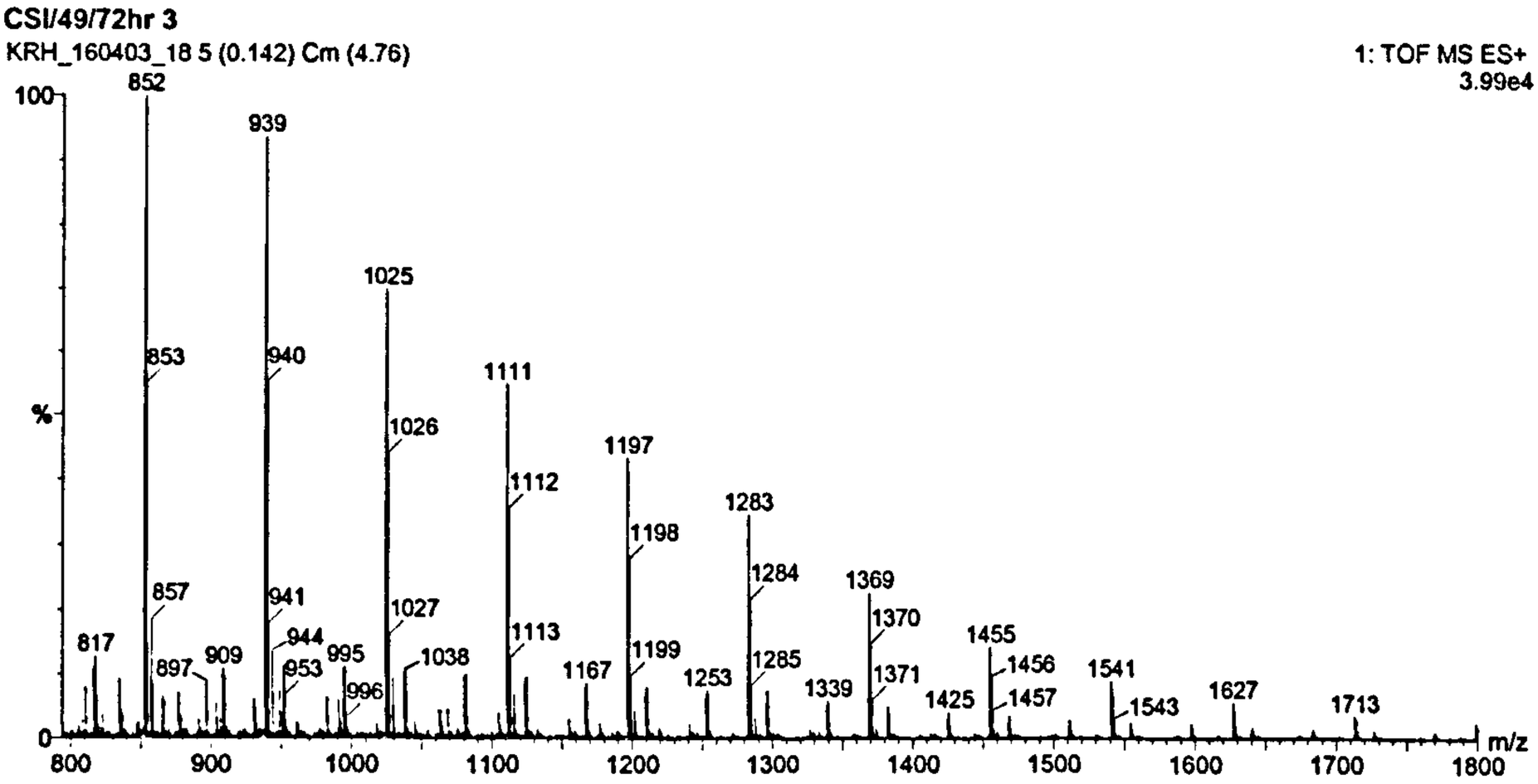


Figure 8-13 ESI-MS of poly (VAc-e-CL) sample CS1/49/72hr3

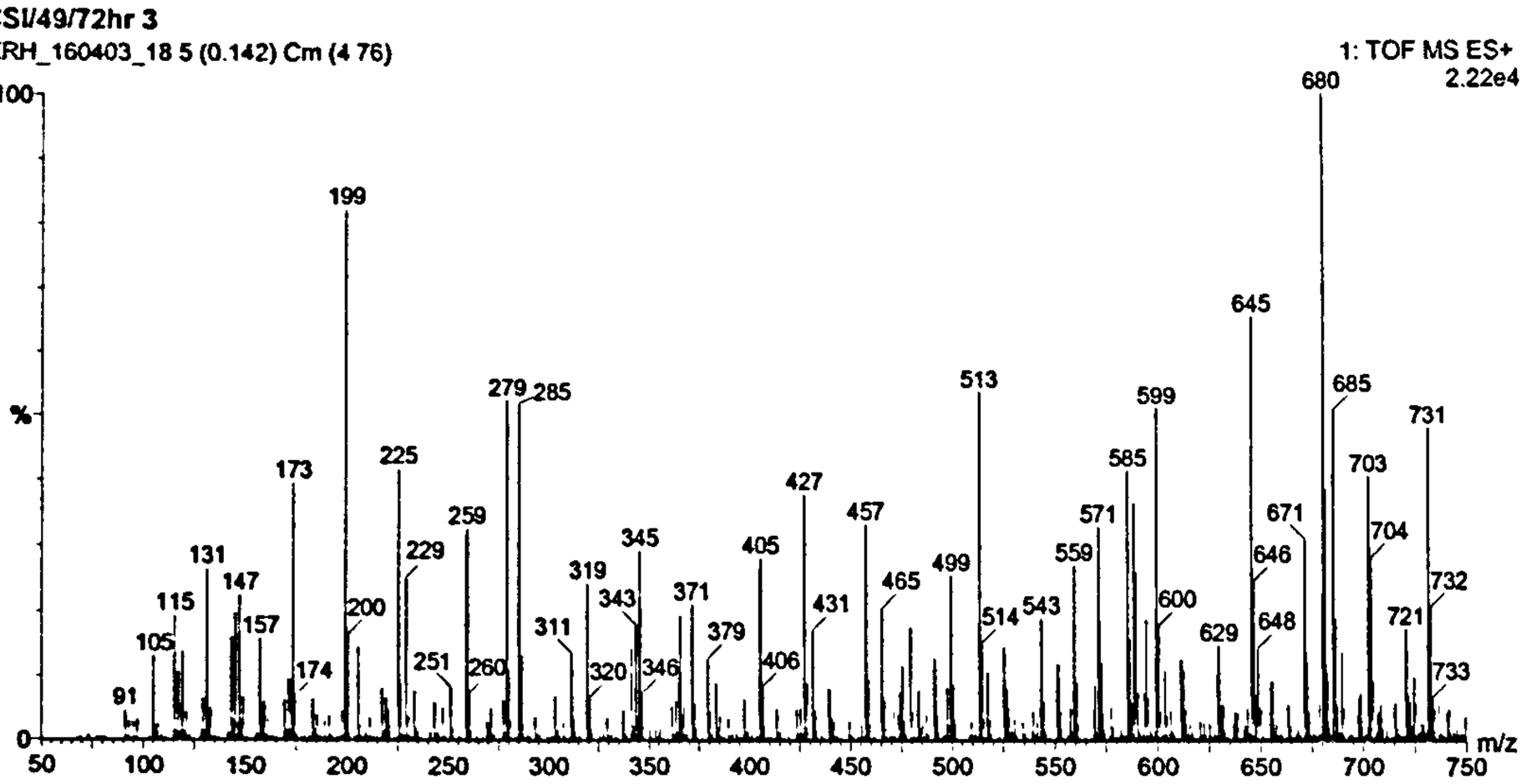


Figure 8-14 ESI-MS of poly (VAc-e-CL) sample CS1/49/72hr3

The three mass spectra shown in figures 12,13 and 14 are of CS1/49/72hr3, a sample containing hydroxy-terminated poly (vinyl acetate) synthesised in isopropanol, ε-caprolactone and catalyst Novozym 435. The first spectrum in figure 12 shows the whole mass range, the second in figure 13 shows the region that has mainly vinyl acetate homopolymer and the third in figure 14 shows the region of low molecular weight VAc homopolymer, which also might contain peaks due to block copolymers of vinyl acetate and ε-caprolactone. An Excel spreadsheet was used to derive a list of numbers that represented the masses that would be expected if copolymerisation had taken place. With the help of this list, an excerpt shown in figure 16, the spectrum was analysed in order to search for peaks due to homopolymers and peaks due to copolymers. A large number of the copolymer peaks that the excel spreadsheet had predicted were indeed found, for example the peak at m/z = 278, is indicative of $P(VAc)_m$-b-$P(\varepsilon CL)_n$ where m and n are both 1, the peak at m/z = 678, has m, n both 3, the peak at m/z = 906, has m = 3, n = 5.

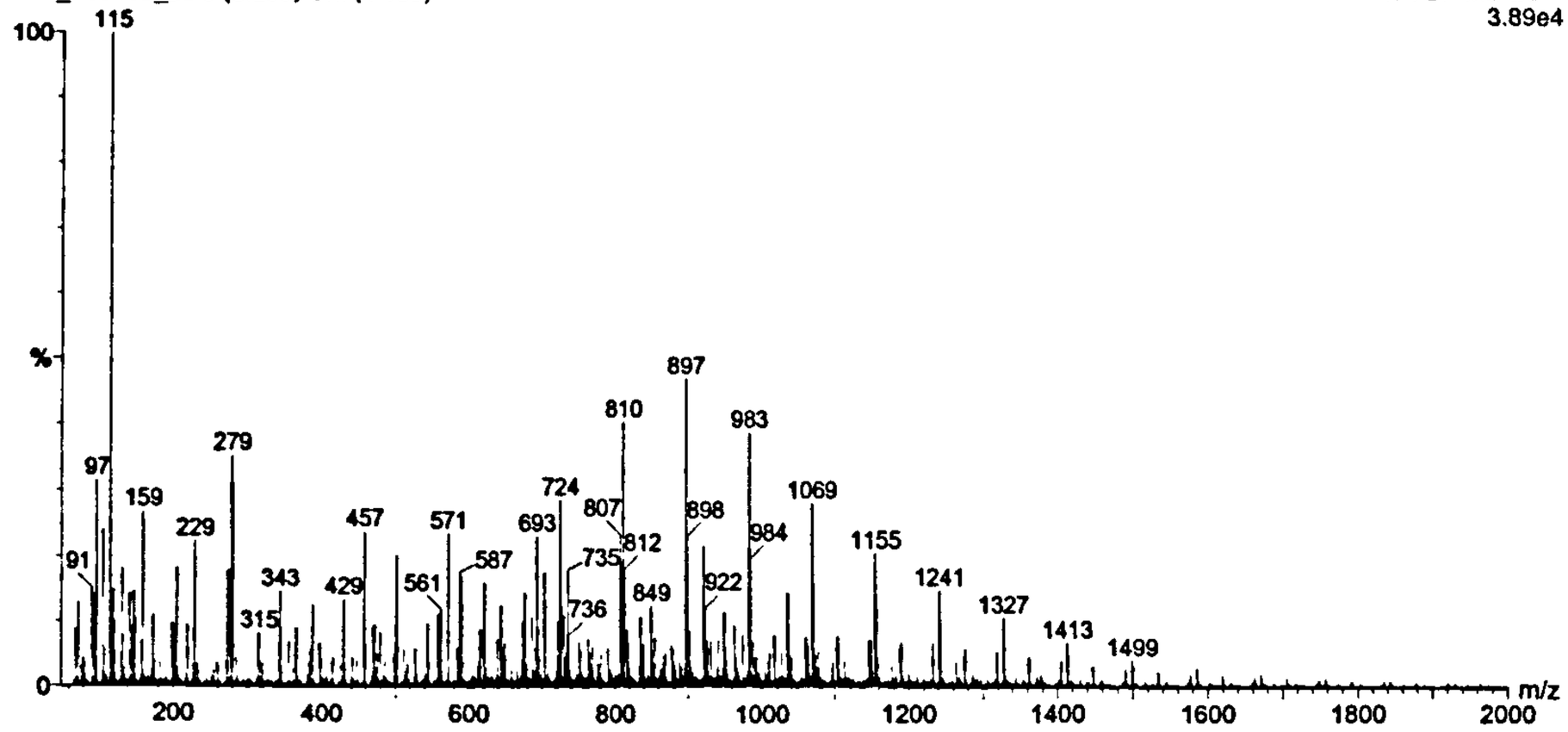


Figure 8-15 ESI-MS of poly (VAc-e-CL) sample CS1/29/72hr8

The above mass spectrum is of sample CS1/49/72hr8, a sample containing hydroxy-terminated poly (vinyl acetate) synthesized in 2-isopropoxy ethanol, ε-caprolactone, and catalyst Novozym 435. This mass spectrum was analysed in much the same way as the previous spectrum, an Excel spreadsheet was generated, and the spectrum was then searched for the requisite peaks. Peaks corresponding to polymers of $P(VAc)_m$-b-$P(\varepsilon CL)_n$, with m =1, n = 1; m = 2, n = 2; m = 2, n = 6 were found in the spectra at m/z = 322, 522, 978, for example.

M	N	PVAc in IPA	PVAc in 2-IPE
1	1	278	322
1	2	392	436
1	4	620	664
1	6	848	892
1	7	962	1006
1	8	1076	1120
1	9	1190	1234
1	10	1304	1348
1	11	1418	1462
1	12	1532	1576
2	1	364	408
2	2	478	522
2	7	1048	1092
2	8	1162	1206
2	10	1390	1434
2	11	1504	1548
2	12	1618	1662
3	1	450	494
3	3	678	722
3	4	792	836
3	5	906	950
3	6	1020	1064
3	7	1134	1178
3	8	1248	1292
3	9	1362	1406
3	10	1476	1520
3	11	1590	1634
3	12	1704	1748

Figure 8-16 Excerpt of excel spreadsheet used to look for copolymer peaks in mass spectra

8.3. Degradation of poly (vinyl acetate)

Because poly (vinyl acetate) is known to degrade in the presence of some enzymes, a follow up experiment was performed where only poly (vinyl acetate) was used in combination with the different enzymes in order to probe the mechanism of the method of degradation. It was also thought that the molecular weight of the polymer in question might have an effect on the amount of degradation observed, to this end a further set of reactions were performed, where

the activity of the enzyme Novosym 435 was checked with regard to increasing molecular weight of the PVAc.

8.3.1. SEC results

The samples were filtered to remove any enzyme, before concentration on a rotary evaporator in order to remove solvent and excess monomer, once isolated they were dissolved in THF (2mg ml^{-1}), and subjected to analysis by size exclusion chromatography. The results of this analysis are tabulated in table 2.

Table 8-2 Table showing SEC results

Sample	Mn / $gmol^{-1}$	Mw / $gmol^{-1}$	Pd	Enzyme
cs1/95/1 24hr	1350	2800	2.1	CA
cs1/95/2 24hr	1300	2440	1.9	PPL
cs1/95/3 24hr	1280	2360	1.8	NV
cs1/95/4 24hr	1290	2390	1.9	Sup PPL
cs1/95/5 24hr	1290	2390	1.9	Blank
cs1/95/6 24hr	3270	9400	2.9	NV
cs1/95/7 24hr	4030	11200	2.6	NV
cs1/95/8 24hr	4390	13800	3.1	NV
cs1/95/9 24hr	6860	15700	2.3	NV
cs1/95/10 24hr	8840	20200	2.3	NV
cs1/95/1 48hr	1320	2730	2.1	CA
cs1/95/2 48hr	1280	2380	1.9	PPL
cs1/95/3 48hr	1250	2320	1.9	NV
cs1/95/4 48hr	1210	2260	1.9	Sup PPL
cs1/95/5 48hr	1280	2370	1.9	Blank
cs1/95/6 48hr	3520	9410	2.7	NV
cs1/95/7 48hr	4540	11000	2.4	NV
cs1/95/8 48hr	6400	14400	2.2	NV
cs1/95/9 48hr	7530	16100	2.1	NV
cs1/95/10 48hr	9100	19200	2.1	NV
cs1/95/1 96hr	730	1960	2.7	CA
cs1/95/2 96hr	750	1920	2.6	PPL
cs1/95/3 96hr	700	1800	2.6	NV
cs1/95/4 96hr	880	1940	2.2	Sup PPL
cs1/95/5 96hr	840	1870	2.2	Blank
cs1/95/6 96hr	3040	7110	2.3	NV
cs1/95/7 96hr	2980	7420	2.5	NV
cs1/95/8 96hr	4730	10700	2.3	NV
cs1/95/9 96hr	4910	11400	2.3	NV
cs1/95/10 96hr	5010	13500	2.7	NV

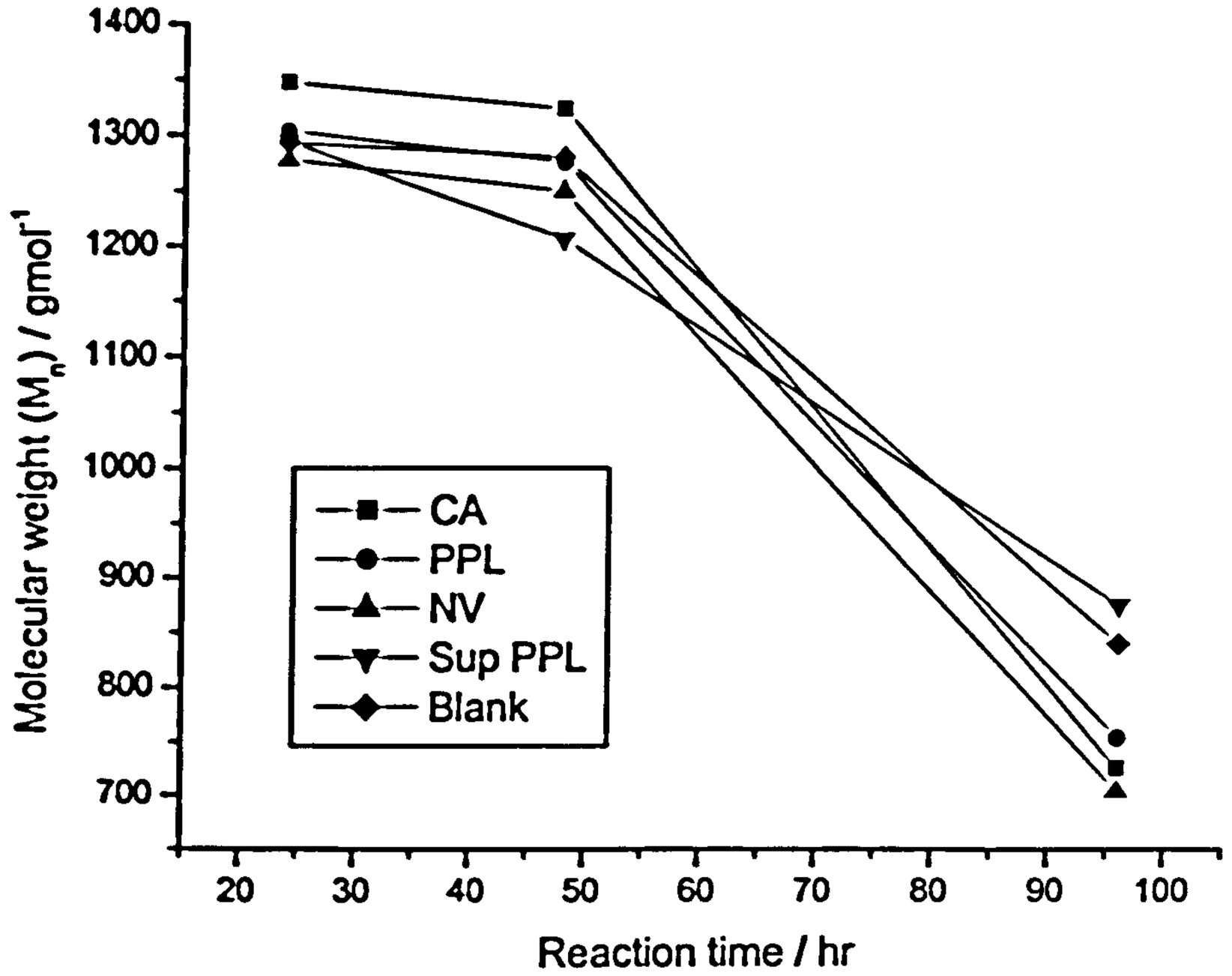


Figure 8-17 Graph showing the degradation of PVAc-OH in the presence of differnt enzymes

The graph in figure 17 shows the degradation of poly (vinyl acetate) with respect to altering enzyme type. From the graph it must be noted that the traces corresponding to supported PPL and the blank test are effectively the same as there was no supported PPL left to run that sample. From this graph it is clear that there is some degradation of the poly (vinyl acetate) samples even without enzyme being present. This in contrast to the previous results where the only sample that showed any change was the sample with Novozym 435 present (see figures 4 and 5). It can be concluded from this graph that the reaction conditions play a large part in the degradation of such samples, the choice of solvent, reaction temperature, reaction time and rate of stirring are all variables that could be investigated.

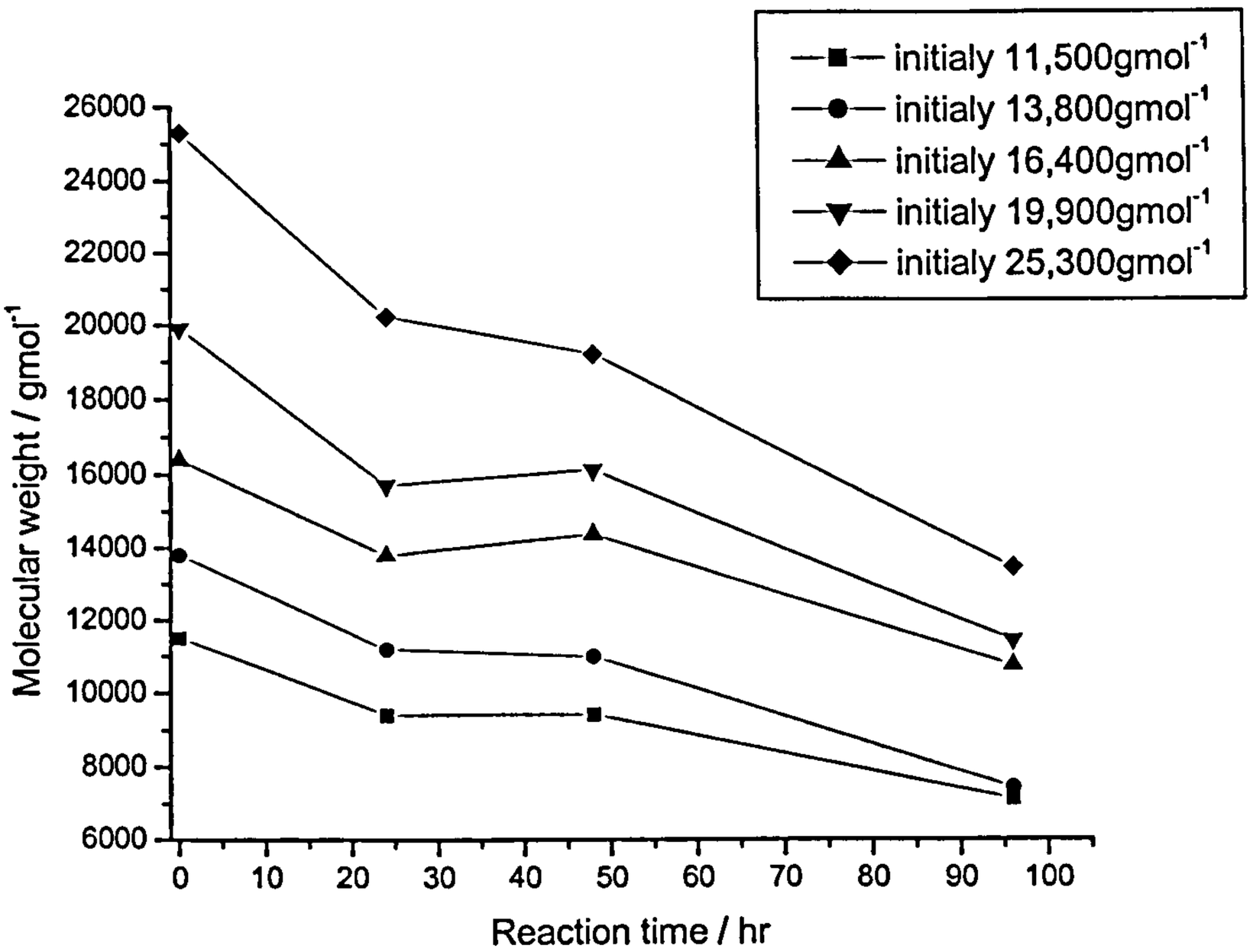


Figure 8-18 Graph to show the degradation of PVAc-OH's of differing molecular weight by Novozym 435

The graph in figure 18 shows the degradation of poly (vinyl acetate) by Novozym 435, here the traces represent the different starting weight of the polymers investigated. Some general trends can be noted from this graph. The first is that the data gives quite good straight line trends, if the second point is ignored and the second point of note is that in general the slope of the line increases as the starting weight of the polymer is increased. This might be an indication of increased activity of the enzyme to higher molecular weight species.

