CRANFIELD UNIVERSITY

LUIS MIGUEL GARCIA CON

DORMANT RADICAL TECHNOLOGY
SYNTHESIS OF MATERIALS AND POTENTIAL APPLICATIONS

CRANFIELD BIOTECHNOLOGY CENTRE

PhD
Academic Year: 2011 - 2012

Supervisor: Dr. Michael J. Whitcombe
Prof. Sergey A. Piletsky

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This thesis is submitted in partial fulfilment of the requirements for the degree of PhD

ABSTRACT

This research was focused on the study of the polymer dormant radical systems, species containing free radical structures that have longer lifetimes and greater stability than radicals in general.

In order to understand the nature and reactivity of the dormant radicals, polymeric systems capable of producing dormant free radicals were synthesised.

In addition, the use of these novel polymeric materials in a range of applications were studied. Those applications exploited the nature of the dormant radical groups and included controlled modifications in the polymeric structure, heterogeneous catalysis and chromatographic separations.

Keywords:

Dithiocarbamates, polymers, macrocycles, flexible cross-linking, chiral resolution.

"Chemists are a strange class of mortals,

impelled by an almost maniacal impulse to seek

their pleasures amongst smoke and vapour,

soot and flames, poisons and poverty,

yet amongst all these evils I seem to live

so sweetly that I would rather die than

change places with the King of Persia".

Johann Joachim Becher

***Physica subterranea* (1667)**

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Symbols:

°C	Celsius degree
α	Separation factors
µ	Micro
Å	Angstrom
Da	Dalton, mass
g	Gram, mass
h	Hour, time
Hz	Hertz, frequency
J	Joule, energy
K	Kelvin
κ	Retention factor
L	Litre, volume
M	Molar, concentration
m	Metre, length
min	Minute, time
mol	Mole, amount
s	Second, time
t	Time
V	Volt, electric potential
W	Watt, power

Abbreviations:

3D	Three dimensional
ACN	Acetonitrile
AIBN	2,2’-Azobisisobutyronitrile
ap	Antiperiplanar
aq	Aqueous
ATRP	Atom Transfer Radical Polymerisations
AU	Arbitrary units

Auto-Poly(BBVC)	Auto-poly(benzyl N-butyl-N-(4-vinylbenzyl)dithiocarbamate)
bar	Bar, pressure
BB	Benzyl bromide
BBTD	N,N'-bis(4-bibenzyl)-N,N'-dibutyldithiuram disulphide
BDD	Benzyl-N,N-diethyldithiocarbamate
BET	Brunauer, Emmett and Teller theory
BBVC	Benzyl N-butyl-N(4-vinylbenzyl)dithiocarbamate
BEDC	Benzyl N,N'-bis(ethyl)dithiocarbamate
S-BPVD	(S)-Benzyl 1-phenylethyl(4-vinylbenzyl)dithiocarbamate
Branched poly(TMSPMA-BVPD)]	poly(3-(trimethoxysilyl)propyl methacrylate-*co*-(S)-Benzyl 1-phenylethyl(4-vinylbenzyl)dithiocarbamate
CD	Carbon disulphide
$CDCl_3$	Deuterated chloroform
CU	Cranfield University
DC	Degree of cross-linking
DBE	1,2-Dibromoethane
De-cross-Poly(BBVC)	De-cross-linked polymer from the auto-poly(benzyl N-butyl-N-(4-vinylbenzyl)dithiocarbamate)
DTC	Dithiocarbamate
DMSO	Dimethylsulfoxide
DMSO-d_6	Deuterated dimethylsulfoxide
EBDCs	Ethylenebisdithiocarbamates
EBVD	Ethylene bis(N-butyl-N-(4-vinylbenzyl)dithiocarbamate)
EGDMA	Ethylene glycol dimethacrylate
EPR	Electron Paramagnetic Resonance
GPC	Gel Permeation Chromatography
HPLC	High Performance Liquid Chromatography
I	Initiator
k_{tc}	Carbon-carbon radical termination rate constant
k_{ts}	Carbon dithiocarbamyl radical termination rate constant
M	Molar mass of a polymer
M_0	Molar mass of a repeat unit within a polymer
MA	Methacrylic acid
MMA	Methyl methacrylate