9.Conclusion to the synthesis of poly (vinyl acetate-*block*-ε-caprolactone)

The aim of this work was an attempt to synthesise block copolymers containing vinyl acetate and ε-caprolactone repeat units. And whilst it is possible to find evidence of these block copolymers in the mass spectra, the peaks assignable to block copolymer species have a low relative intensity with respect to the peaks due to the poly (vinyl acetate) and homopolymer caprolactone present.

The samples were also subjected to analysis by size exclusion chromatography, here the results were analysed in order that changes in the molecular weight of the polymers could be determined. The use of "change in molecular weight" is more accurate in this case than "increase in molecular weight" as initially the molecular weights of the samples were found to decrease. After a period of reaction of 72 hours however the molecular weight was starting to increase, though it only exceeded the starting molecular weight for the polymers synthesised in isopropanol, the polymers synthesised in 2-isopropoxy ethanol, although increasing in molecular weight towards the end of the reaction period had not at that stage exceeded the starting value

This was thought to be due to a combination of competing reactions taking place. Primarily it is thought that the enzyme (Novozym 435) and the reaction conditions initially promoted the degradation of the poly (vinyl acetate), it was only after a certain period of time that the polymerisation of ε-caprolactone, catalysed by the enzyme and initiated by water present either in the reaction medium or bound water of the enzyme started to raise the overall molecular

weight of the entire system. The alcoholic end groups of the poly (vinyl acetate) could also be responsible for initiating some of the ε-caprolactone polymerisation reactions, giving rise to block copolymers. However, given the relatively low concentration of hydroxyl groups present associated with PVAc, it can be assumed that the amount of block copolymer produced is quite low. When the mass spectra were analysed, nearly all the peaks that were calculated by allowing for different copolymers of the form $(VAc)_m(\varepsilon\text{-}CL)_n$ were found, up to m/z = 2000. However most of the peaks assigned as being due to block copolymers are quiet small and whilst peak intensity in mass spectra is not usually a good indication of relative abundance, it must be thought that the levels of block copolymer are quite small.

Two experiments that might have indicated the presence of block copolymers better would have been to perform the enzymatic reaction with i) commercially available PVAc, ii) no PVAc at all. Then if there was incidence of poly ε-caprolactone, it would not be due to the hydroxyl end-groups of the PVAc.

Part 3: The synthesis of hyperbranched polymers

10. Introduction to the synthesis of hyperbranched poly (vinyl acetate)

The final part of this thesis is concerned with the synthesis of highly branched or hyperbranched polymers, henceforth referred to as hyperbranched polymers. The term "hyperbranched polymers" means that the polymer molecules in question have a larger number of branching points than that of a linear polymer molecule. However many so-called "linear" polymers contain low levels of branching, an example of this is poly (vinyl acetate)[86].

Many hyperbranched polymers are synthesised using AB_n type monomer systems, where A represents a chemical group capable of reacting with chemical group B. Here the ratio of A groups to B groups will affect the amount of branching that is present in the final polymer molecule.

10.1. Dendrimers

Dendrimers, which can be thought of as "perfect" or "ideal" hyperbranched polymers are often produced in this way[87]. Often the reaction is a simple one: for example between an amine and ester functionalised monomer, forming an amide linkage.

The formation of dendrimers, i.e. perfect hyperbranched polymers is not straightforward. Each time a reaction is performed, the resulting compound must be rigorously purified in order to remove any species that have less than 100%

conversion in order to avoid incomplete branching, and thus deficiencies in the shape and resultant properties of the dendrimer. This problem is mainly encountered when the dendrimer is "grown outwards", i.e. the divergent method, where the dendrimer is started from a poly-valent core molecule. If one of the reactive groups does not react with the other monomer it can be seen that the dendrimer will not form properly. A method which has gained much favour of late is the formation of dendrimers using a convergent approach. In this route, the outer segments of the dendrimer, the dendrons, are grown first. Once they have reached a suitable size, a core molecule is reacted with the fully formed dendrons in order to make the dendrimer. However, the synthesis of dendrimers via either method tends to be laborious and wasteful. Because dendrimer synthesis is both economically and environmentally expensive, attention has turned to viable alternatives which include hyperbranched polymers. These are non-ideal dendrimers, but they have similar desirable properties. For example, if they are amphiphilic they can be designed to have a hydrophobic cavity at their core, as can dendrimers, and therefore they can be used to increase the solubility of hydrophobic compounds in a water rich or polar solvent system; that is they can be used as molecular micelles.

10.2. Non-dendritic hyperbranched polymers

Hyperbranched polymers are easier to make, require little or no purification of the starting reagents and the purification of the resulting polymer is simpler. Most methods for making hyper-branched polymers can be done using a "one-pot" synthesis. Hyperbranched polymers, can also be synthesized from AB_n type monomers, in a radical initiated polymerization. This leads to a random polymer

with lots of branching due to the multi-functional monomers used in the synthesis.

10.2.1. Radical polymerisation methods

Previous work by Sherrington *et al* [18] describes a method for the production of hyperbranched polymers composed of a vinyl monomer and a cross-linking compound with two double bonds, via radical polymerisation. There is a drawback with this system; without some method of controlling the polymerisation a crosslinked gel results, much in the same fashion as the poly (styrene-co-divinyl benzene) gels used in SEC columns are formed. In order to stop this gel formation, 1-dodecanethiol (DDT), a chain transfer agent was added. The chain transfer agent in this reaction stops the polymers from becoming a cross-linked gel by abstracting from the transfer agent and initiating a new polymer chain. However the choice of transfer agent is vital for the successful production of hyperbranched polymers and it is believed that thiol transfer agents will only work for vinyl monomers if the radical is stabilised, i.e. in monomers where the radical can be delocalised by the formation of resonance hybrids. These monomers include methacrylates and styrene. Transfer to thiols in the polymerisation of VAc and N-vinyl pyrrolidinone (NVP) is far too rapid to be useful in batch processes. Another aspect of the work by Sherrington[88], is that a cross linking agent, but-2-ene-1,4-diacrylate, is employed which has an internal double bond when incorporated into a polymer network. This double bond can be readily cleaved by the use of ozonolysis, to break down the branched structure and give the linear components of which the branched network is comprised.

10.2.2. ATRP methods

The work of Yoo *et al* [89], describes the preparation of hyperbranched polymers in emulsion via ATRP. It was thought that ATRP was sufficiently robust to be unaffected by the presence of water and other contaminants. Copper(I)bromide mediated ATRP of 2-(2-bromopropionyloxy)ethyl acrylate and its chlorine analogue were investigated. It was discovered that gelation could be suppressed by using certain ligands. Towards this end, a number of bipyridyl compounds were synthesized. The most successful ligands for reducing gelation were those with long alkyl chains, 4,4-dinonyl-2,2-dipyridyl for example. However, the longer alkyl chains increased the solubility of the Cu(II) species, and so the rate of polymerisation was lower with 4,4-dinonyl-2,2-dipyridyl than with 4,4-dipentyl-2,2-dipyridyl ligands. Because of this, high Mn was only achieved with 4,4-dinonyl-2,2-dipyridyl at high reaction temperatures.

10.2.3. Condensation methods

Hao *et al* [90], have reported on the synthesis of aromatic polyimides, using an A_2+B_3 synthetic approach. In contrast to the AB_x approach, the monomers are often commercially available, removing the need for the multistep organic synthesis of starting materials. However, with a 1:1 molar feed ratio of monomers, conversion past a particular point will lead to gelation. This theory was elucidated by Flory in 1953 and was based on the assumptions (i) that all A or B groups have equal reactivity throughout the reaction, (ii) there is no intramolecular cyclisation and (iii) the condensation reactions are limited to those between an A group and a B group. A reaction scheme that avoids these criteria might not experience the same problems with gelation as one that fulfils the

above assumptions. A non-ideal synthesis was devised using tri(phthalic acid ethyl ester) (B_3), and 1,4-phenylenediamine (A_2) as the monomers and diphenyl(2,3-dihyro-2-thioxo-3-benzoxazolyl)phosphonate (DBOP) as a condensation agent. The DBOP reacts *in situ*, to activate the carboxylic acid groups of the B_3 monomer; this activated intermediate can either react with an amine or react with the by product of the activation reaction, which itself can then react with amine. The ability of the activated intermediate to react with more than one compound removes the system from ideality and stops the formation of a gel.

Gao *et al* [76, 91, 92], have reported the synthesis of novel hyperbranched materials. Their work has looked at synthesis using an A_2+CB_n approach. Here the A_2 monomer was a diisocyanate and the CB_n monomer a multifunctional alcohol. Later an AB+CD_n approach was used to yield AD_n type intermediates, that can be self-condensed at high temperature to yield hyperbranched polyesters that are water soluble and biodegradable. It was also noted that fluorescent hyperbranched polymers had non-linear optical properties. To this end a hyperbranched polyether with numerous hydroxyl groups was synthesized and this was then reacted with dimethylaminobenzaldehyde, thus forming a fluorescent polymer.

Cheng[93], used a kinetic model to study the effect of the feed rate of AB_2 type monomers to a C_3 core molecule. The dependency of molecular weight, polydispersity, degree of branching and number of structural units were examined by the use of this model. Nasar *et al* [94], have reported on the synthesis of hyperbranched polyamides, formed from a self-condensation polymerisation of an AB_2 type monomer, in this case, 3,5-bis(4-aminophenoxy)benzoic acid. The product was then separated by the use of fractional precipitation and the products used as crosslinking agents in the preparation of polyurethane elastomers. Ishizu *et al* [95], have performed a study of the kinetics of the polymerisation of an AB^*

type monomer, 2-(N,N-diethyldithiocarbamyl)ethyl methacrylate, leading to a hyperbranched polymer. Through the use of a semi-logarithmic plot the reaction was found to be first order with respect to monomer. Kricheldorf *et al* [96], have studied the effect of formation of cyclic structures during the polycondensation reactions of AB_n type monomers. They came to the following conclusions: cyclisation competes with propagation irrespective of concentration and at all stages of the polycondensation, and that formation of cycles limits chain growth and at 100% conversion all reaction products have a cyclic structure.

Bo and Schluter[97], have reported the synthesis of hyperbranched polymers using an AB_2+AC_2 synthetic approach using a palladium catalysed Suzuki coupling reaction. Choi and Kwak[98], have synthesized hyperbranched poly (ε-caprolactone)s from the polycondensation reaction of multifunctional macromonomer units. This was performed by the synthesis of benzyl protected AB_2 macromonomers, followed by deprotection and further reaction with ε-caprolactone to form a hyperbranched polymer. Lin and Long[99], reported their work on the synthesis of hyperbranched poly (aryl ester)s using a A_2+B_3 synthetic route. Here, the monomers were bisphenol A and 1,3,5-benzenetricarbonyltrichloride. The reaction was performed at 25°C under dilute conditions, with the ratio of A_2:B_3 kept at 1:1. Such reaction conditions avoided the problems of gelation that are known to be problematic with these types of polycondensations. Twyman *et al* [100], have recently reported on the synthesis of hyperbranched polyamidoamine (PAMAM) polymers using an AB_2 type monomer system. The monomer was heated at 165°C under vacuum for 30 hours. The crude product was purified by dialysis, and analysed by GPC, NMR and MALDI-TOF mass spectrometry, and the molecular weight was found to be in the range of a perfect second generation dendrimer analogue.

In an interesting piece of work, Jiang *et al* [101] report on a self-condensing vinyl polymerisation of a novel AB* type monomer and its copolymerisation with styrene. Here two monomer species can react together to give a dimer with two active sites. These can then react with more monomer to form trimers with three active sites and so on until a polymer is formed. The reaction is catalysed by the use of bipyridyl and CuCl. Linear analogues of the branched polymers formed by this route were synthesized through the use of AIBN as a radical initiator.

10.2.4. Properties and uses

Rodlert *et al* [102] have used hyperbranched polymers to modify the mechanical properties of montmorillonite clays. These nanocomposites show significant increases in elongation at break, a higher modulus and increased tensile strength compared to the neat resin, especially above the T_g.

Karger-Kocsis *et al* [103] have reported on the modification of vinylester-urethane resins by the reaction between reactive hyperbranched polymers and small molecule analogues. It was found that the star-like hyperbranched polymers, when covalently reacted to form cross-links, increased the toughness of the vinylester-urethane resins. The hyperbranched polymers with the longest "arms" had the greatest effect.

Hyperbranched polymers have a number of interesting properties; one of these has been reported by Seiler *et al* [104]. The authors performed a novel study on the properties of vapour-liquid, liquid-liquid and solid-liquid-liquid equilibria, modified by the addition of hyperbranched polymers. The polymers studied were commercial products, one a polyester, the other a poly (esteramide). These polymers were shown to break the ethanol-water and THF-water azeotrope,

allowing selective purification to be achieved. Further work by Seiler *et al* [105] has examined the effect that the branching has on the separation of azeotropic mixtures, and on the phase behaviour and thermodynamic properties of hyperbranched polymer solutions[106]. The Newtonian flow behaviour of hyperbranched polymers were studied by Ye and Zhu[107], SEC and rheology of AB/AB_2 hyperbranched polymers were studied by Kunamaneni *et al* [108].

Mizutani and Matsuda[85, 109] have synthesized a series of biodegradable polymers, which are liquids in their natural state, and can be crosslinked, by photocuring, in order to give solid three dimensional objects. The polymers were copolymers of ε-caprolactone, and trimethylene carbonate, initiated with low molecular weight multifunctional alcohols. The resulting polymers were endcapped by acryloyl chloride. These polymers were then crosslinked by visible-light irradiation, using camphorquinone as the initiator. The crosslinked polymers were then subjected to degradation studies in phosphate buffered saline, at pH 7.4.

Hyperbranched polymers are also used in the field of supported catalysis; enzymes are often supported on polymer substrates, and there is much research into the field of solid phase synthesis. Karjalainen *et al* [110] have reported on the use of hyperbranched crosslinked polymers as heterogeneous ligands for the complexation of $Ti(O^iPr)_4$, and the use of the resulting insoluble catalyst in the epoxidation of trans-allylic alcohols. The insoluble polymer ligated catalyst is easy to remove by filtration.

Britton *et al* [43] have made use of ^{13}C NMR in order to look at the effect of feed rate on chain transfer to polymer, in the emulsion polymerisation of vinyl acetate. They discovered that even with high frequency NMR it was hard to distinguish the branch point CH_2 carbons, however it was possible to look at a well resolved

signal from the ultimate CH_2 carbon. These signals were used to calculate the amount of branching in the sample, as each branching incident would give rise to one of these ultimate CH_2 carbon species.

10.2.5. Vinyl acetate based hyperbranched polymers

In the research discussed here, vinyl monomers with unstabilised radicals, such as vinyl acetate and N-vinyl pyrrolidinone can be polymerised successfully. As mentioned in earlier sections of this thesis, this type of monomer has no resonance stabilization of the monomer, and therefore the monomer radical is extremely active and capable of transfer to solvent, monomer or polymer. Thiol transfer agents can be used with these monomers[18], however, it is generally necessary to negate the high transfer rate by feeding the transfer agent into the reaction medium. Work in the first section of this thesis looked at the use of solvents to act as chain transfer agents. The solvents used had low transfer constants, and so were ideal for use in such systems.

In many cases the fact that vinyl acetate readily undergoes chain transfer is seen as a problem but it has also been used as an effective method to control the molecular weight of the polymers produced. The types of chemical motifs that could act as a suitable branching agent for vinyl acetate, N vinyl pyrrolidinone (NVP) and other monomers that propagate from unstabalised radicals therefore needs consideration. To this end the use of solvents such as isopropanol and an analogue have already been discussed here.

In order to get a highly branched polymer a branching agent may be required. Liu *et al* [111, 112] copolymerised a 5-fluorouracil diallyl carbonate macromonomer with NVP. This allowed the compound to be taken across cell membranes as it is

was incorporated into a water-soluble but amphiphilic polymer. Hydrolytic scission of the carbonate linking groups allowed the release of the active compound. It was thought that a similar compound might be used to promote branching in vinyl acetate and n-vinyl pyrrolidinone polymerisations. However after incorporation into the growing polymer chain a suitable branching agent must then be able to initiate a new polymer chain.

Isopropyl groups are known to have a chain transfer constant that makes them suitable for the control of the polymerisation of VAc and NVP. Work has been performed in this area by Haff *et al* [113], Ferruti *et al* [114, 115], Carter *et al* [40] and Liu and Rimmer[116]. From this and the work performed in the first part of this thesis, it was thought that by combining an isopropyl group motif with a vinyl or allyl motif, it might be possible to synthesise branched polymers. To this end a branching agent was synthesised, with a double bond at one end of the molecule and an isopropyl group at the other. This allowed the incorporation of the molecule into the growing polymer chain, but also allowed the formation of polymer chains from the branching agent because of its ability to act as a transfer agent. In this respect the work is similar to that of Yamada, where a branching agent with two polymerisable double bonds and a transfer moiety was used[117].

Thus the advantage of this method is that the transfer agent is also a comonomer. A similar approach has been adopted by Yamada *et al*[117] for the synthesis of hyperbranched polymers, however the polymers are formed from monomers that form stabilised radicals. In contrast, Sherrington's work[18], which also uses monomers that propagate from stabilised radicals, a transfer agent has to be added in order that the polymerisation does not result in a crosslinked gel.

11. Synthesis of hyperbranched poly (vinyl acetate)

11.1. Synthesis of the branching agent

11.1.1. Materials

Isopropanol was dried by refluxing over calcium hydride and then distilled. 2-isopropoxy ethanol (Aldrich) was used as received. Allyl chloroformate (Aldrich) was used as received. Distilled water was ultra-purified through the use of Elga Option4, then Milipore Simplicity 185. Triethylamine was dried over calcium hydride, then distilled.

11.1.2. Method

A three necked round bottom flask was set up in an ice/water bath, on a stirrer hotplate (IKA RCT basic), to this was added a nitrogen inlet, a condenser, and a pressure-equalised addition funnel. The flask was charged with isopropanol (13g, 0.216mol), and triethylamine (22.75g, 0.225mol) and the apparatus was purged with nitrogen. The allyl chloroformate (25g, 0.207mol) was added slowly, via the dropping funnel, to the pre-cooled isopropanol and triethylamine over the course of half an hour. Once all of the allyl chloroformate was added, the ice bath was removed and the reaction allowed to warm up to room temperature; once at room temperature it was left for a further 5 hours to react fully. The reaction was then

quenched by the addition of distilled water. This dissolved the white solid that had formed (triethylamine hydrochloride). The mixture was transferred to a separating funnel and the mixture was separated, the aqueous layer was discarded and the organic layer retained. The organic layer was firstly washed with 1M hydrochloric acid, followed by washing with saturated sodium hydrogen carbonate, then by distilled water. The organic layer was shaken with distilled water once more, followed by addition of dichloromethane. The mixture was shaken again and allowed to settle. The organic layer was retained. The dichloromethane was removed by rotary evaporation, and the oil that was left was mixed with water once more before addition of more dichloromethane. The organic layer was dried with anhydrous magnesium sulphate, before filtering and removal of solvent, to leave the pure compound. This procedure was necessary in order to remove the triethylamine hydrochloride which is slightly soluble in organic media and is therefore quite difficult to remove.

The procedure was repeated to synthesise an analogous branching agent from 2-isopropoxy ethanol. The amount of allyl chloroformate and triethylamine employed was similar to the above reaction. The amount of 2-isopropoxy ethanol used was 22.9g, 0.22mol. In both cases, the yield of the isolated and purified products was about 25%.

11.2. Synthesis of hyperbranched poly (vinyl acetate)

11.2.1. Materials

Vinyl acetate (Aldrich) was passed through an inhibitor removal column (Aldrich) before fractional distillation (fraction collected at 73°C). AIBN was recrystallised from diethyl ether. Allyl isopropyl carbonate (branching agent 1), allyl 2-isopropoxyethyl carbonate (branching agent 2) were synthesised and purified as described above.

11.2.2. Method

An ampoule of 100cm^3 capacity was filled with a solution of vinyl acetate, solvent, AIBN and branching agent. The ampoule was degassed using 6 freeze pump thaw cycles on a vacuum line at 10^{-5}mbar. Once the degassing cycles had been completed, the ampoule was flame sealed then frozen at –20°C until use. Once a series of ampoules had been prepared, four of the ampoules were taken and clamped in a thermostatically controlled water bath which had been pre-set at 60°C at which point the polymerisations commenced. The reactions were left to proceed for 4 hours after which time they were removed and returned to the freezer in order to quench the reaction. Further sets of polymerisations were then performed under the same conditions until the series was complete. Once all the polymerisations had been completed, the ampoules were thawed and the contents were dissolved in THF (100 ml), prior to being precipitated into 40-60 petroleum ether (1litre). The precipitated polymer was dried *in vacuo*, before being

redissolved in THF, reprecipitated and dried. A range of polymers was produced, and the compositions are listed below. The polymers produced were analysed by GPC, triple detector GPC, and 250MHz NMR. In the table below samples cs1/71/1-5 used isopropanol and cs1/77/1-5 used 2-isopropoxy ethanol as solvent.

Table 11-1 Table showing composition of reactions

Sample	Vol Solvent /ml	Amount solvent /mol	Vol Monomer /ml	Amount Monomer /mol	Amount Branching agent /mol	Mass Initiator /mg
cs1/71/1	10	0.1306	10	0.109	0.0033	54
cs1/71/2	10	0.1306	10	0.109	0.0066	56
cs1/71/3	10	0.1306	10	0.109	0.0131	56
cs1/71/4	15	0.1959	10	0.109	0.0033	52
cs1/71/5	20	0.2612	10	0.109	0.0033	54
cs1/77/1	10	0.0867	10	0.109	0.0027	62
cs1/77/2	10	0.0867	10	0.109	0.0055	58
cs1/77/3	10	0.0867	10	0.109	0.0109	58
cs1/77/4	15	0.1301	10	0.109	0.0027	63
cs1/77/5	20	0.1734	10	0.109	0.0027	65

In this first set of reactions the experiments were performed in such a way that the effects of changing the concentration of either the branching agent or the solvent could be probed, whilst keeping the number of separate reactions to a minimum.

11.3. Hyperbranched polymers without the use of chain transfer to solvent

The polymers produced previously were made in the presence of a solvent that acts as a chain transfer agent. It was decided to try and produce hyperbranched polymers without the use of this chain transfer agent. Sherrington and Slark have published patents and papers[88] on the manufacture of hyperbranched vinyl polymers using a difunctional branching compound and an alkyl thiol as a chain

transfer agent. The chain transfer agent is necessary in order to stop the polymerization forming an intractable gel.

11.3.1. Materials

Optical grade NVP was distilled under vacuum, n-Butyl acetate was purified by refluxing with potassium permanganate, dried with anhydrous magnesium sulfate, then filtered and distilled under vacuum. Other materials were purified as described above.

11.3.2. Method

A series of ampoules were charged with NVP, AIBN, varying quantities of branching agent, and n-butyl acetate, the latter being a solvent which is known to be inert with respect to transfer of radicals from vinyl acetate. The ampoules were degassed by 3 freeze pump thaw cycles on a vacuum line at to 10^{-5} mbar. The ampoules were then flame sealed and polymerised in a thermostatically controlled water bath set at 60°C, for a period of 2 1/2 hours. The reactions were quenched by placing the ampoules in a freezer. When an attempt was made to recover the polymers by dissolving in dichloromethane it became clear that the polymers had in fact cross-linked, and had to be removed by swelling the gel and using compressed air to force the gel from the ampoule. A control made with no branching agent was an homogeneous solution in dichloromethane, and was precipitated into diethyl ether, to give a white powder.

When a similar reaction was performed with vinyl acetate, using the same conditions that were used for the NVP polymerizations, a cross-linked gel was formed once more.

Table 11-2 Table showing composition of reactions

Sample	Vol solvent /ml	Amount solvent /mol	Vol monomer /ml	Amount monomer /mol	Amount Branching agent /mol	Mass initiator /mg
cs1/91/1	10	0.0759	10	0.0936	0.0033	60
cs1/91/2	10	0.0759	10	0.0936	0.0066	60
cs1/91/3	10	0.0759	10	0.0936	0.0098	60
cs1/91/4	10	0.0759	10	0.0936	0.0131	60
cs1/91/5	10	0.0759	10	0.0936	0.0027	60
cs1/91/6	10	0.0759	10	0.0936	0.0055	60
cs1/91/7	10	0.0759	10	0.0936	0.0082	60
cs1/91/8	10	0.0759	10	0.0936	0.0068	60
cs1/91/9	10	0.0759	10	0.0936	0	60

11.4. High temperature reactions

The problems encountered with the cross-linking of NVP and VAc in the absence of radical transfer to solvent lead to the decision to try the polymerisations in an autoclave, where the temperature could be increased to a suitably high level.

11.4.1. Materials

Optical grade NVP was distilled under vacuum, n-Butyl acetate was purified by refluxing with potassium permanganate, dried with anhydrous magnesium sulfate, then filtered and distilled under vacuum. Other materials were purified as described above.

11.4.2. Method

Butyl acetate (30ml), plus the monomer (10ml) and branching agent (2ml) were charged to the autoclave's glass liner, and polymerized at 150°C under nitrogen. The NVP formed an insoluble layer at the bottom of the liner vessel. The vinyl

acetate, being more soluble in butyl acetate than NVP, formed a clear colourless solution.

In the case of NVP, the solvent was decanted off and the polymer was dissolved in dichloromethane, before precipitation into diethyl ether. The precipitated polymer was then redissolved and reprecipitated. They were analysed by using an SEC system running on DMF; NVP sticks to the polystyrene gel columns if THF is used as a solvent.

The poly vinyl acetate, was precipitated into 40-60 pet ether and was filtered off, redissolved in THF, before precipitation in to 40-60 pet ether. This process was repeated and the polymer dried. The hyperbranched poly (vinyl acetate) was then analysed by SEC and TD-SEC.

Table 11-3 Table showing composition of reactions

Sample	Vol Solvent /ml	Amount Solvent /mol	Vol monomer /ml	Amount monomer /mol	Amount branching agent /mol	Mass initator /mg
cs1/101/1	30	0.2278	10	0.0936	0.0109	65
cs1/101/2	30	0.2278	10	0.0936	0	62
cs1/103/1	30	0.2278	10	0.109	0.0109	60
cs1/103/2	30	0.2278	10	0.109	0	61

12. Results and discussion for the synthesis of hyperbranched poly (vinyl acetate)

The hyperbranched polymers produced were analysed by NMR and triple detection SEC. The branching agent has easily identifiable peaks in the NMR; unreacted branching agent and that which has been incorporated into hyperbranched polymers can be differentiated. By evaluating the integral of the polymerised branching agent and comparing it to the integral of the signal for the acetate methyl protons, a degree of branching can be calculated. This method assumes that a new vinyl acetate chain propagates from the new radical site. The results of SEC and triple detection SEC (TD-SEC) were compared. As expected for a highly branched polymer, quite different answers were obtained depending on which method of analysis was employed.

It is well known that for two polymers of equal molecular mass, a highly branched polymer will have a smaller hydrodynamic volume compared to a linear analogue. For branched and hyperbranched polymers, the value for the molecular weight obtained by SEC using the usual linear polystyrene standards for calibration, will be lower than expected due to the smaller hydrodynamic volume which allows it a greater residence time in the SEC column.

12.1. Synthesis of the branching agents

The branching agents were isolated as pale yellow clear liquids. These liquids were stored in the freezer until they were needed. Samples from the two branching agents were analysed through the use of 250MHz NMR. A scheme representing the synthesis of the two branching agents used is shown below.

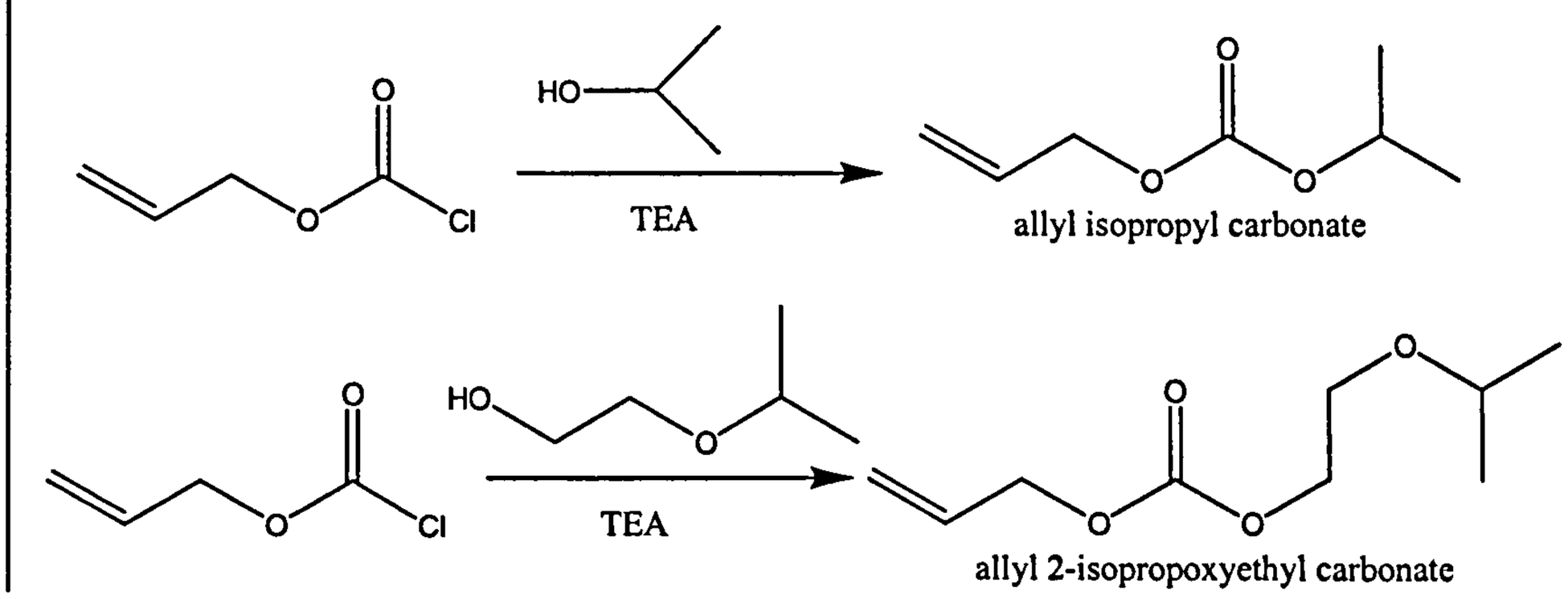


Figure 12-1 Reaction scheme showing the fomation of the branching agents

The presence of the tertiary carbon atom allows the transfer of a propagating polymer radical to another compound, terminating the propagating chain. A new chain grows from the site to which the radical has transferred.

12.1.1. NMR analysis

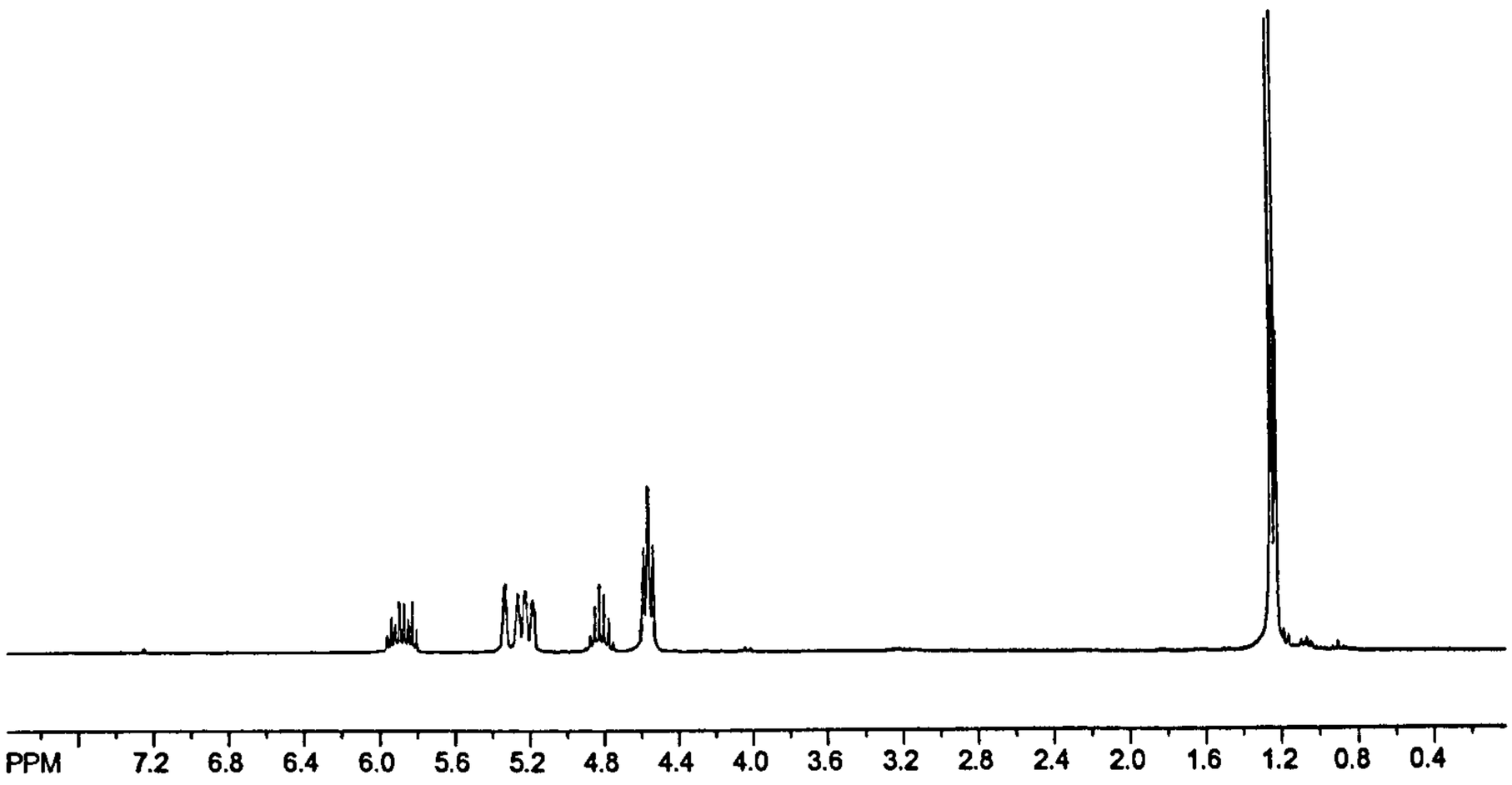


Figure 12-2 ^{1}H NMR spectrum of allyl isopropyl carbonate

The NMR spectrum shown in figure 2 is of allyl isopropyl carbonate (branching agent 1), synthesized from allyl chloroformate and isopropanol. The assignments are: C*H*CH_2 δ≈5.9; CHC*H*$_2$ δ≈5.3; $(CH_3)_2$C*H* δ≈4.5; OC*H*$_2$CH δ≈4.8; $(CH_3)_2$C δ≈1.2.

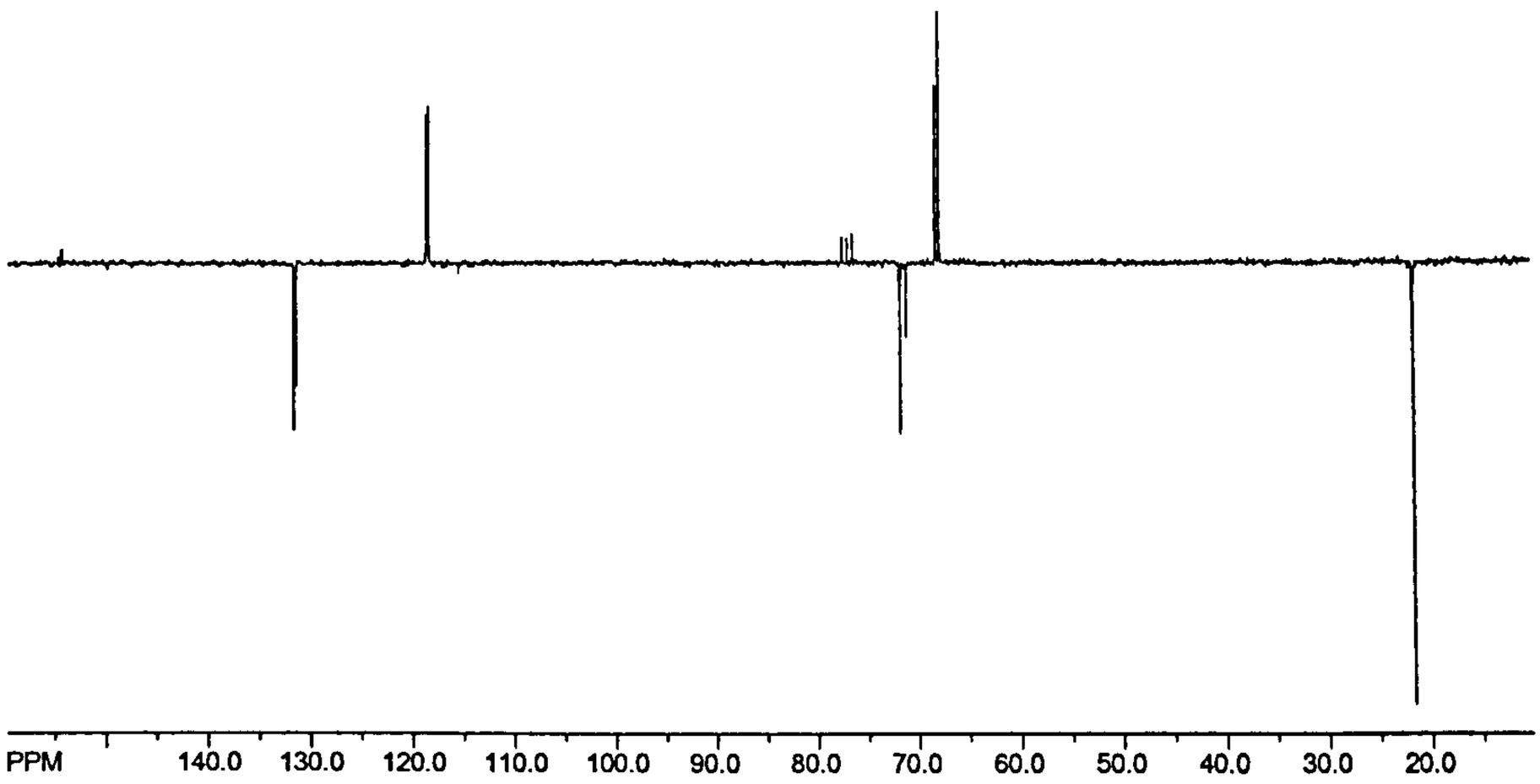


Figure 12-3 ^{13}C PENDANT NMR spectrum of allyl isopropyl carbonate

The NMR spectrum shown in figure 3 is of allyl isopropyl carbonate (branching agent 1), synthesized from allyl chloroformate and isopropanol. The assignments are: carbonyl δ≈155; $CHCH_2$ δ≈132; $CHCH_2$ δ≈118; $(CH_3)_2CH$ δ≈71; CH_2CHCH_2 δ≈68; $(CH_3)_2CH$ δ≈22. The peaks at δ≈77 are due to $CDCl_3$.

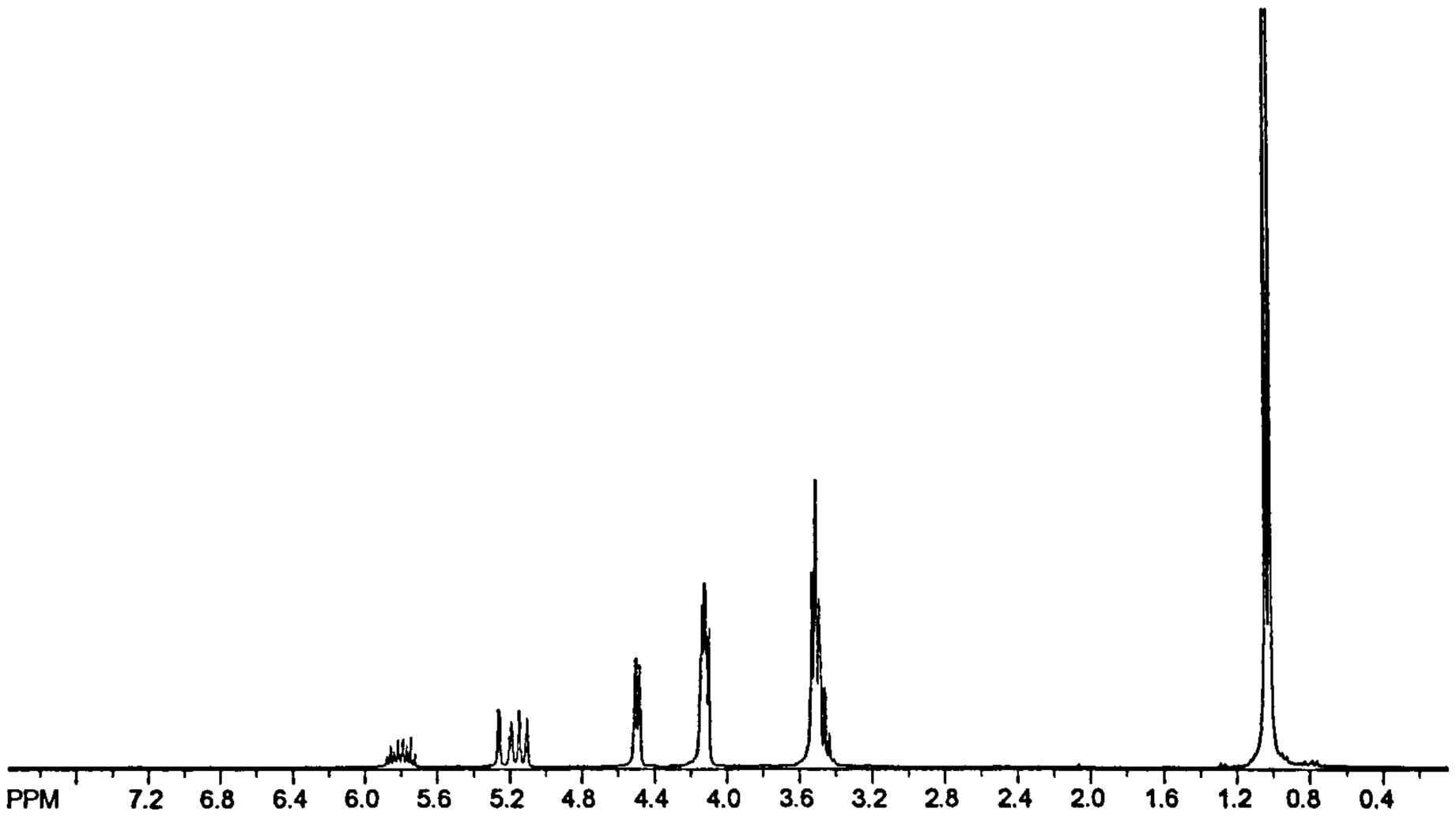


Figure 12-4 ^{1}H NMR spectrum of allyl 2-isopropoxyethyl carbonate

The NMR spectrum shown in figure 4 is of allyl 2-isopropoxyethyl carbonate (branching agent 2). The assignments are: CH_2CH δ≈5.8; CH_2CH δ≈5.2; $CHCH_2$ δ≈4.5; OCH_2CH_2 δ≈4.1; OCH_2CH_2 δ≈3.5; $(CH_3)_2CH$ δ≈3.5; $(CH_3)_2$ δ≈1.0.

12.2. Synthesis of hyperbranched polymers

The polymers synthesised using this method were isolated first by rotary evaporation in order to remove any solvent and excess monomers. The samples thus isolated were then dissolved in THF (100ml) and precipitated into 40-60 petroleum ether (2000ml). The resulting powder like polymer was removed from the solvents by filtration. The samples were then dried *in vacuo*.

12.2.1. SEC analysis

The isolated and dried polymers were dissolved in THF (2mg ml^{-1}), and subjected to Size Exclusion Chromatography, and Triple Detection-Size Exclusion Chromatography (TD-SEC). The TD-SEC data was analysed using two different methods. Firstly, the molecular weights of the polymers could be determined through the use of a combination of results from light scattering, viscometry, and refractive index detection. Secondly, an indication of the amount of branching of each molecule could be examined through the use of Mark-Houwink plots. Here, the log of the intrinsic viscosity is plotted against the log of the viscosity average molecular weight, giving a straight line. Ideally, the Mark-Houwink plots corresponding to the branched species are compared to a plot of linear samples having similar chemistry, the intrinsic viscosity of branched species being considerably lower as a function of molecular weight. Due to the nature of the polymerisation of the poly(vinyl acetate), the graphs can be used only to compare

the various branched species, linear samples being unavailable. The results of these analyses are shown below.

Table 12-1 Table showing SEC results

Sample	Ordinary SEC		Triple Detector SEC		Branching agent
	Mn	Mw	Mn	Mw	
cs1/71/1	13610	46380	15850	77990	1
cs1/71/2	12440	46560	10200	102250	1
cs1/71/3	13050	47100	11100	85480	1
cs1/71/4	8900	24720	30050	322950	1
cs1/71/5	7030	17660	5920	25800	1
cs1/77/1	13310	38590	27160	47140	2
cs1/77/2	13930	44220	25630	59380	2
cs1/77/3	21020	71520	98250	142430	2
cs1/77/4	9320	23720	12390	21910	2
cs1/77/5	8430	20230	15440	23100	2

The Mark-Houwink plots shown in Fig 5 are the results obtained for increasing concentration of branching agent, for the series cs1/71, the amount of monomer and solvent remaining constant for the three samples studied.

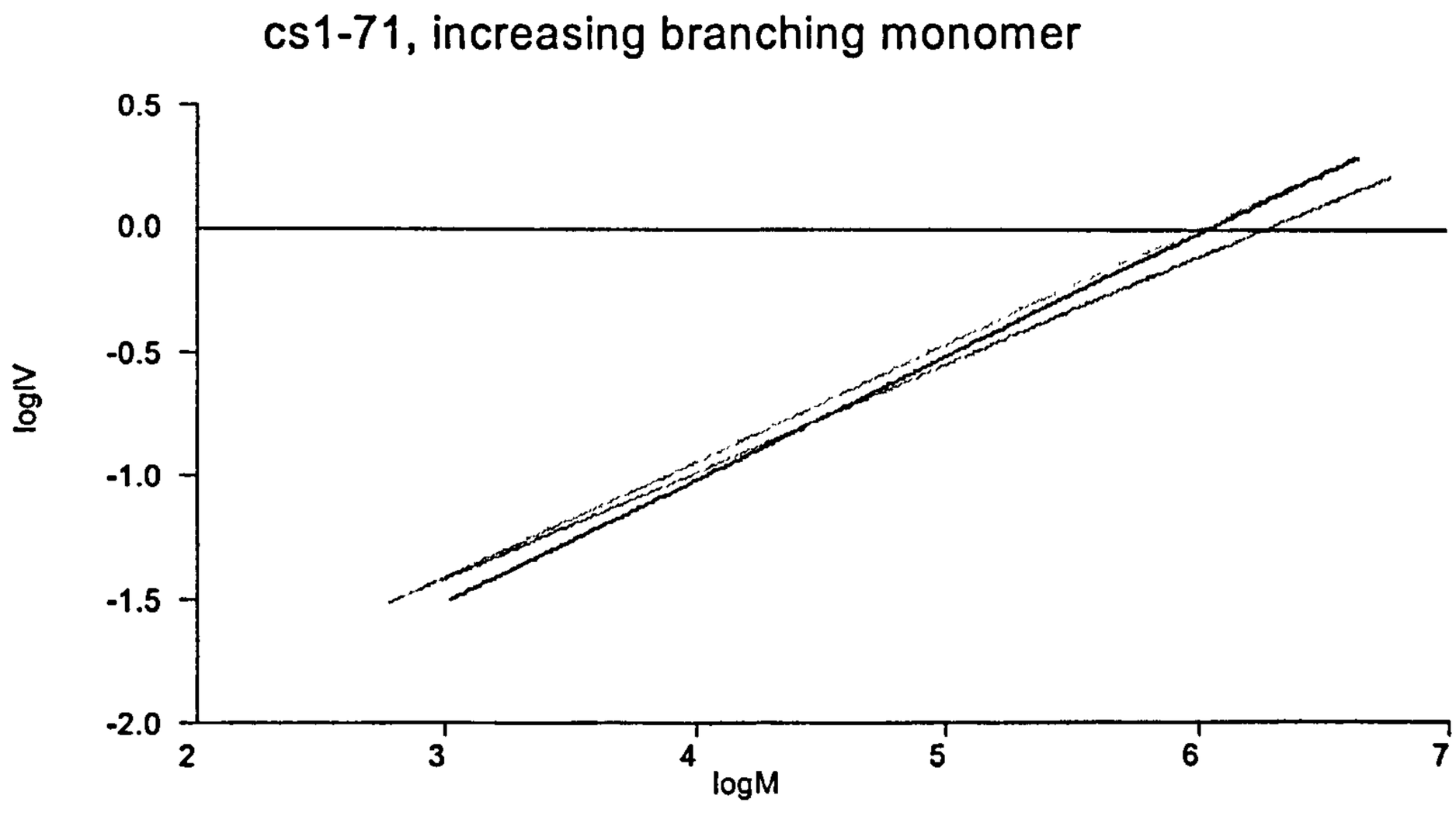


Figure 12-5 Mark-Houwink plot

Shown in Fig 6 are the results obtained for the series cs1/71. Here the amount of monomer and branching agent remained constant for the three samples studied but the solvent concentration increased.

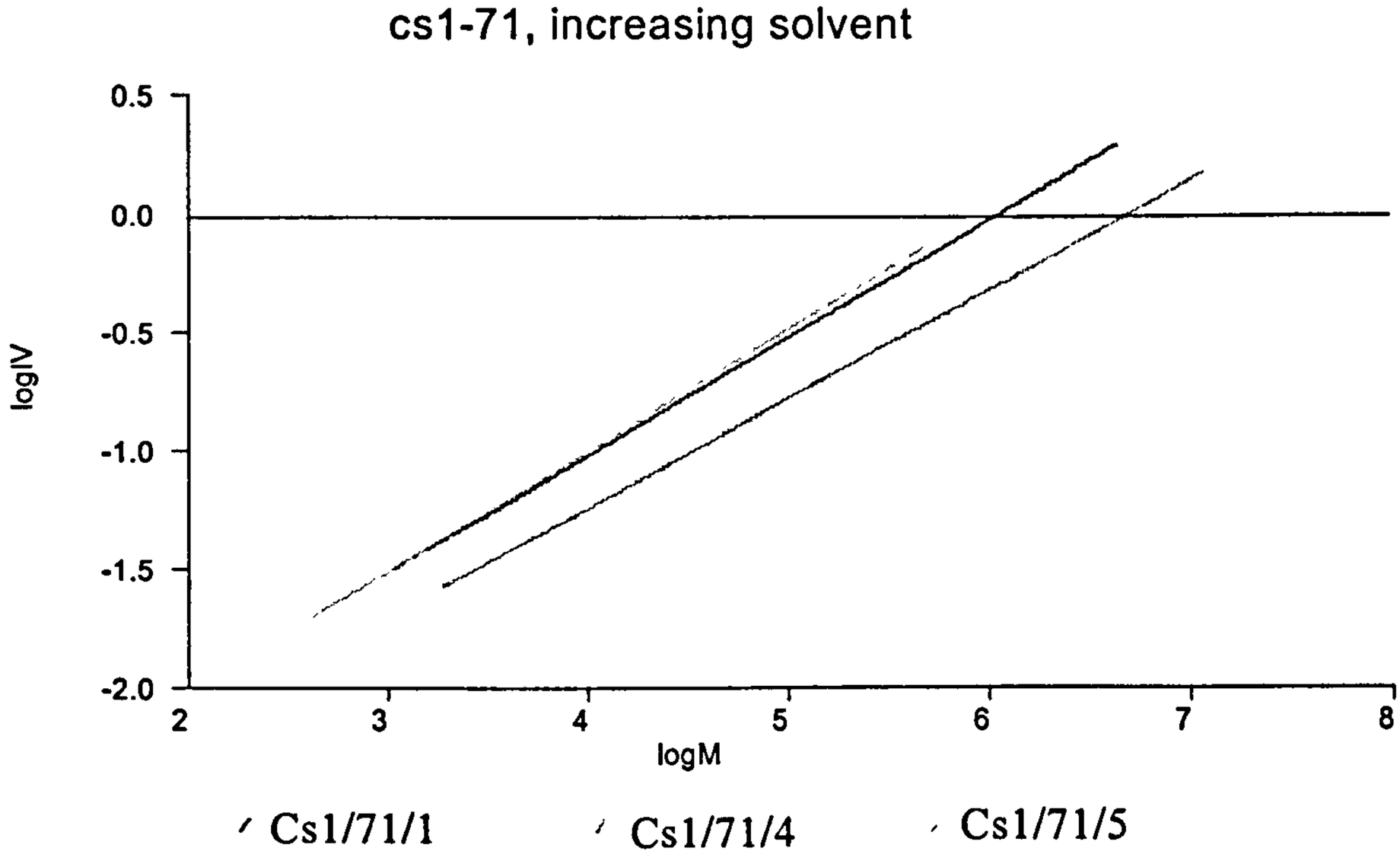


Figure 12-6 Mark-Houwink plot

The results obtained for the series cs1/77, where the amount of monomer and solvent remained constant but the concentration of branching agent increased are shown in Figure 7.

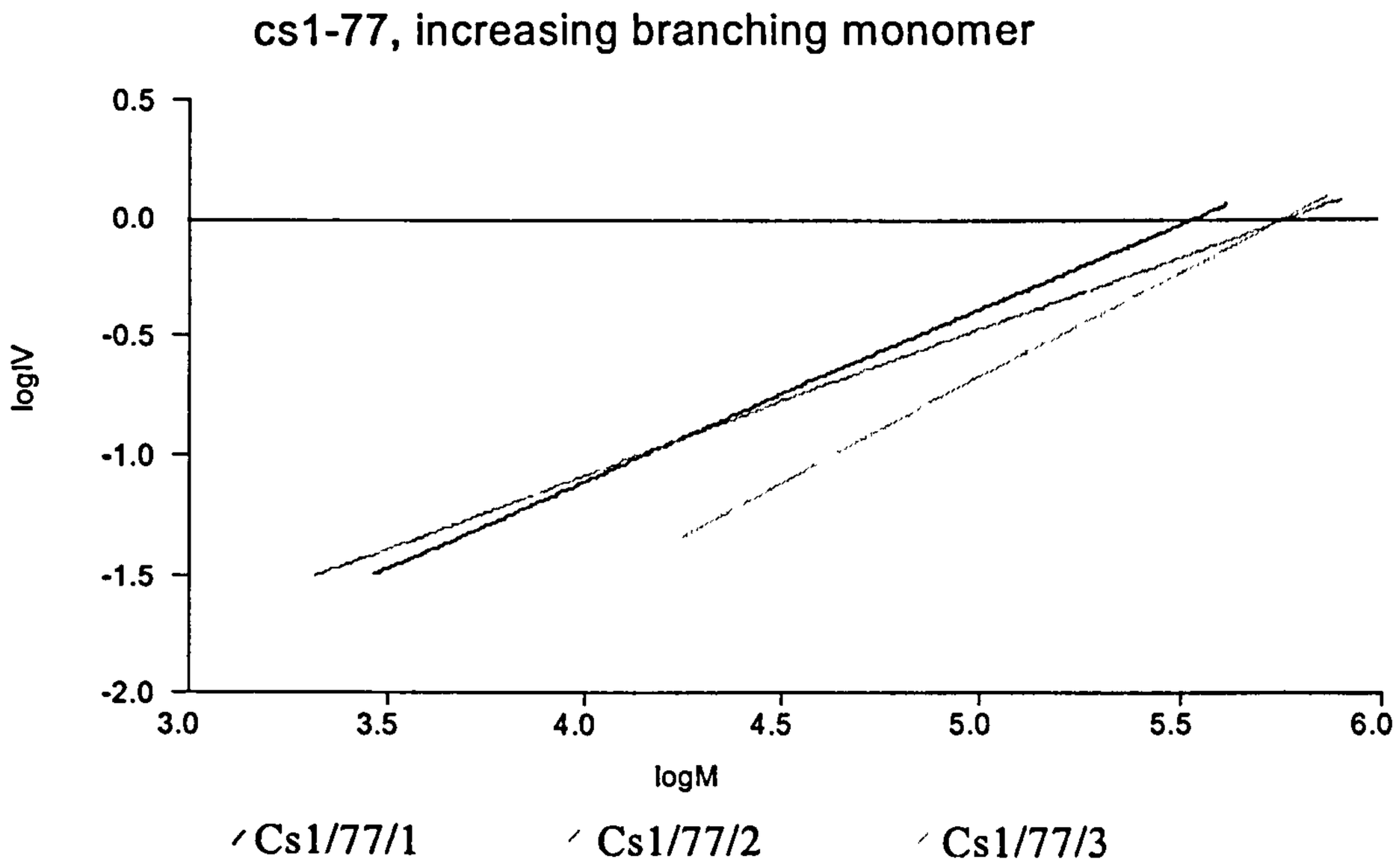


Figure 12-7 Mark-Houwink plot

The results obtained for the series cs1/77 are shown in Figure 8. Here the amount of monomer and branching agent remained constant, the solvent concentration being the variable for the three samples studied.

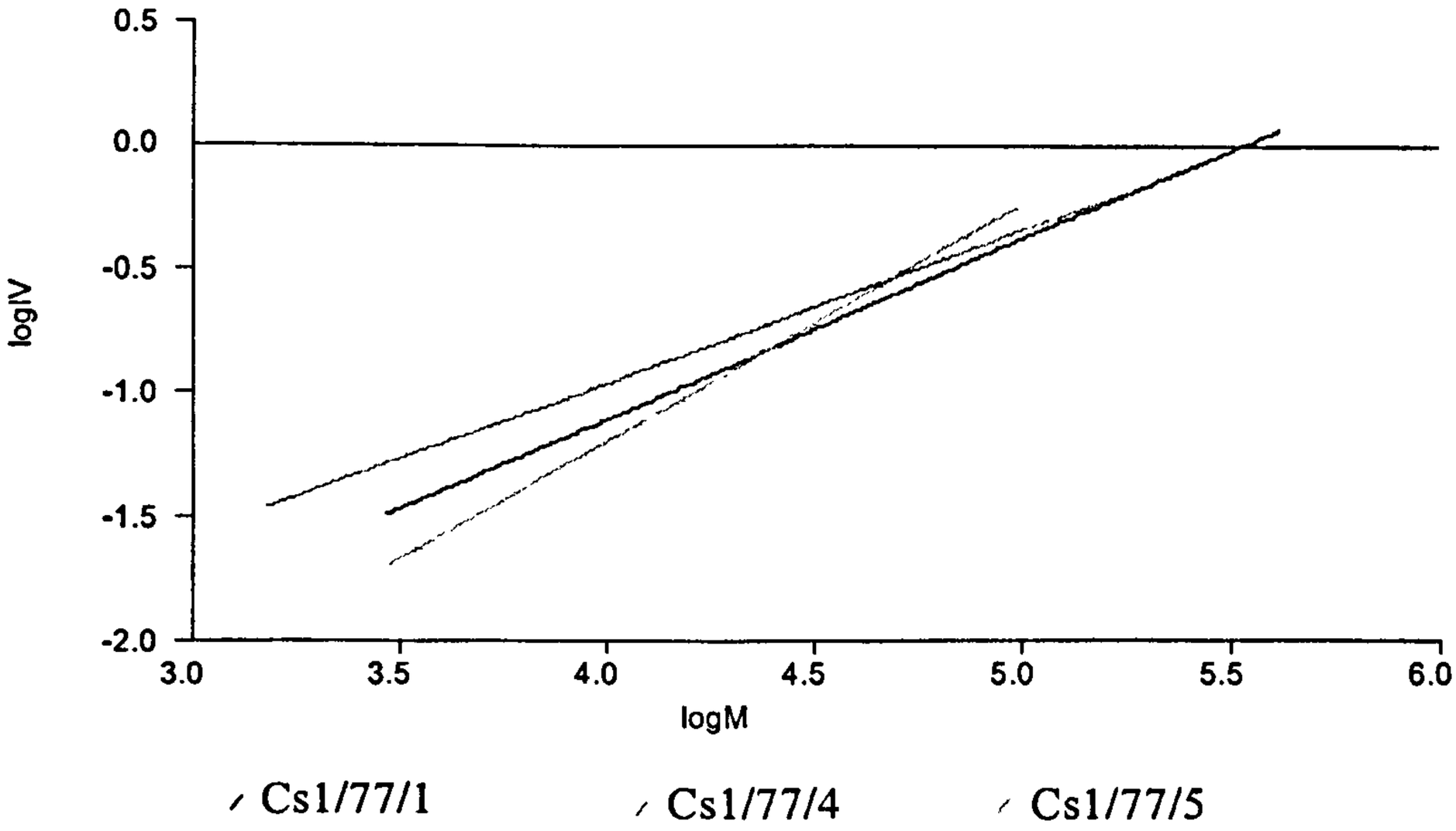


Figure 12-8 Mark-Houwink plot

It must be noted that in each of these graphs there are no simple correlations between the experimental conditions employed and the apparent intrinsic viscosities of the products as a function of the molecular weight. This is due to the range of different processes that can occur during the polymerisation. As has already been discussed, there are two possible transfer reactions, one of which causes a crosslinking reaction, the other leading to the formation of shorter chains. These events occur in varying amounts during each polymerisation, making it difficult to determine the amount of branching present in the samples using this method.

12.2.2. NMR analysis

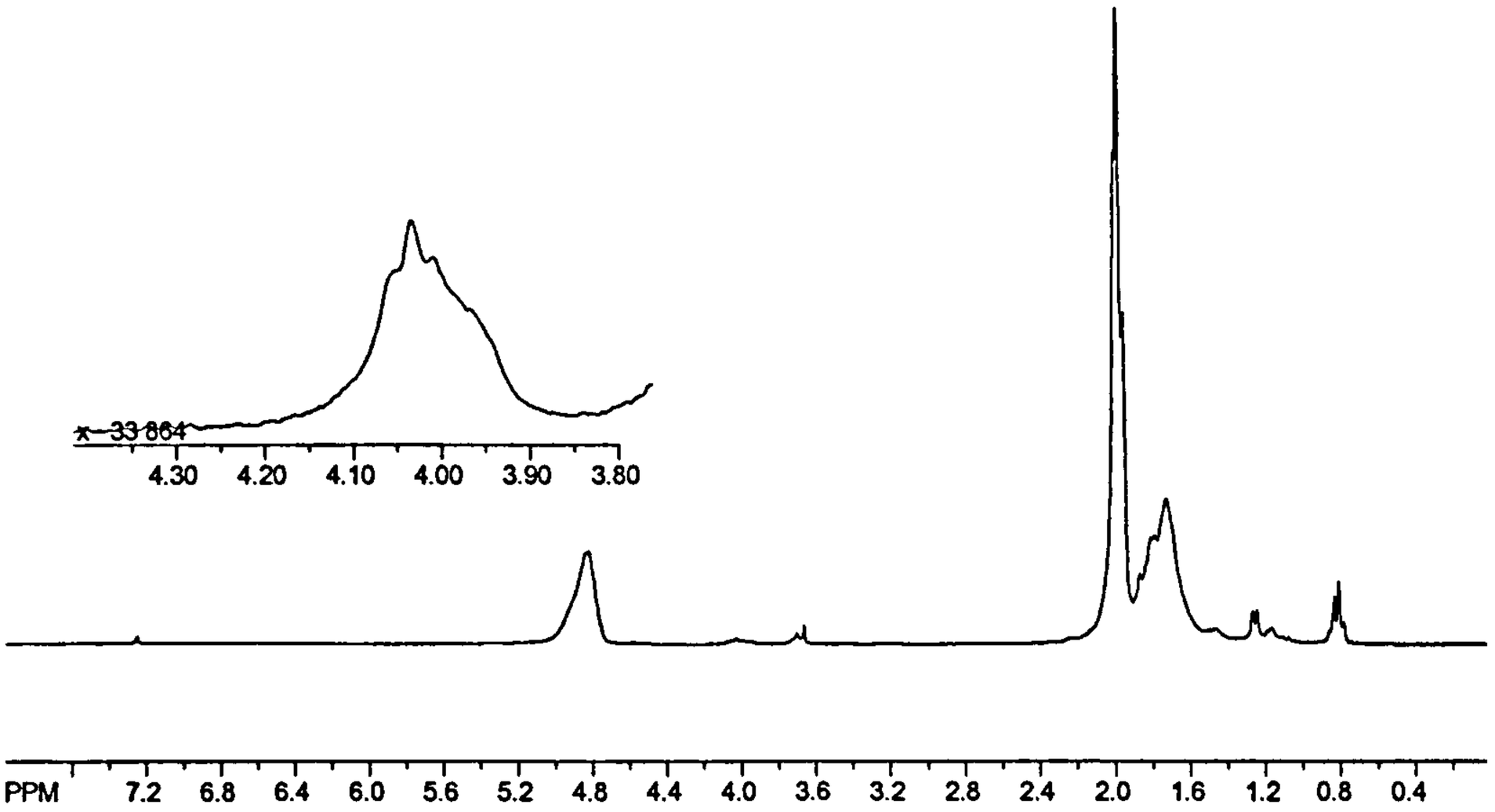


Figure 12-9 ^{1}H NMR spectrum of PVAc sample CS1/71/1

The NMR spectrum shown in figure 9 is of sample cs1/71/1, poly (vinyl acetate) synthesized in the presence of isopropanol and branching agent 1. The expanded section is a peak due to the branching agent. The integral of this peak $\delta \approx 4.0$ was

compared with the integral for the pendant methoxy methyl peak δ≈2.0, in order to estimate the extent of branching. The other assignments are: VAc backbone C*H* δ≈4.8; VAc backbone CH_2 δ≈1.6.

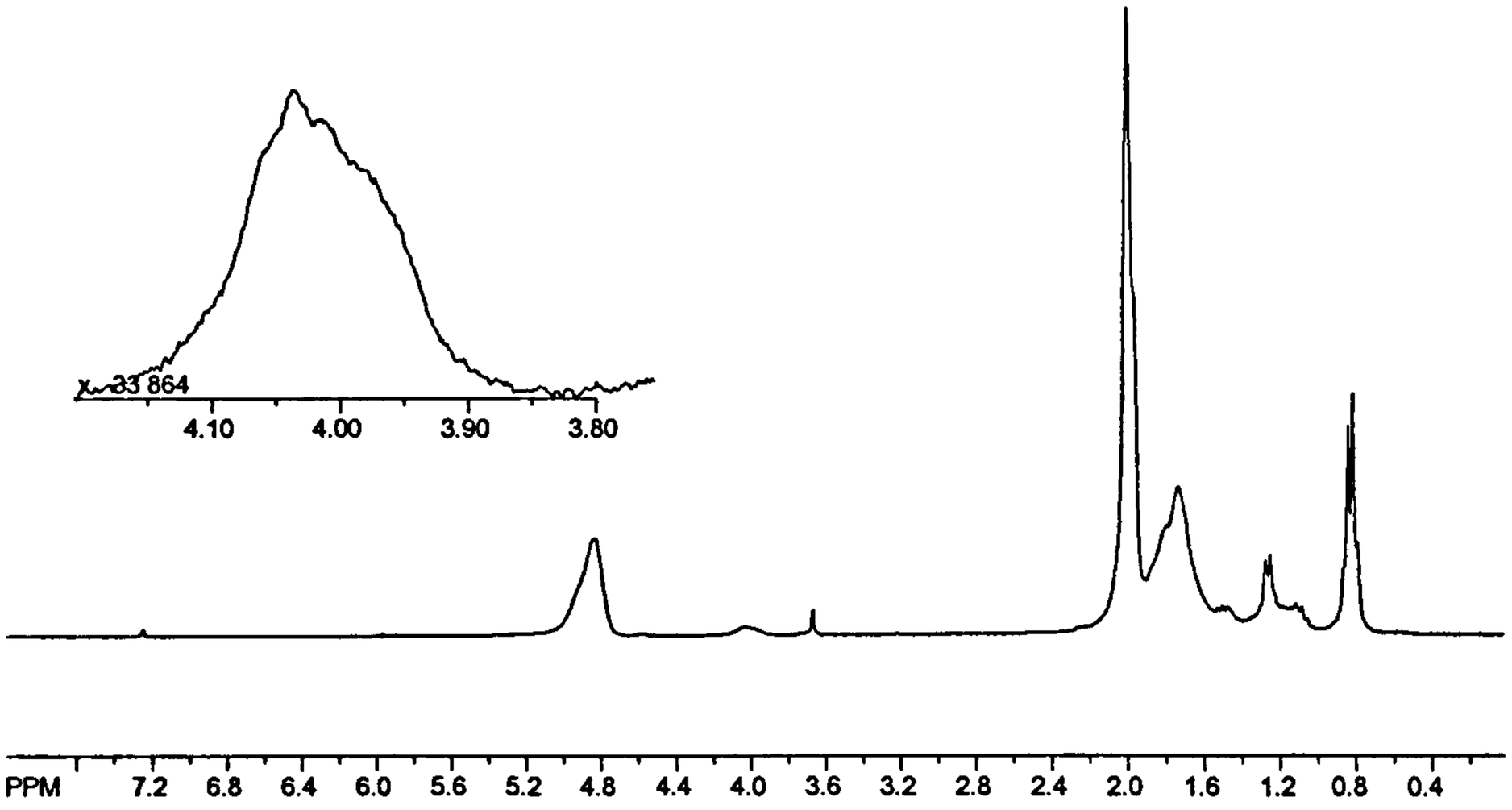


Figure 12-10 ^{1}H NMR spectrum of PVAc sample CS1/71/2

The NMR spectrum shown in figure 10 is of sample cs1/71/2, poly (vinyl acetate) synthesized in the presence of isopropanol and branching agent 1. The assignments are the same as for figure 4. The spectrum was analysed in the same way as the spectrum for cs1/71/1.

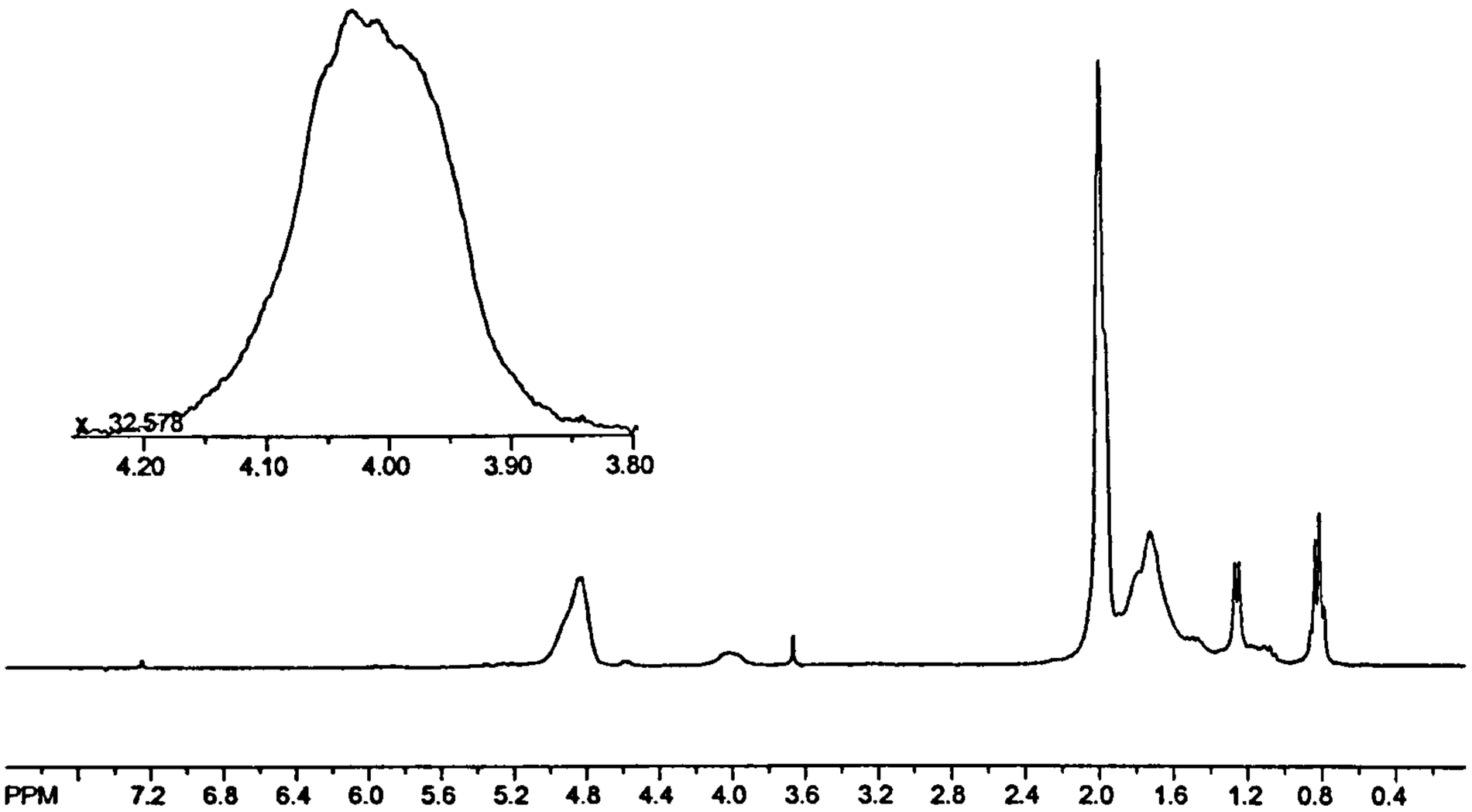


Figure 12-11 ^{1}H NMR spectrum of PVAc sample CS1/71/3

The NMR spectrum shown in figure 11 is of sample cs1/71/3, poly (vinyl acetate) synthesized in the presence of isopropanol and branching agent 1. The assignments are the same as for figure 4. The spectrum was analysed in the same way as the spectra for cs1/71/1 and cs1/71/2.

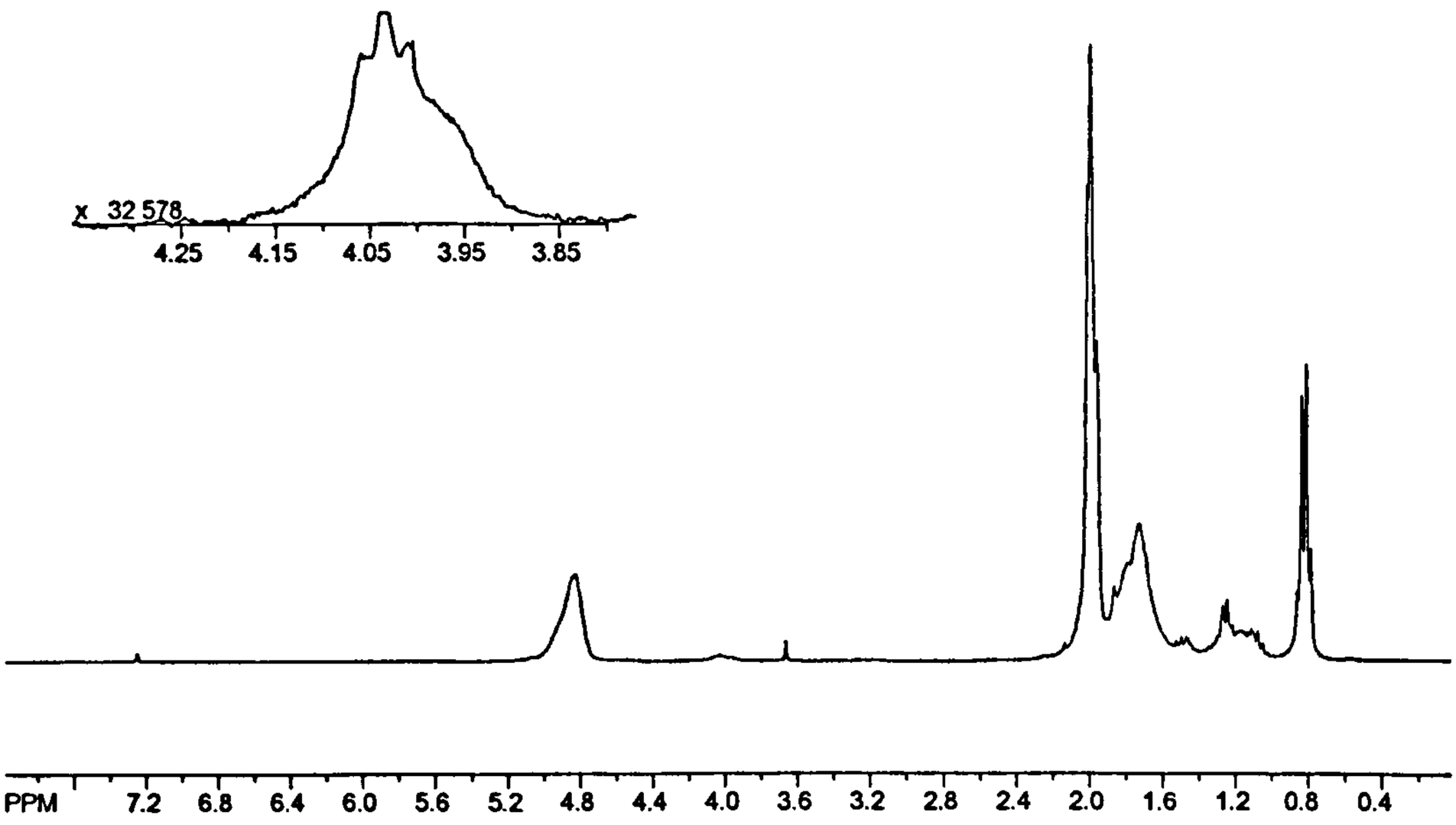


Figure 12-12 ^{1}H NMR spectrum of PVAc sample CS1/71/4

The NMR spectrum shown in figure 12 is of sample cs1/71/4, poly (vinyl acetate) synthesized in the presence of isopropanol and branching agent 1. The assignments are the same as for figure 4. The analysis of the spectrum was performed in the same way as the previous 3 samples.

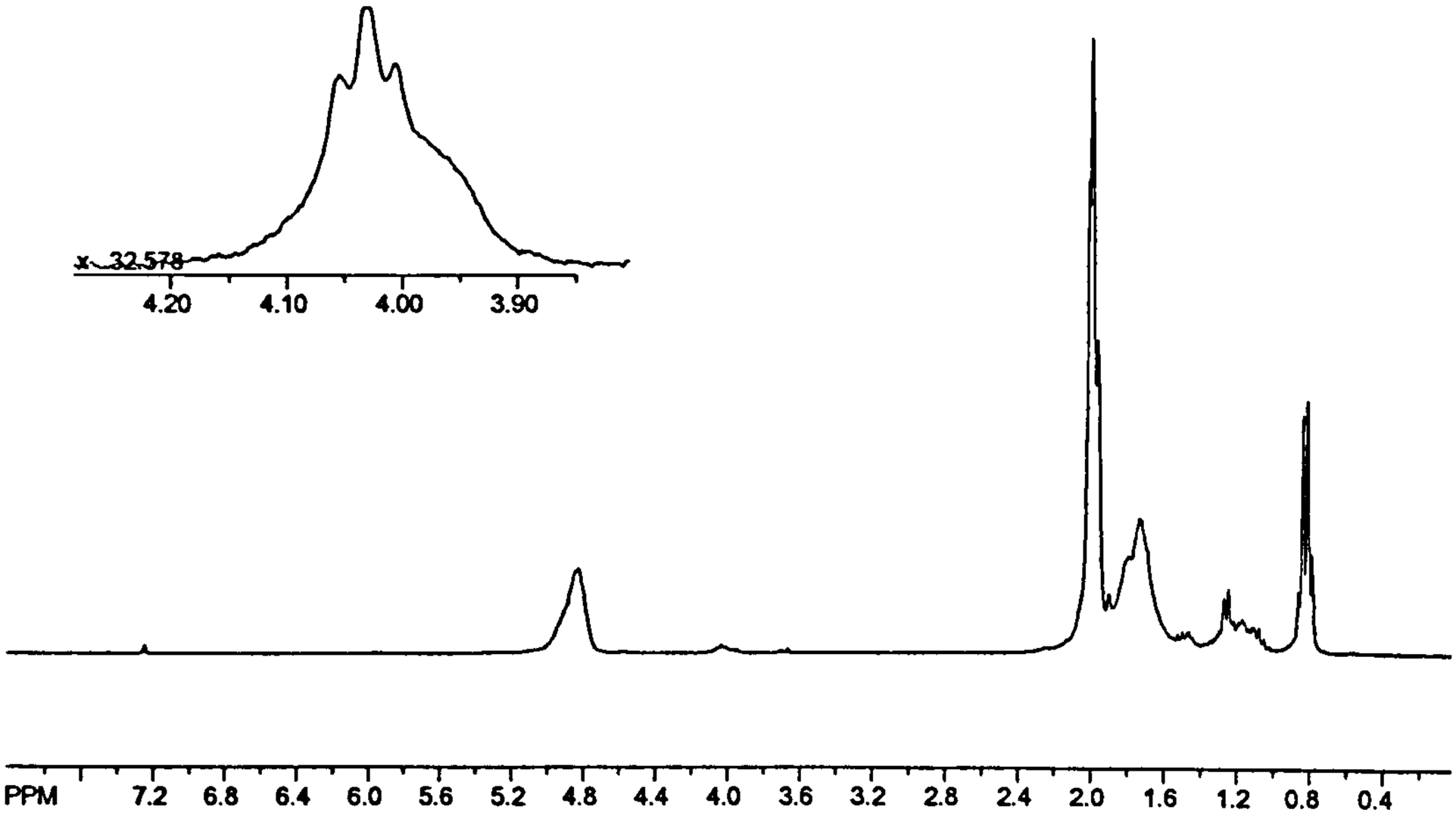


Figure 12-13 ^{1}H NMR spectrum of PVAc sample CS1/71/5

The NMR spectrum shown in figure 13 is of sample cs1/71/5, poly (vinyl acetate) synthesized in the presence of isopropanol and branching agent 1. The assignments are the same as for figure 4. The analysis of the spectrum was performed in the same was as the previous 4 samples.

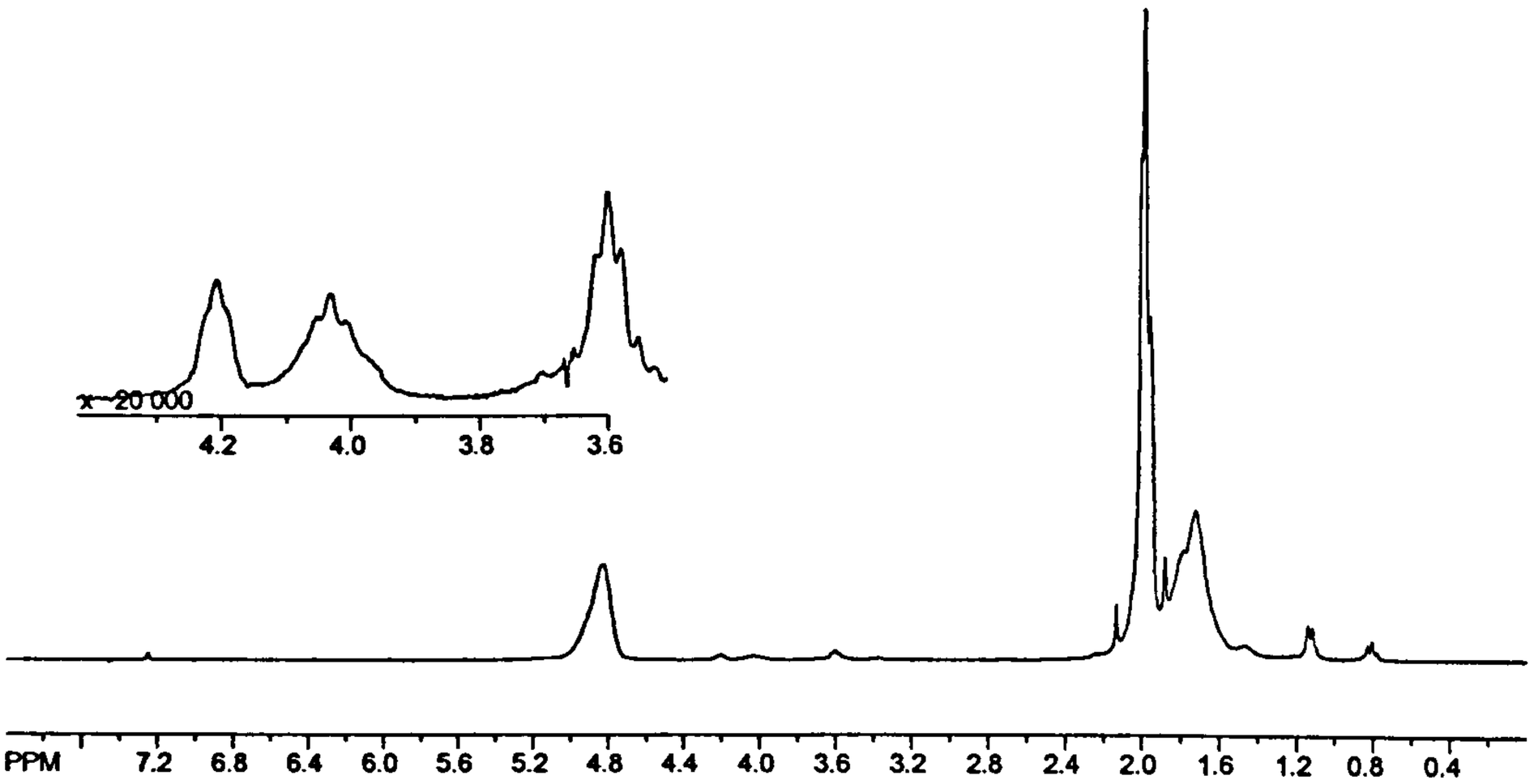


Figure 12-14 ^{1}H NMR spectrum of PVAc sample CS1/77/1

The NMR spectrum shown in figure 14 is of sample cs1/77/1, poly (vinyl acetate) synthesized in the presence of 2-isopropoxy ethanol and branching agent 2. The expanded section shows the peaks due to the branching agent. The integral of one of the peaks at δ≈4.0 was compared to the integral of the peak at δ≈2.0, which is due to the pendant methoxy methyl, in order to evaluate the level of branching. The assignments are: VAc backbone C*H* δ≈4.8; VAc backbone CH_2 δ≈1.7 The same procedure was applied to the NMR spectra of the other 4 samples.

The results for the calculation of the level of branching for vinyl acetate produced in isopropanol in the presence of ally isopropyl carbonate and vinyl acetate produced in 2-isopropoxy ethanol in the presence of allyl 2-isopropoxyethyl carbonate are detailed below. The analysis was performed as follows,

Equation 12-1

$$\frac{I_{B}/_{2}}{I_{B}/_{2}+I_{P}/_{3}} = branching$$

equation 1 was used to evaluate the branching for the hyperbranched poly (vinyl acetate), here, the integral of the peak due to the polymerised branching agent (I_B) was divided by the sum of the integrals for the peak due to the branching agent and the peak due to the polymer (I_P). The integrals are divided by the number of protons that gave rise to the signal.

Table 12-2 Table showing branching fractions

Sample	Branching fraction / branches per repeat	Mole fraction branching agent
cs1/73/1	0.027	0.0295
cs1/73/2	0.042	0.0563
cs1/73/3	0.07	0.107
cs1/73/4	0.027	0.0295
cs1/73/5	0.033	0.0295
cs1/79/1	0.018	0.024
cs1/79/2	0.03	0.048
cs1/79/3	0.056	0.091
cs1/79/4	0.022	0.024
cs1/79/5	0.024	0.024

12.3. Synthesis of hyperbranched polymers without chain transfer agents

The polymers synthesised from NVP using butyl acetate as the solvent and a branching agent formed crosslinked gels. Because of this it was decided to run the experiments at high temperatures in order to increase the rate of transfer, and so avoid the formation of crosslinked gels. It was thought that the reason for this was that the rate of termination via combination was higher than the rate of chain transfer. In the first set of reactions the solvent used was either isopropanol or 2-isopropoxy ethanol, and it is thought that the polymers produced using this method did not form crosslinked gels because of this added transfer agent.

12.4. High temperature reactions

12.4.1. SEC analysis

In order to get hyperbranched polymers that were not cross-linked in the absence of chain transfer agents, the synthesis was performed at high temperature, in an autoclave. These polymers proved to be soluble and were analysed by SEC and NMR. There was a slight problem with the analysis of the polymers produced in this fashion. Whilst with poly (vinyl acetate) SEC analysis was straightforward, NVP, when dissolved in THF sticks to the polystyrene of the SEC column, and is not eluted. Thus it was not possible to obtain TD-SEC data for these polymers, and any indication of branching is taken from NMR data.

Table 12-3 Table showing SEC results

Sample	Ordinary SEC		Triple Detector SEC	
	Mn	Mw	Mn	Mw
cs1/101/1	4490	19360		
cs1/101/2	3300	10900		
cs1/103/1	7130	17100	12310	21960
cs1/103/2	7630	17300	9550	15020

12.4.2. NMR analysis

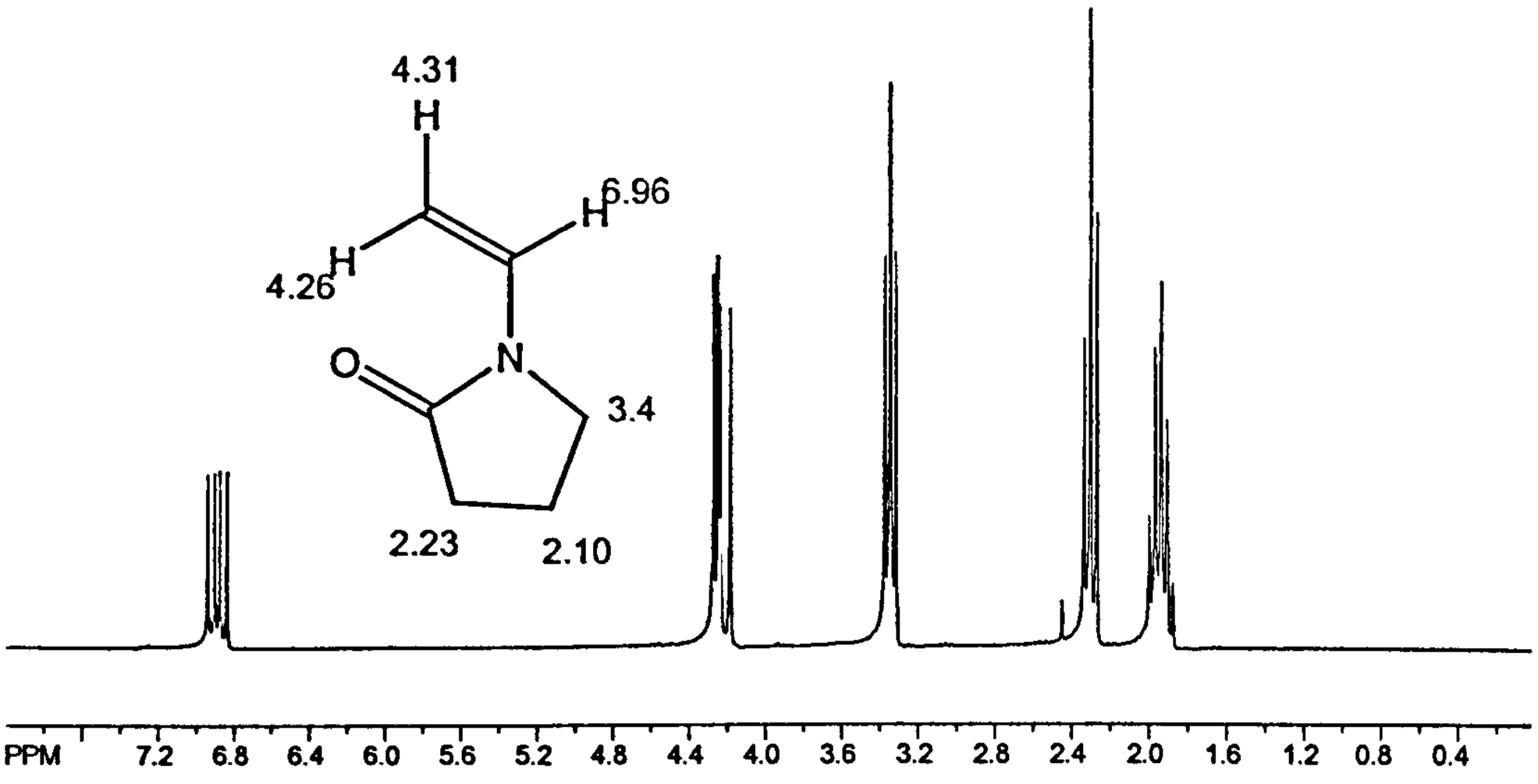


Figure 12-15 ^{1}H NMR spectrum of NVP monomer

The NMR spectrum shown in figure 15 is of NVP monomer, in $CDCl_3$, the assignments are shown in the figure.

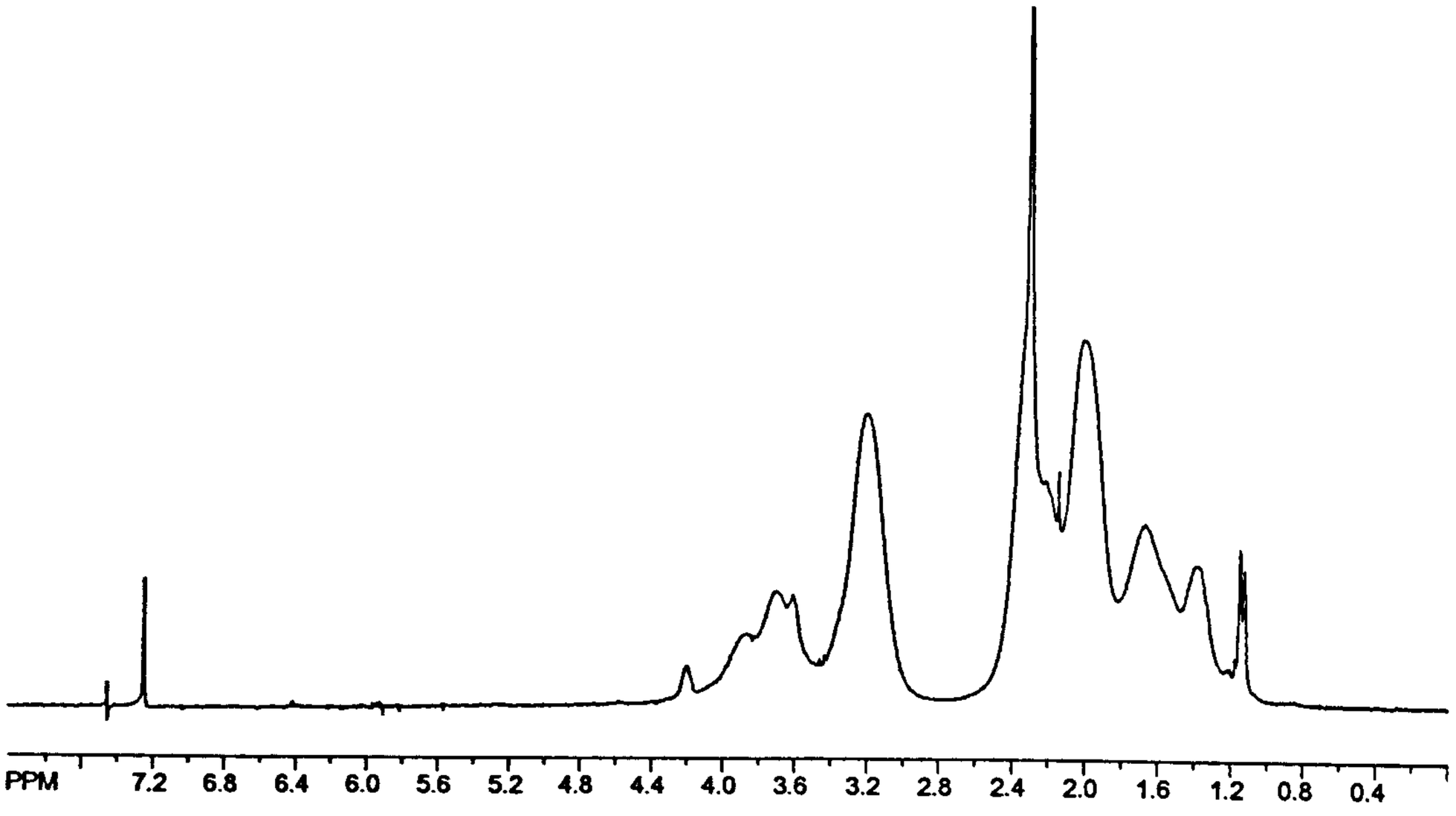


Figure 12-16 ^{1}H NMR spectrum of poly (NVP), synthesised at 150°C, with branching agent 2

The NMR spectrum shown in figure 16 is of poly (N-vinyl pyrrolidinone) synthesized in butyl acetate, in the presence of branching agent 2, at 150°C. The assignments are: backbone C*H* δ≈3.8; backbone CH_2 δ≈1.6; ring NCH_2 δ≈3.2; ring NCH$_2$CH_2 δ≈2.0; ring NCOCH_2 δ≈2.3. The branching agent peaks are at δ≈4.2, 3.6.

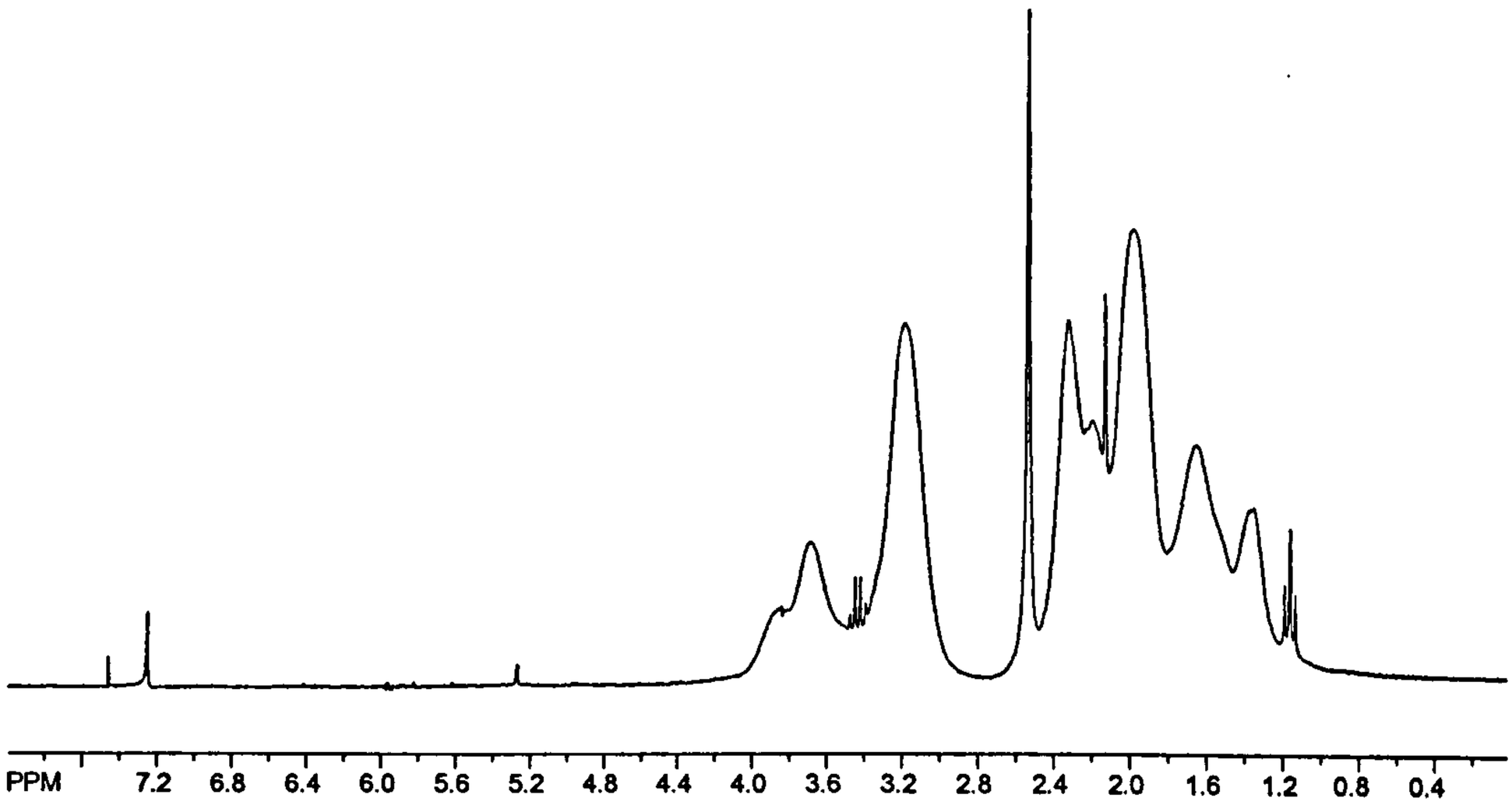


Figure 12-17 ^{1}H NMR spectrum of poly (NVP), synthesised at 150°C

The NMR spectrum shown in figure 17 is of poly (N-vinyl pyrrolidinone) synthesized in butyl acetate, at 150°C. The assignments are: backbone C*H* δ≈3.8; backbone CH_2 δ≈1.6; ring NCH_2 δ≈3.2; ring NCH$_2$CH_2 δ≈2.0; ring NCOCH_2 δ≈2.3. The peaks at δ≈3.4, 1.1, are due to diethyl ether still present.

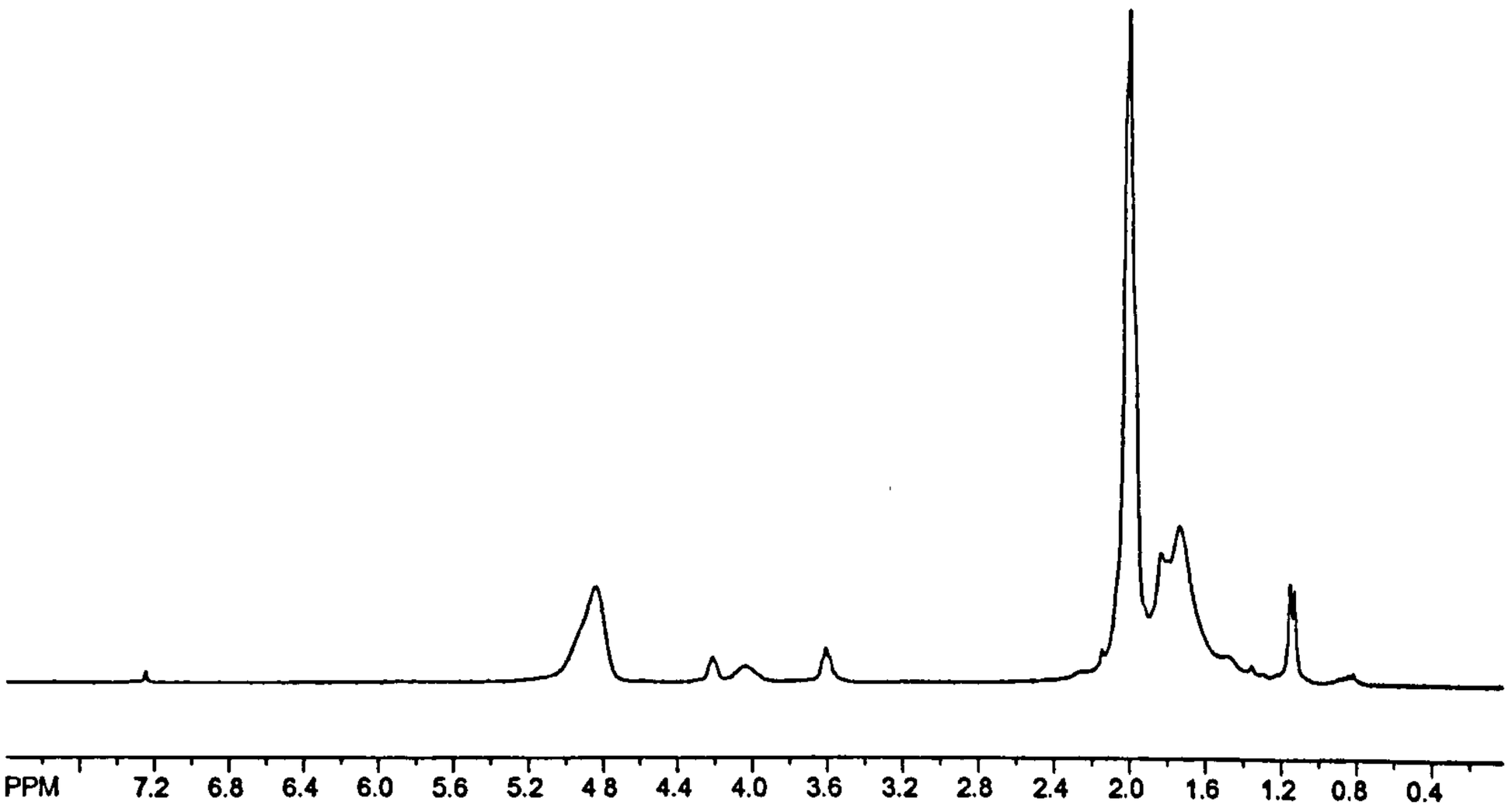


Figure 12-18 ^{1}H NMR spectrum of PVAc, synthesised at 150°C, with branching agent 2

The NMR spectrum shown in figure 18 is of poly (vinyl acetate) synthesized in butyl acetate (autoclave), in the presence of branching agent 2, at 150°C. The assignments are: VAc backbone C*H* δ≈4.8; VAc backbone CH_2 δ≈1.6; pendant methoxy methyl δ≈2.0; branching agent δ≈4.2, 4.0.

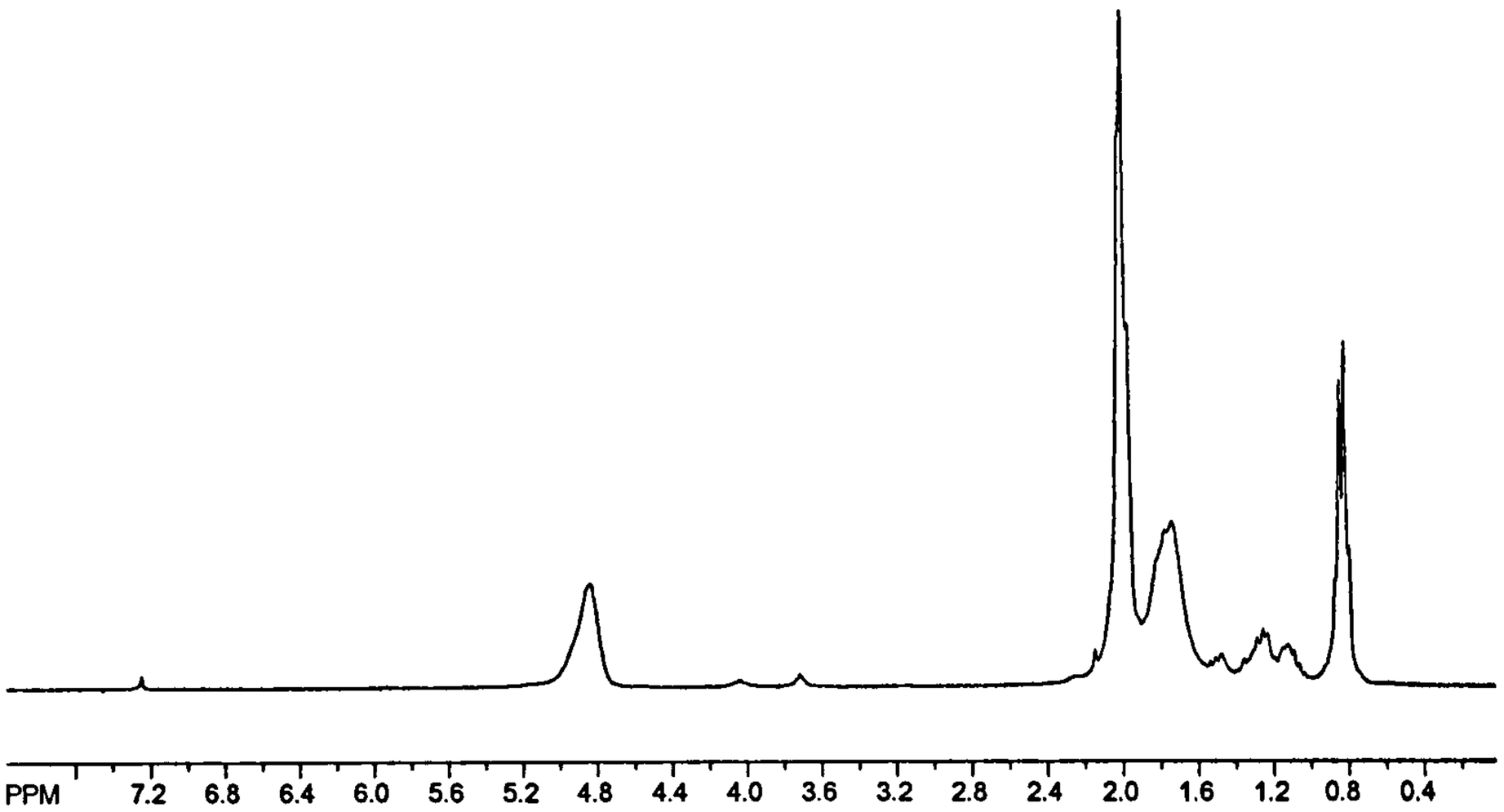


Figure 12-19 ^{1}H NMR spectrum of PVAc, synthesised at 150°C

The NMR spectrum shown in figure 19 is of poly (vinyl acetate) synthesized in butyl acetate, at 150°C. The assignments are: VAc backbone C*H* δ≈4.8; VAc backbone CH_2 δ≈1.6; pendant methoxy methyl δ≈2.0.

The level of branching was evaluated using the same method as was used for the first set of hyperbranched polymers. However the equation used for the polymers synthesised from NVP is slightly different from the equation used for the polymers synthesised from VAc.

Equation 12-2

$$\frac{I_{B/2}}{I_{B/2} + I_{P/2}} = branching$$

Equation 2 was used to evaluate the branching of the hyperbranched poly (N-vinyl pyrrolidinone). Here the integral of the non-branching monomer is divided by 2 this time instead of 3, as the integral is only from 2 protons, not 3 like with vinyl acetate. The branching of the poly (vinyl acetate) was analysed using the same method as used for the first series of polymerisations. The results from this analysis are shown in the table shown below.

Table 12-4 Table showing the branching fractions

Sample	Branching fraction / branches per repeat	Mole fraction branching agent
cs1/101/1	0.036	0.104
cs1/103/1	0.064	0.091

12.5. Discussion

Even if we assumed that vinyl acetate does not form branched polymers, which in fact it does, then the only branching points would be due to the branching agent, copolymerised into the polymer backbone. Assuming that these branching molecules subsequently transfer a radical, then a new polymer chain would grow from the site of radical transfer. Into this new polymer chain would be incorporated more of the branching agent molecules, these could then in turn start more new polymer chains.

A schematic representation of the branched polymers produced using this method is shown below. In this representation, the position of a branching monomer is highlighted by the use of a dashed bond in the polymer backbone.

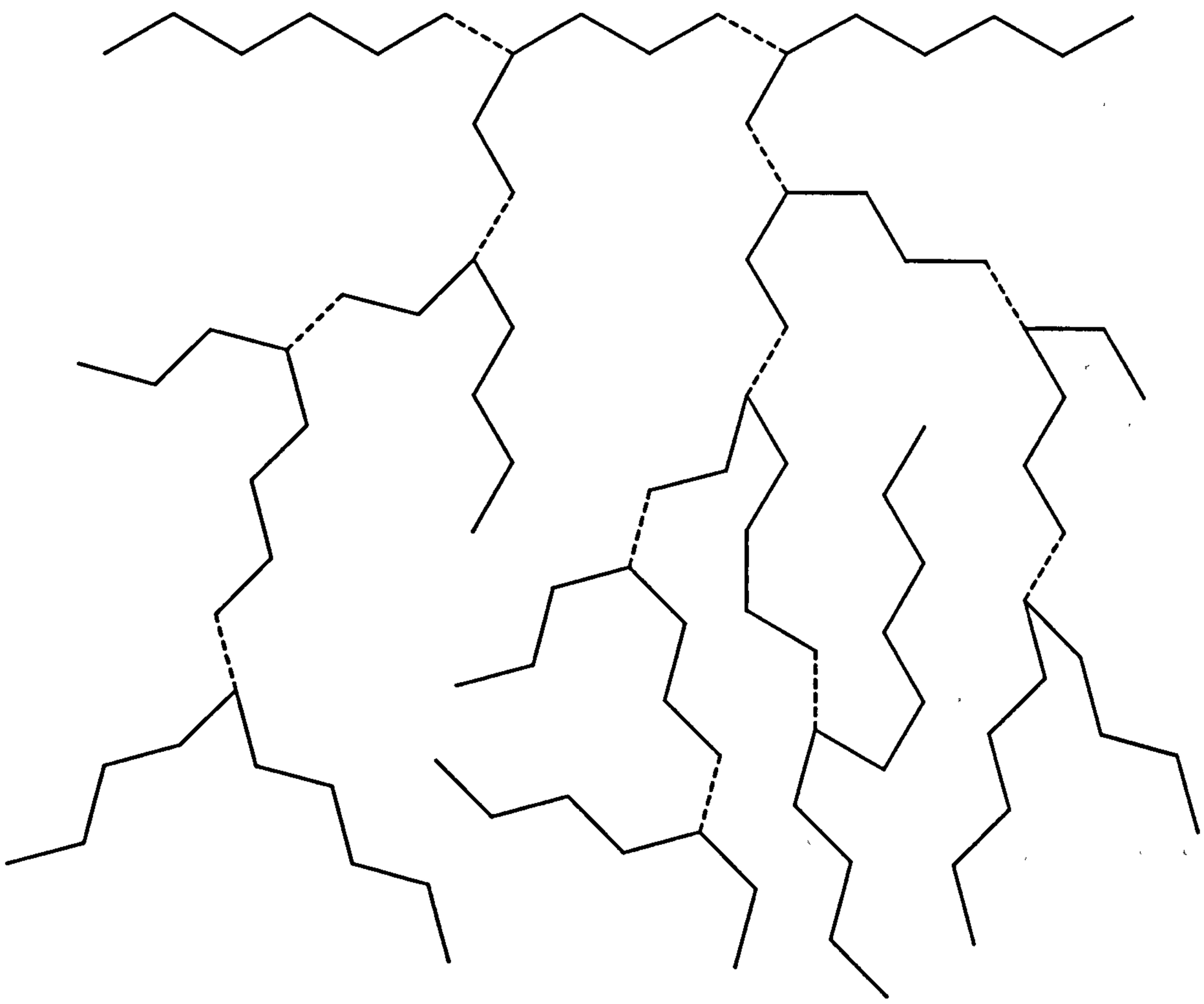


Figure 12-20 Sechematic diagram of branched polymer

As the transfer agents possessed their own transfer moiety it was hoped that there would be no need to add a further transfer agent. In the first series of polymerisations which were carried out in solvents known to chain transfer, the hyperbranched polymers produced were soluble in THF, and were analysed by SEC and NMR. However it was discovered that if the polymerisations were performed at 60°C without an additional chain transfer agent, gelation occurred. If the temperature was raised, to promote transfer reactions with respect to propagation reactions, the chain transfer agent could be omitted. Thermodynamics of polymers tells us that if the reaction temperature is raised

high enough then the polymerisation will not occur. This threshold is known as the depolymerisation temperature; it is the temperature above which the probability of a transfer or depolymerisation reaction occurring is greater than that of a propagation or combination reaction. Owing to the transfer reaction either not happening rapidly enough or without sufficient frequency, it was decided to raise the temperature of the reaction to increase the chance of these types of process occurring.

To this end, owing to the low boiling points and high vapour pressure of the solvent and monomers, it was decided to perform the reactions in an autoclave where the temperature could be raised with less of a risk of the reaction vessel shattering due to the increased pressure.

Work by Lebedev and Kulagina[118] has investigated the thermodynamic properties of vinyl acetate and poly (vinyl acetate), it is interesting to note that their calculated depolymerisation temperature is substantially higher than that of the polymer's decomposition temperature.

These values are 926K and 440K, for the ceiling temperature and degradation temperature respectively. It was decided to run the polymerisation of vinyl acetate and NVP at 150°C (423K). No data pertaining to the ceiling temperature for the polymerisation of NVP appeared to be available.

13. Conclusion to the synthesis of hyperbranched poly (vinyl acetate)

The final section of this thesis has been concerned with the synthesis of polymers of a highly branched or hyper branched nature. These polymers have found many uses, and indeed, dendrimers, ideal hyper branched polymers, have been proposed as candidates for use in drug delivery systems. Here the potential for a dendrimer to act as a "molecular micelle" would be exploited in order that a hydrophobic drug could be transported across a cell membrane at the core of a molecule which has hydrophilic groups at its extremities.

It is known already that many polymers form branched structures during polymerisation, indeed, vinyl acetate, one of the monomers used in this study is known to form branches during polymerisation through chain transfer. It is thought that the formation of branching is a function of the temperature at which the reaction was performed.

However a greater extent of branching is present in hyper branched molecules, in these cases, either a poly functional monomer is employed or a monomer with a crosslinking agent are used. For the latter case, the addition of a chain transfer agent is also necessary to avoid the formation of a crosslinked gel. Taking these points into consideration, it was decided to make use of vinyl acetate's facile transfer to solvent. To this end, a branching agent was synthesised, with the intention that it should act as a co-monomer, inducing branching through chain transfer, whilst being added to the reaction, at initiation, at relatively low concentrations.

Initially it was found that the rate of transfer was not great enough to ensure branching but not the formation of a gel. It was thought that the ability of the branching agent to act through a chain transfer pathway would stop the formation of a gel. To that end, two routes were open, the first; addition of an additional transfer agent, such as a solvent in this case, or the second; increase the temperature at which the reaction was performed at, promoting transfer reactions. As work has already been performed with the use of additional transfer agents, it was decided that an increase in the reaction temperature was the correct method to pursue.

By using an autoclave, it was possible to perform the polymerisations at temperatures significantly higher than was used for the polymerisations that formed gels. The reason for the use of the autoclave is that at the higher temperature the vapour pressure of the monomer would be significant.

Part 4: Methods of analysis and further work

14. Characterisation methods

There are many methods that can be used in the characterisation of polymeric materials. Some of these, used during this work, are detailed below.

14.1. Nuclear Magnetic Resonance (NMR) methods

NMR can be used to give information on the chemical structure of polymers: how the monomer units have been added to the chain; how much, if any, branching has taken place; the tacticity and/or microstructure of the polymer chain; the composition, and the number average molecular weight can be calculated from NMR spectra.

Work performed by Britton *et al*[43, 119] has looked at using NMR to calculate the amount and type of branching found in a poly (vinyl acetate) system. In their case the polymer was a seeded emulsion polymerisation, performed at different monomer feed rates, this was in order to check the effect of the monomer feed rate on the amount of branching in the polymer.

The work concentrated on two types of branching, the first where a proton was abstracted from the polymer backbone and the second where the proton was abstracted from the methyl of the side group.

Their theory was, as there were three times as many side group protons than backbone protons, the branching points were more likely to be from the side groups rather than the polymer backbone.

However, it is hard to prove this as the NMR signals from the two adjacent CH_2 groups of interest fall within the region of the spectrum where non-ideal polymerisation events such as tail-tail and head-head additions have taken place.

An accurate figure can be put upon the level of branching because the terminal CH_2 gives a clearly resolved peak at, or around, 60-62 ppm. In many cases ^{13}C NMR cannot be taken to be quantitative due to the lower signal intensities and the relaxation times of the carbon atoms. However, if the NMR is run using a pulse sequence, also known as "inverse-gated", then it is possible to suppress the Nuclear Overhauser Effect (NOE) and thereby have a quantitative NMR spectrum.

In this case however they ran most of the spectra with continuous proton decoupling using a pulse interval of 0.5 seconds, and a pulse flip angle of 70°. This was done in order to maximise the signal to noise ratio of the spectra. In a previous study they had produced similar spectra and then used the inverse-gated method in order to quantify the amounts of each carbon atom present. They then worked out a calibration factor as the fast pulse sequence underestimates the amount of primary and quaternary carbons relative to CH and CH_2 carbons.

A similar procedure was used by Hill *et al*[24] to determine if they had AIBN initiator fragments, rather than solvent fragments, as end groups on their polymers

14.2. Vapour pressure osmometry (VPO)

The technique of vapour pressure osmometry is a widespread, convenient method for determining the number average molecular weight of a polymer. It is not an absolute method because the osmometer has to be calibrated with a sample of known mass. In most cases this will be a small organic molecule such as Benzil. It is however, the most precise method for determining the absolute number average molecular weight of polymers, for Mn<20,000g mol^{-1}.

For the calibration, a series of solutions of known concentration of calibrant are made up. The solutions are then run, and as the mass of the calibrant is known, a calibration constant, also known as the cell constant, is determined. This cell constant is dependent on the solvent must be determined for each solvent used.

The osmometer its self is a simple instrument, even if it is not that easy to use. Briefly it consists of a glass container for the solvent, a paper wick to ensure a saturated layer of solvent vapour above the liquid, and two sensitive thermisters, all set within a heating block to keep the solvent at the right temperature.

The thermisters are connected in a wheatstone bridge circuit, so that the device can measure temperature differences of as little as $1x10^{-4}$ °C. It is this accuracy that is the basis on which the VPO works. On one of the probes a droplet of pure solvent is placed, on the other probe a droplet of polymer solution is placed, these two probes are kept surrounded by solvent vapour.

As the solution probe has a lowered vapour pressure, solvent from the vapour surrounding the probe condenses onto the probe, this raises the temperature difference between the two probes. The amount of solvent that condenses onto the probe is a measure of the number of molecules of polymer in the solution. As the concentration by mass of the polymer solution is known the molecular weight of the polymer can be calculated.

For the Gonotec machine used in this work (see appendix A figure 2), a graph is drawn and the intercept of the line with the Y axis, which has concentration equal to zero, determined. The cell constant when divided by the intercept gives the molecular weight.

Most of the mathematics is performed by the machine, however the equation that is used is $\frac{\Delta R}{Kc} = \left(\frac{1}{M_n}\right)\left(1+\frac{1}{2}\Gamma_2 c^2\right)$ where ΔR=difference in resistance, K=calibration constant, c=concentration of solution.

The value of Mn is determined by extrapolating the data to c→0,

14.3. Size Exclusion Chromatography (SEC)

As Size Exclusion Chromatography (SEC), or Gel Permeation Chromatography (GPC) as it is otherwise known, is a widely used polymer characterisation technique and as many articles have been written on its application and uses in the characterisation of polymers[120] it will not be dealt with in any detail, save to say that all the SEC analyses performed during the course of this work were carried out using a system with 3x30cm PLGel mixed B columns for high molecular weight species and 2x60 cm PLGel 100Å and 500Å columns in series for low molecular weight species, running on THF, and calibrated with respect to narrow poly styrene standards, excepting the analysis of the polymers based on N-Vinyl Pyrrolidinone (NVP), which were performed on a system with 3x30cm PLGel mixed B columns using DMF as solvent, at 70°C, calibrated with poly (ethylene oxide) standards.

The results given by the SEC software are not the same as the absolute values of molecular weight for the polymer being analysed. This is partly because the

calibrant was not of the same repeat unit as the analyte molecules. The Mark-Houwink Equation

$$[\eta] = KM^{\alpha}$$

relates the molecular weight M to the intrinsic viscosity $[\eta]$ of a solution of polymer, it must be remembered that the residence time of a polymer molecule in an SEC column will have a dependency upon the viscosity of the solution injected. The Mark-Houwink parameters, K being the Mark-Houwink constant, and α the Mark-Houwink exponent are put into the software when the machine is calibrated, and normally the same constants as the calibrant are used for the analyte molecules, and the result is simply quoted as being relative to a particular standard, for example poly styrene. The values for K and α for polystyrene in THF are taken to be $14.1 \times 10^{-3} cm^3\ g^{-1}$ and 0.70 respectively, however for poly (vinyl acetate) in THF the values, obtained from the Polymer Handbook were $16.0 \times 10^{-3}\ cm^3\ g^{-1}$ and 0.70 for K and α respectively. These values were imputed in the analysis page of the SEC software, and when the calculation of molecular weight was performed, the software allows for the difference in the Mark-Houwink parameters in the calculations.

A schematic depiction of the SEC apparatus is shown below.

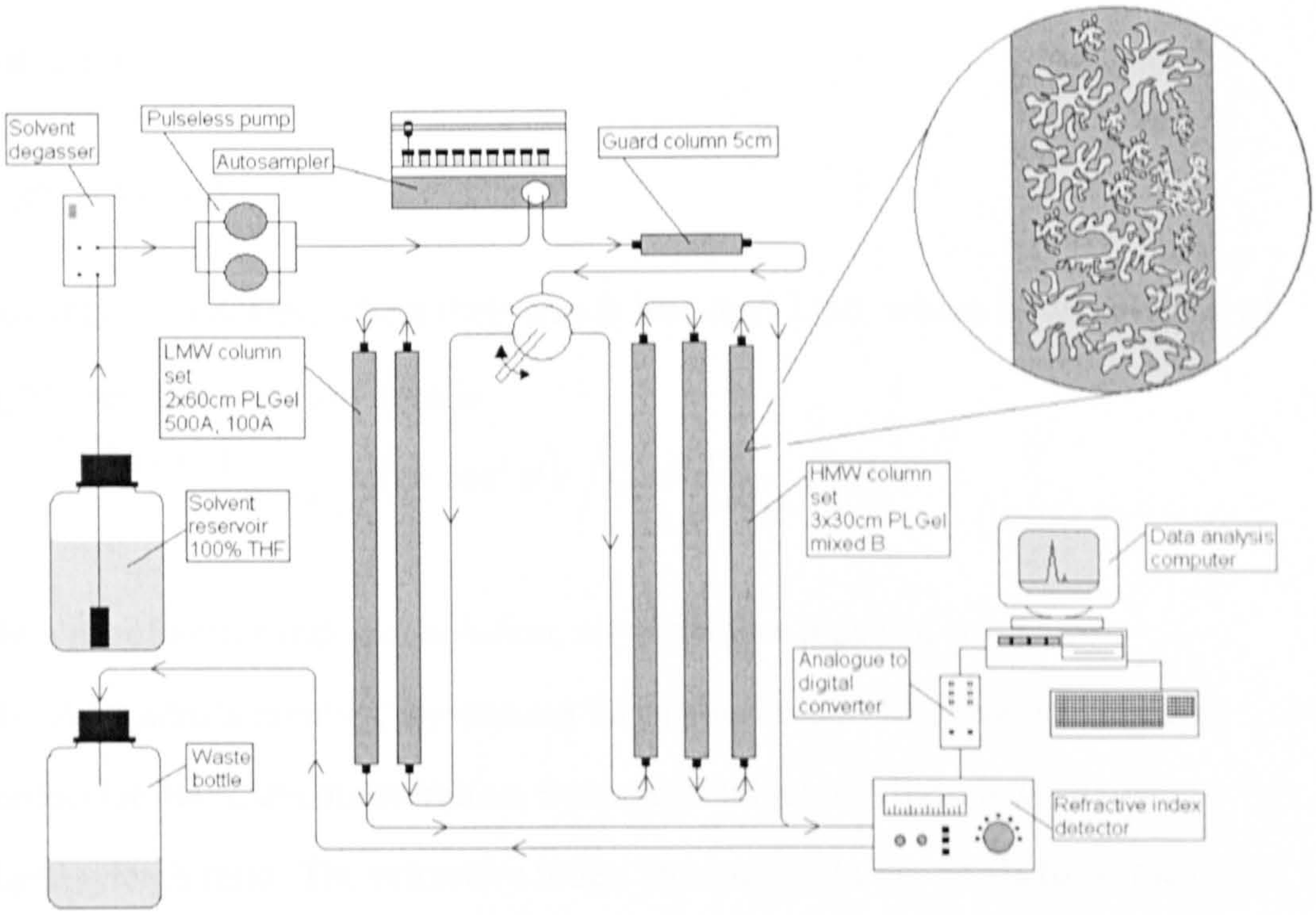


Figure 14-1 Schematic of SEC system

14.3.1. Triple Detector-Size Exclusion Chromatography TD-SEC (TD-GPC)

Many of the hyper-branched samples synthesized during the course of this work were analysed by the technique of Triple Detector-Size Exclusion Chromatography. This is a technique where a sample is not only analysed by the change in its refractive index (R.I) relative to pure solvent, but is also analysed by the change in the viscometry of the sample and the light scattered from the sample. This is where the technique gets its name, the three types of characterization used are, RI, Viscometry and Light Scattering.

The SEC equipment (see appendix A figure 3) has both Right Angle Light Scattering (RALS) and Low Angle Light Scattering (LALS); these two methods

are used together, although the LALS loses sensitivity for lower molecular weight polymers.

Light scattering

For small molecules, where their size is less than λ/20, where λ=wavelength of light used, the equation used is

$$\left\{2\pi^2 n_0^2 (dn/dc)^2 \Big/ (\lambda^4 N_A)\right\}(1+\cos^2 0)c \Big/ R_0 = 1/M_w + 2A_2 c$$

Here n=refractive index of solution, n_0=refractive index of solvent, N_A=Avagadro's number, A_2=second virial coefficient, M_W=weight average molecular mass, c=concentration, 0=angle at which the light is scattered, R_0=Rayleigh ratio. The refractive index increment, dn/dc, needs to be measured separately, on a differential refractometer.

Viscosity

The following relationships are used in order to determine the molecular weight of the polymers being analysed.

$$\eta_r = (t/t_0) = (\eta/\eta_0),$$

where η_r=relative viscosity, t=flow time for polymer solution, t_0=flow time for pure solvent, η=viscosity of polymer solution, η_0=viscosity of pure solvent

$$\eta_{sp} = \eta_r - 1 = (t - t_0)/t_0$$

where η_{sp}=specific viscosity, η_{sp} is related to the mass of the analyte by the equation $\eta_{sp} = K\Sigma C_i M_i^v$.

14.4. Mass spectrometry (MS) methods

Of the many mass spectrometry methods available to the polymer chemist, the two that have found the most use have been Matrix Assisted Laser Desorption/Ionisation-Time Of Flight (MALDI-TOF) and ElectroSpray Ionisation (ESI) mass spectrometry. MALDI-TOF has been used quite extensively for the analysis of biological samples such as proteins, as well as synthetic polymers. ESI is an ionisation method that is used to ionise molecules that might be damaged by MALDI or one of the other ionisation methods.

ElectroSpray ionisation has been used to analyse poly (vinyl acetate) that has been subject to enzymatic modification, Carter *et al*[40], used this method to show that some of the pendant acetate groups of a vinyl acetate oligomer had been converted to the alcohol by some enzymes and not been touched by other enzymes. In the past they had found that MALDI had been too aggressive an ionisation method and had broken down some of the molecules leading to a false mass spectrum.

A widely employed analytical method is Liquid Chromatography -Mass Spectrometry LC-MS, this method allows the separation of a mixture of compounds immediately prior to acquisition of mass spectra. A method that has received less attention is Size Exclusion Chromatography-Mass Spectrometry SEC-MS. This is a more efficient method of polymer analysis, which involves the "on-line" detection by ESI of polymers as they are eluted from SEC columns, than simply running an SEC of a compound, and waiting until the peak starts to elute from the column, then manually collecting samples from the waste flow of the system. These samples are then individually analysed by mass spectrometry, usually MALDI-TOF. The MALDI process, however, can lead to unwanted fragmentation in some cases, particularly with aliphatic polyesters so in this work

ESI was the preferred technique. An LC-MS system (see appendix A figure 4) with a set of SEC columns was set up in order to separate the polymers by hydrodynamic volume then perform "on-line" mass spectrometry on the eluted products This is similar work to that of Nielen *et al*[121], where comparisons of SEC, Gradient Polymer Elution Chromatography (GPEC) and Liquid Chromatography at the Critical point of adsorption (LCCC) are made.

However, there is a problem with this method, in that most mass spectrometry methods require a catinating agent for ESI, usually ammonium acetate, made up in the form of an aqueous solution.

Herein lies the problem; normal polystyrene based SEC columns are sensitive to water, it causes the gel to collapse. Because of this, another method had to be used in order to introduce the ammonium acetate into the analyte flow.

On the LC-MS a splitter valve is used to divert 80% of the flow away from the mass spectrometer towards an evaporative light scatterer (ELS), this is to stop the mass spectrometer becoming flooded with sample.

Because of these constraints the ammonium acetate had to be added after the SEC column to avoid damaging the column and before the splitter to avoid damaging the mass spectrometer. A separate HPLC pump was used to supply the aqueous ammonium acetate to the analyte flow, this was achieved through the use of a 3-way High Performance Liquid Chromatography (HPLC) fitting.

The results of the mass spectra, when analysed, show that the polymers have alcohol based end groups, with a vinyl acetate backbone, indicating chain transfer to solvent, as was expected, following on from the work performed previously by Carter *et al*[40].

14.4.1. Tandem mass spectrometry (MS:MS)

In a novel technique, known as "tandem mass spectrometry" or more simply as MS:MS, molecules are separated according to their mass, these separated molecules are then bombarded with highly accelerated noble gas atoms in order to break them apart. The results of this fragmentation are then analysed further using a second mass spectrometry technique. This technique is considered in greater depth in a separate chapter within this thesis.

15. Final conclusions and further work

The work contained within this thesis can be used a starting point for studies into the interesting behaviour and properties of the polymers synthesised herein.

15.1. Chain transfer

The work reported on in the first section of this thesis has already been studied in some depth, and although this is the case, the search for other solvents capable of chain transfer when used in a vinyl acetate system would be advantageous. A small study was performed here, where 3-methyl-2-butanone was used as a solvent, this has already been used for vinyl acetate and n-vinyl pyrrolidinone, and as expected, acted as a chain transfer agent, resulting in polymers with a different chain end when compared to the two sets of polymers synthesised within the boundary of this report.

Poly (vinyl acetate) synthesised using this method have useful properties, they can be low molecular weight oligomers, or higher molecular weight polymers. Indeed their molecular weight can be chosen by the ratio of monomer to solvent used. Further reaction of these polymers with other chemical species can lead to new and useful products. It might be possible to synthesise a polyurethane block copolymer from these vinyl acetate polymers, if one of the pendant acetate groups could be hydrolysed selectively. Further work looking at the use of enzymes to perform this sort of selective hydrolysis might lead to an interesting application,

where the vinyl acetate based polyurethane, could then be chemically hydrolysed to give a vinyl alcohol based poly urethane.

15.2. Enzymatic modification

The use of enzymes in this work showed the potential that they have for the catalysis for unusual polymerisation reactions. Here an hydroxyl terminated poly (vinyl acetate) was used in an attempt to initiate an ε-caprolactone ring opening polymerisation. A further study this time using commercial PVAc and using no PVAc at all would help to confirm the presence of block copolymers. This work followed on from that previously performed in the area in order to examine the effect that enzyme has on the polymerisation.

15.3. Hyperbranched polymers

The last section of this thesis was about the work performed in the area of hyperbranched polymers synthesised from unstabilised radical forming monomers. Here the work was new and the polymers synthesised have the potential to be of much interest to further research. The comonomer used to effect the branching is a carbonate, this can be hydrolytically cleaved through the use of base mediated hydrolysis.

Branched polymers have different properties when compared to their linear analogues, for example they have a smaller radius of gyration, lower intrinsic viscosity. For this reason branched polymers are often added to linear polymers in

the melt to stop chain entanglements, and lower the viscosity of the melt, thereby making the processing of the polymers easier.

Hyperbranched polymers can also be used as the dispersion agent in a dispersion polymerisation, useful for the synthesis of microparticles. Here it is thought that the use of a hyperbranched polymer as the dispersion agent would induce changes in the size of particle formed due to the different effect the shape of the polymer molecule would have with respect to the reactant species. For example it is thought that hyperbranched polymers would lead to smaller particles due to the ability of the hyperbranched molecules increased ability to stabilise the smaller particles, when compared to their linear analogues.

16. References

[1] R. Jerome, M. Henrioulle-Granville, B. Boutevin, J. J. Robin, *Progress in Polymer Science* 1991, *16*, 837.

[2] O. W. Webster, *Science (Washington, D. C., 1883-)* 1991, *251*, 887.

[3] C. Zune, P. Dubois, R. Jerome, J. Kriz, J. Dybal, L. Lochmann, M. Janata, P. Vlcek, T. M. Werkhoven, J. Lugtenburg, *Macromolecules* 1998, *31*, 2731.

[4] M. Kobayashi, M. Hirata, M. Takeishi, *Polymer Journal (Tokyo, Japan)* 2004, *36*, 238.

[5] D. Y. Sogah, W. R. Hertler, O. W. Webster, G. M. Cohen, *Macromolecules* 1987, *20*, 1473.

[6] U. Tunca, *Polymer* 1995, *36*, 3955.

[7] E. Walch, R. J. Gaymans, *Polymer* 1993, *34*, 412.

[8] W. Lang, S. Rimmer, *Macromolecular Rapid Communications* 2001, *22*, 194.

[9] D. Mardare, K. Matyjaszewski, *Macromolecules* 1994, *27*, 645.

[10] C. Granel, R. Jerome, P. Teyssie, C. B. Jasieczek, A. J. Shooter, D. M. Haddleton, J. J. Hastings, D. Gigmes, S. Grimaldi, P. Tordo, D. Greszta, K. Matyjaszewski, *Macromolecules* 1998, *31*, 7133.

[11] M. Kamigaito, T. Ando, M. Sawamoto, *Chemical Reviews (Washington, D. C.)* 2001, *101*, 3689.

[12] M. Wakioka, K.-Y. Baek, T. Ando, M. Kamigaito, M. Sawamoto, *Macromolecules* 2002, *35*, 330.

[13] J. Yang, S. Ding, M. Radosz, Y. Shen, *Macromolecules* 2004, *37*, 1728.

[14] U. Meyer, A. R. A. Palmans, T. Loontjens, A. Heise, *Macromolecules* 2002, *35*, 2873.

[15] A. J. Clark, G. M. Battle, A. M. Heming, D. M. Haddleton, A. Bridge, *Tetrahedron Lett.* 2001, *42*, 2003.

[16] C. M. Wager, D. M. Haddleton, S. A. F. Bon, *Eur. Polym. J.* 2004, *40*, 641.

[17] S. Liu, S. P. Armes, *Polym. Mater. Sci. Eng.* 2001, *84*, 145.

[18] S. Durie, K. Jerabek, C. Mason, D. C. Sherrington, *Macromolecules* 2002, *35*, 9665.

[19] J. P. A. Heuts, T. P. Davis, G. T. Russell, *Macromolecules* 1999, *32*, 6019.

[20] G. Moad, C. L. Moad, *Macromolecules* 1996, *29*, 7727.

[21] K. G. Suddaby, D. R. Maloney, D. M. Haddleton, *Macromolecules* 1997, *30*, 702.

[22] J. Filley, J. T. McKinnon, D. T. Wu, G. H. Ko, *Macromolecules* 2002, *35*, 3731.

[23] W. S. Lyoo, S. S. Han, J. H. Kim, W. S. Yoon, C. J. Lee, I. C. Kwon, J. Lee, B. C. Ji, M. H. Han, *Angew. Makromol. Chem.* 1999, *271*, 46.

[24] D. J. T. Hill, L. Y. Shao, P. J. Pomery, A. K. Whittaker, *Polymer* 2001, *42*, 4791.

[25] P. Liu, H. Ding, J. Liu, X. Yi, *Eur. Polym. J.* 2002, *38*, 1783.

[26] J. C. Bevington, T. N. Huckerby, *Eur. Polym. J.* 1995, *31*, 99.

[27] S. Boileau, L. Bouteiller, A. Kowalewska, *Polymer* 2003, *44*, 6449.

[28] M. R. Gagne, M. R. Korn, in *U.S. Pat. Appl. Publ.*, (The University of North Carolina at Chapel Hill, USA). Us, 2002, pp. 20 pp.

[29] K. Hiltunen, M. Harkonen, J. V. Seppala, T. Vaananen, *Macromolecules* 1996, *29*, 8677.

[30] J. R. Ebdon, N. J. Flint, *Eur. Polym. J.* 1996, *32*, 298.

[31] J. R. Ebdon, N. J. Flint, S. Rimmer, *Macromolecular Reports* 1995, *A32*, 603.

[32] J. R. Ebdon, S. Rimmer, *J. Chem. Res., Synop.* 1997, 408.

[33] J. R. Ebdon, S. Rimmer, *J. Polym. Sci., Part A: Polym. Chem.* 1997, *35*, 3255.

[34] S. Rimmer, J. R. Ebdon, M. J. Shepherd, *Reactive & Functional Polymers* 1995, *26*, 145.

[35] T. Sawaguchi, H. Saito, S. Yano, M. Seno, *Polym. Degrad. Stab.* 2001, *72*, 383.

[36] T. Sawaguchi, M. Seno, *Polym. J. (Tokyo)* 1996, *28*, 817.

[37] A. O. Helminen, H. Korhonen, J. V. Seppaelae, *J. Polym. Sci., Part A: Polym. Chem.* 2003, *41*, 3788.

[38] A. O. Helminen, H. Korhonen, J. V. Seppala, *Macromolecular Chemistry and Physics* 2002, *203*, 2630.

[39] A. O. Helminen, H. Korhonen, J. V. Seppala, *J. Appl. Polym. Sci.* 2002, *86*, 3616.

[40] S. Carter, A. Kavros, S. Rimmer, *Reactive & Functional Polymers* 2001, *48*, 97.

[41] T. Ohnaga, T. Sato, *Polymer* 1996, *37*, 3729.

[42] J. Xia, H.-j. Paik, K. Matyjaszewski, *Macromolecules* 1999, *32*, 8310.

[43] D. Britton, F. Heatley, P. A. Lovell, *Macromolecules* 2000, *33*, 5048.

[44] J. M. G. Cowie, *Polymers: Chemistry and Physics of modern materials*, Chapman & Hall, 1991.

[45] P. Rizzarelli, G. Impallomeni, *Biomacromolecules* 2003.

[46] M.-S. Giguere, P. M. Mayer, *International Journal of Mass Spectrometry* 2002, *231*, 59.

[47] R. Z. Greenley, in *The Polymer Handbook* (Eds.: J. Brandrup, E. H. Immergut, E. A. Grulke), Wiley, 1999, p. II/181.

[48] G. Moad, D. H. Solomon, *The chemistry of free radical polymerization*, Pergamon, 1995.

[49] M. Bankova, A. Kumar, G. Impallomeni, A. Ballistreri, R. A. Gross, *Macromolecules* 2002, *35*, 6858.

[50] A. Dyal, K. Loos, M. Noto, S. W. Chang, C. Spagnoli, K. V. P. M. Shafi, A. Ulman, M. Cowman, R. A. Gross, *J. Am. Chem. Soc.* 2003, *125*, 1684.

[51] R. A. Gross, A. Kumar, in *USPTO*, 200211269001-62-1, USA, 2002, p. 33 pp.

[52] R. A. Gross, A. Kumar, B. Kalra, *Chemical Reviews (Washington, D. C.)* 2001, *101*, 2097.

[53] B. Kalra, R. A. Gross, *Biomacromolecules* 2000, *1*, 501.

[54] A. Kumar, R. A. Gross, *Biomacromolecules* 2000, *1*, 133.

[55] A. Kumar, R. A. Gross, Y. Wang, M. A. Hillmyer, *Macromolecules* 2002, *35*, 7606.

[56] S. M. Li, X. H. Chen, R. A. Gross, S. P. McCarthy, *Journal of Materials Science: Materials in Medicine* 2000, *11*, 227.

[57] A. Mahapatro, B. Kalra, A. Kumar, R. A. Gross, *Biomacromolecules* 2003, *4*, 544.

[58] Y. Mei, A. Kumar, R. A. Gross, *Macromolecules* 2002, *35*, 5444.

[59] A. Charusheela, L. Arvind, *Enzyme Microb. Technol.* 2002, *30*, 19.

[60] Y. Mei, L. Miller, W. Gao, A. Gross Richard, *Biomacromolecules* 2003, *4*, 70.

[61] S. J. Bryant, K. L. Durand, K. S. Anseth, *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* 2001, *42*, 86.

[62] J. H. De Groot, H. W. Kuijper, A. J. Pennings, *Journal of Materials Science: Materials in Medicine* 1997, *8*, 707.

[63] B. L. Seal, T. C. Otero, A. Panitch, *Materials Science & Engineering, R: Reports* 2001, *R34*, 147.

[64] Y. Aoyagi, K. Yamashita, Y. Doi, *Polym. Degrad. Stab.* 2002, *76*, 53.

[65] J. H. De Groot, A. J. Pennings, J. M. F. H. Coenen, *J. Mater. Sci. Lett.* 1997, *16*, 152.

[66] V. Hasirci, K. Lewandrowski, J. D. Gresser, D. L. Wise, D. J. Trantolo, *J. Biotechnol.* 2001, *86*, 135.

[67] M. Taira, Y. Araki, J. Takahashi, *J. Mater. Sci. Lett.* 2001, *20*, 1773.

[68] M. J. A. van Luyn, J. A. Plantinga, L. A. Brouwer, I. M. S. L. Khouw, L. F. M. H. de Leij, P. B. van Wachem, *Biomaterials* 2001, *22*, 1385.

[69] T. G. van Tienen, R. G. J. C. Heijkants, P. Buma, J. H. de Groot, A. J. Pennings, R. P. H. Veth, *Biomaterials* 2002, *23*, 1731.

[70] O. Persenaire, M. Alexandre, P. Degee, P. Dubois, *Biomacromolecules* 2001, *2*, 288.

[71] C. Eldsater, B. Erlandsson, R. Renstad, A. C. Albertsson, S. Karlsson, *Polymer* 1999, *41*, 1297.

[72] D. R. Chen, J. Z. Bei, S. G. Wang, *Polym. Degrad. Stab.* 2000, *67*, 455.

[73] S. Chawla Jugminder, M. Amiji Mansoor, *Int. J. Pharm.* 2002, *249*, 127.

[74] H. Tsuji, K. Suzuyoshi, *Polym. Degrad. Stab.* 2002, *75*, 357.

[75] H. Tsuji, K. Suzuyoshi, *Polym. Degrad. Stab.* 2002, *75*, 347.

[76] C. Gao, Y. Xu, D. Yan, W. Chen, *Biomacromolecules* 2003, *4*, 704.

[77] S. Chattopadhyay, G. Sivalingam, G. Madras, *Polym. Degrad. Stab.* 2003, *80*, 477.

[78] G. Sivalingam, S. Chattopadhyay, G. Madras, *Chem. Eng. Sci.* 2003, *58*, 2911.

[79] G. Sivalingam, S. Chattopadhyay, G. Madras, *Polym. Degrad. Stab.* 2003, *79*, 413.

[80] J. W. Park, S. S. Im, *Polymer* 2003, *44*, 4341.

[81] A. W. P. Jarvie, N. Overton, C. B. St Pourcain, *J. Chem. Soc., Perkin Trans. 1* 1999, 2171.

[82] D. Cohn, T. Stern, M. F. Gonzalez, J. Epstein, *Journal of Biomedical Materials Research* 2002, *59*, 273.

[83] C. J. Han, M. S. Lee, D.-J. Byun, S. Y. Kim, *Macromolecules* 2002, *35*, 8923.

[84] A. Kavros, T. N. Huckerby, S. Rimmer, *J. Mater. Chem.* 1999, *9*, 1071.

[85] M. Mizutani, T. Matsuda, *Journal of Biomedical Materials Research* 2002, *62*, 387.

[86] A. Chatterjee, W. S. Park, W. W. Graessley, *Chem. Eng. Sci.* 1977, *32*, 167.

[87] S. Merino, L. Brauge, A.-M. Caminade, J.-P. Majoral, D. Taton, Y. Gnanou, *Chemistry--A European Journal* 2001, *7*, 3095.

[88] N. O'Brien, A. McKee, D. C. Sherrington, A. T. Slark, A. Titterton, *Polymer* 2000, *41*, 6027.

[89] S. H. Yoo, J. H. Lee, J.-C. Lee, J. Y. Jho, *Macromolecules* 2002, *35*, 1146.

[90] J. Hao, M. Jikei, M. Kakimoto, *Macromolecules* 2002, *35*, 5372.

[91] C. Gao, J. Hou, D. Yan, Z. Wang, *Reactive & Functional Polymers* 2004, *58*, 65.

[92] C. Gao, D. Yan, *Macromolecules* 2003, *36*, 613.

[93] K.-C. Cheng, *Polymer* 2003, *44*, 1259.

[94] A. S. Nasar, M. Jikei, M.-a. Kakimoto, *Eur. Polym. J.* 2003, *39*, 1201.

[95] K. Ishizu, T. Shibuya, S. Kawauchi, *Macromolecules* 2003, *36*, 3505.

[96] H. R. Kricheldorf, L. Vakhtangishvili, G. Schwarz, R.-P. Krueger, *Macromolecules* 2003, *36*, 5551.

[97] Z. Bo, A. D. Schlueter, *Chemical Communications (Cambridge, United Kingdom)* 2003, 2354.

[98] J. Choi, S.-Y. Kwak, *Macromolecules* 2003, *36*, 8630.

[99] Q. Lin, T. E. Long, *Macromolecules* 2003, *36*, 9809.

[100] L. J. Twyman, A. S. H. King, J. Burnett, I. K. Martin, *Tetrahedron Lett.* 2004, *45*, 433.

[101] B. Jiang, Y. Yang, X. Jin, R. Zhu, J. Hao, W. Wang, *Eur. Polym. J.* 2001, *37*, 1975.

[102] M. Rodlert, C. J. G. Plummer, L. Garamszegi, Y. Leterrier, H. J. M. Grunbauer, J.-A. E. Manson, *Polymer* 2004, *45*, 949.

[103] J. Karger-Kocsis, J. Frohlich, O. Gryshchuk, H. Kautz, H. Frey, R. Mulhaupt, *Polymer* 2004, *45*, 1185.

[104] M. Seiler, D. Kohler, W. Arlt, *Separation and Purification Technology* 2003, *30*, 179.

[105] M. Seiler, M. Buggert, A. Kavarnou, W. Arlt, *J. Chem. Eng. Data* 2003, *48*, 933.

[106] M. Seiler, J. Rolker, W. Arlt, *Macromolecules* 2003, *36*, 2085.

[107] Z. Ye, S. Zhu, *Macromolecules* 2003, *36*, 2194.

[108] S. Kunamaneni, D. M. A. Buzza, D. Parker, W. J. Feast, *J. Mater. Chem.* 2003, *13*, 2749.

[109] T. Matsuda, M. Mizutani, *Journal of Biomedical Materials Research* 2002, *62*, 395.

[110] J. K. Karjalainen, O. E. O. Hormi, D. C. Sherrington, *Tetrahedron: Asymmetry* 1998, *9*, 1563.

[111] Z. Liu, N. Fullwood, S. Rimmer, *J. Mater. Chem.* 2000, *10*, 1771.

[112] Z. Liu, S. Rimmer, *J. Controlled Release* 2002, *81*, 91.

[113] F. Haff, A. Sanner, F. Straub, *Polym. J. (Tokyo)* 1985, *17*, 143.

[114] E. Ranucci, G. Spagnoli, L. Sartore, F. Bignotti, P. Ferruti, *Macromolecular Chemistry and Physics* 1995, *196*, 763.

[115] L. Sartore, E. Ranucci, P. Ferruti, P. Caliceti, S. Schiavon, F. M. Veronese, *J. Bioact. Compat. Polym.* 1994, *9*, 411.

[116] Z. Liu, S. Rimmer, *Macromolecules* 2002, *35*, 1200.

[117] B. Yamada, O. Konosu, K. Tanaka, F. Oku, *Polymer* 2000, *41*, 5625.

[118] B. V. Lebedev, T. G. Kulagina, *Journal of Thermal Analysis and Calorimetry* 1998, *54*, 731.

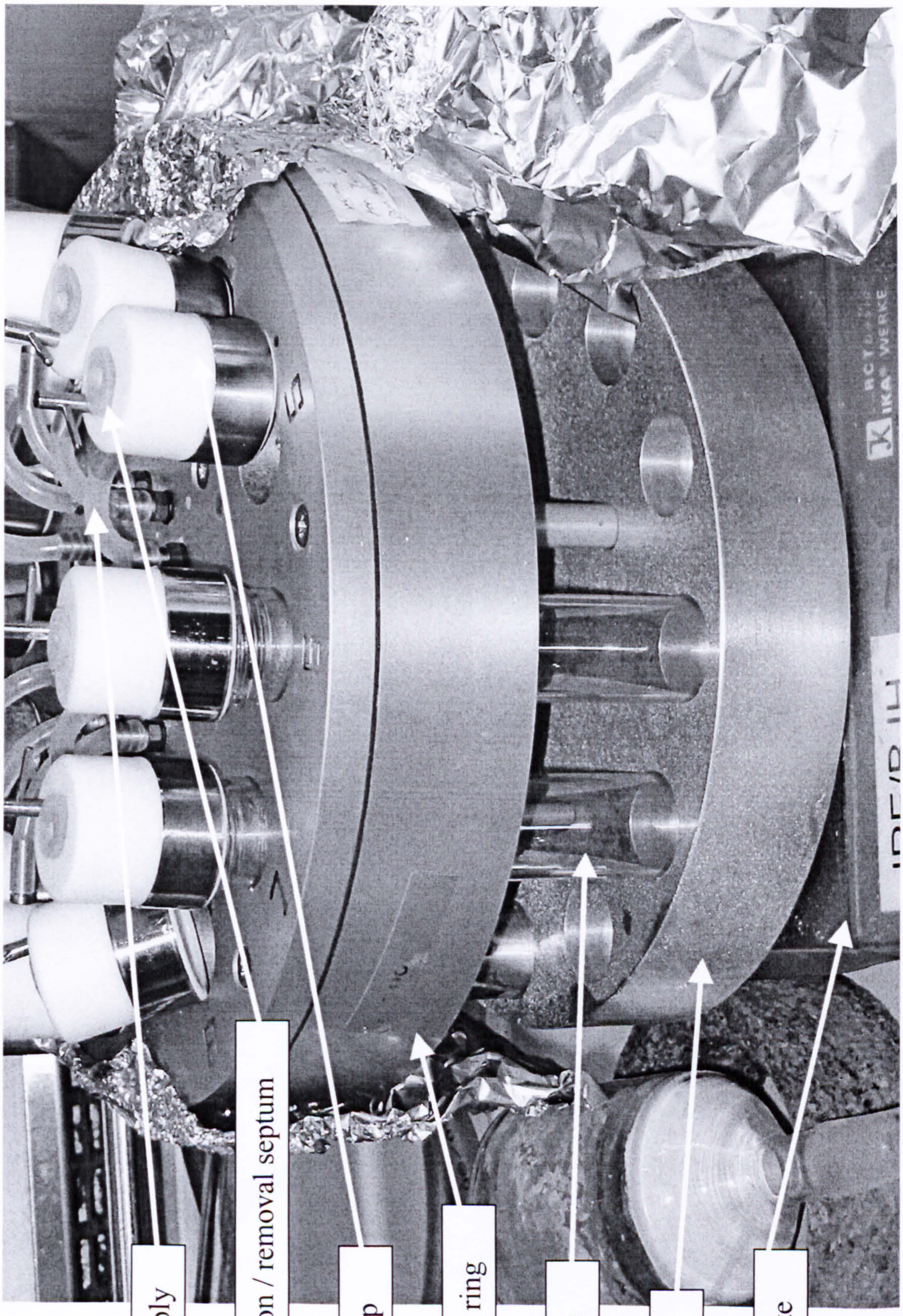
[119] D. Britton, F. Heatley, P. A. Lovell, *Macromolecules* 1998, *31*, 2828.

[120] B. J. Hunt, S. R. Holding, Blackie, 1989.

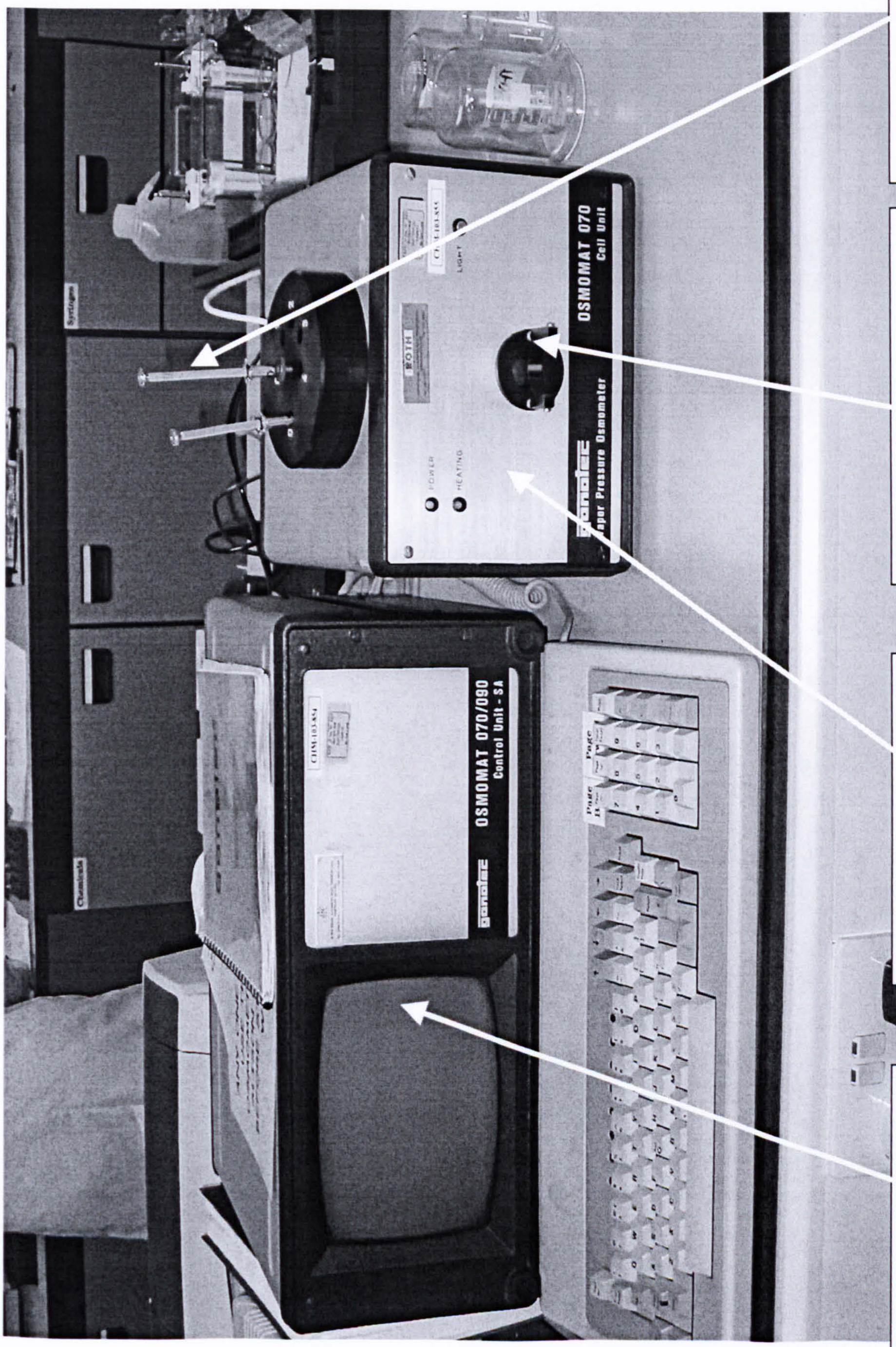
[121] M. W. F. Nielen, F. A. Buijtenhuijs, *Anal. Chem.* 1999, *71*, 1809.

17. Appendix A: Photographs of equipment

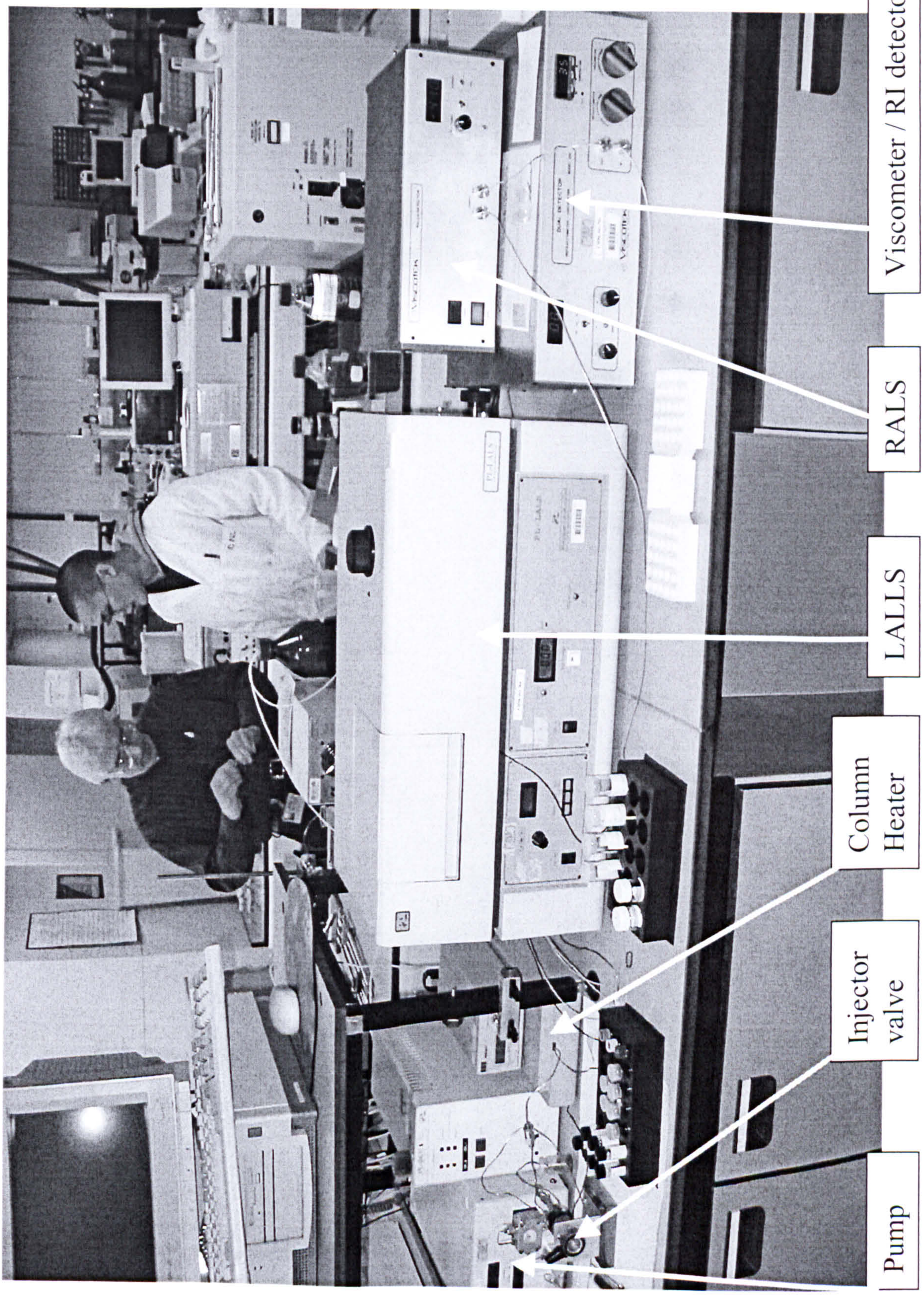
Radley's 12 station reaction Carousel



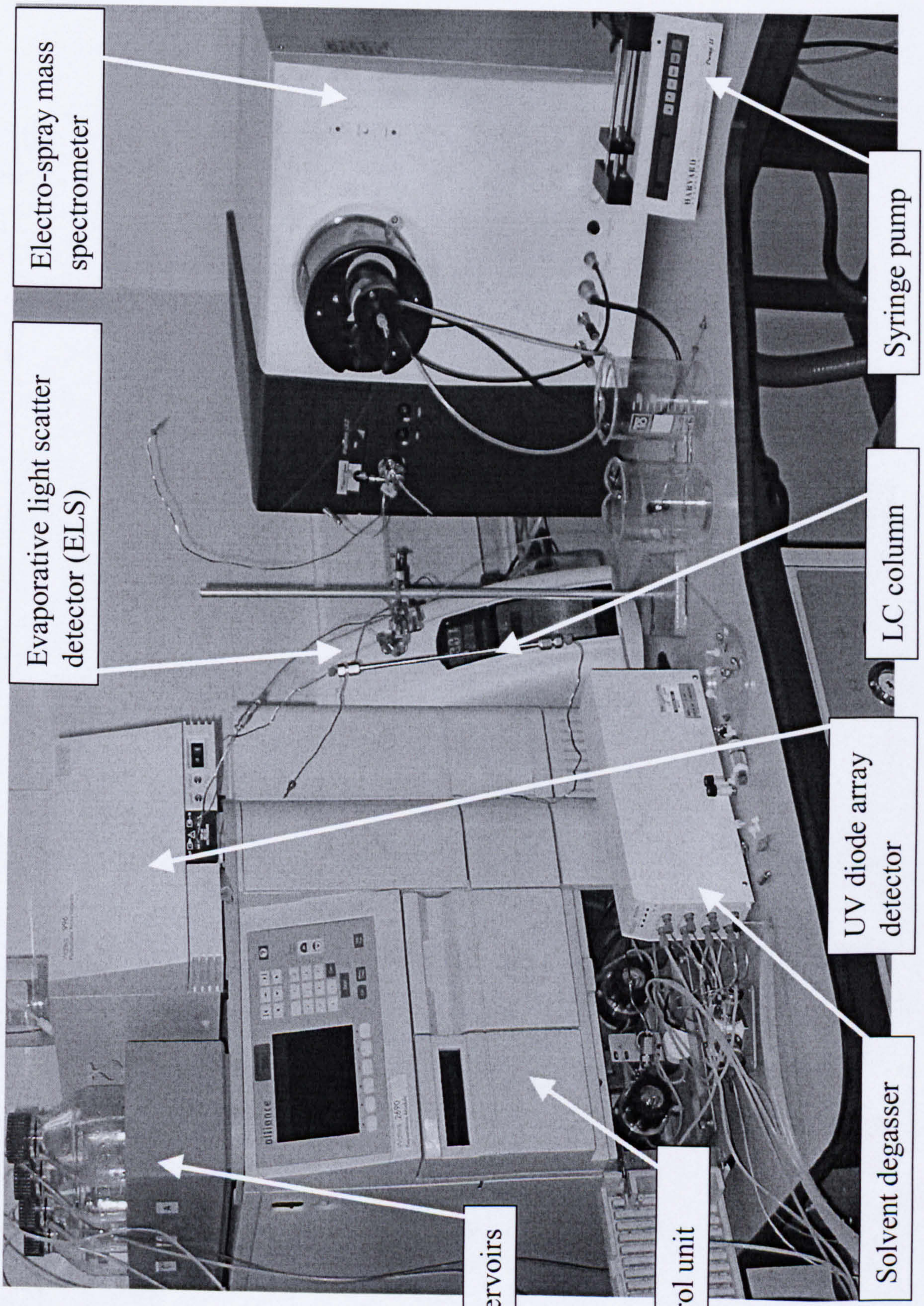
Vapour pressure osmometer



Triple detector SEC system



LCMS System


Electro-spray mass spectrometer
Evaporative light scatter detector (ELS)
LC column
Syringe pump
UV diode array detector
Solvent reservoirs
HPLC control unit
Solvent degasser