MBVC	Methyl N-butyl-N-(4-vinylbenzyl)dithiocarbamate
MS	Mass spectrometry
N_i	Number of molecules having M_i as molecular mass
NBA	n-Butylamine
^{1}H NMR	Proton Nuclear Magnetic Resonance
^{13}C NMR	Carbon Nuclear Magnetic Resonance
NBVA	N-(4-vinylbenzyl)butan-1-amine
o.d.	Outside diameter
Poly(BBVC)	Poly(benzyl N-butyl-N-(4-vinylbenzyl)dithiocarbamate)
Poly(EGDMA)	Poly(Ethylene glycol dimethacrylate)
Poly(EGDMA-*co*-BBTD)	Poly(ethylene glycol dimethacrylate-*co*-N,N'-bis(4-bibenzyl)-N,N'-dibutyldithiuram disulphide
Poly(EGDMA-*co*-BBVC)	Poly(ethylene glycol dimethacrylate-*co*-Benzyl N-butyl-N-(4-vinylbenzyl)dithiocarbamate)
PTFE	Polytetrafluoroethylene
PVC	Polyvinyl chloride
RF	Refractive index
R.T.	Room temperature
Rf	Retention factor
RAFT	Reversible Addition-fragmentation Transfer polymerisation
sp	Synperiplanar
St	Styrene
TEA	Triethylamine
TEMPO	(2,2,6,6-Tetramethylpiperidin-1-yl)oxyl
TETD	Tetraethylthiuram disulphide
THF	Tetrahydrofuran
TLC	Thin Layer Chromatography
Toluene-d_8	Deuterated toluene
TMSPMA	Poly(3-(trimethoxysilyl)propyl methacrylate
UV	Ultraviolet
VBC	4-Vinylbenzylchloride
VBDC	4-vinylbenzyl N,N’-diethyldithiocarbamate
S-VBPE	(S)-N-(4-vinylbenzyl)1-phenyl-ethanamine
x	Degree of polymerisation

1 LITERATURE REVIEW

1.1 Introduction

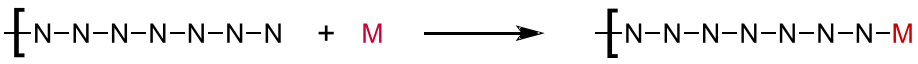
This thesis presents a study of dormant radicals, involving the design and synthesis of a series of monomers and polymers containing functional groups capable of generating such species under controlled conditions. The behaviour and interaction of these dormant radicals with other radicals and functionalities was studied.

This chapter contains the theoretical background that the reader needs to know to understand the work included in the following chapters.

1.2 Polymers and polymerisation

Polymers surround the world in which we live, in natural forms, such as DNA or proteins, and in man-made forms such as nylon or polystyrene. The polymers are used to provide clothing, decoration, tools, weapons, construction materials, and advances in the science have allowed the synthesis of new polymers that can offer new, exciting and complex applications.

A polymer is a substance composed of large molecules called macromolecules. These macromolecules have high molecular weights and their structures are formed by small repeating units with low molecular weights. These units are derived from molecules called monomers which can undergo polymerisation and then contribute their constituent units to the structure of the macromolecule. In that process, chemical reactions take place and the units are linked together, through the formation of covalent bonds (**Scheme 1-1**). The macromolecules can be linear in nature, or consist of a branched structure or a three-dimensional network and are referred to as a polymer (**Figure 1-1**). The size of the chains formed in any polymerisation process will depend on parameters such as the temperature and the reaction time, the concentration of monomer, etc., and it is their long chain nature which sets polymers apart from other materials and gives rise to their characteristic properties.



Scheme 1-1: A monomer (*M*) contributing with a unit (*N*) to a macromolecule in a polymerisation process

In polymer chemistry variations in the structure give rise to major differences in properties. Linear and branched polymers will be soluble in their respective solvents at certain temperatures, while network polymers do not melt and will not dissolve in any solvent, though they may swell considerably in compatible solvents. The cross-link density is important too, with low cross-link densities the product will be a flexible elastomer because the number of bonds between chains is not high and the structure retains some degree of mobility, whereas rigid materials are formed when the cross-link density is high, since the number of bonds between chains are large and they cannot move in any direction.

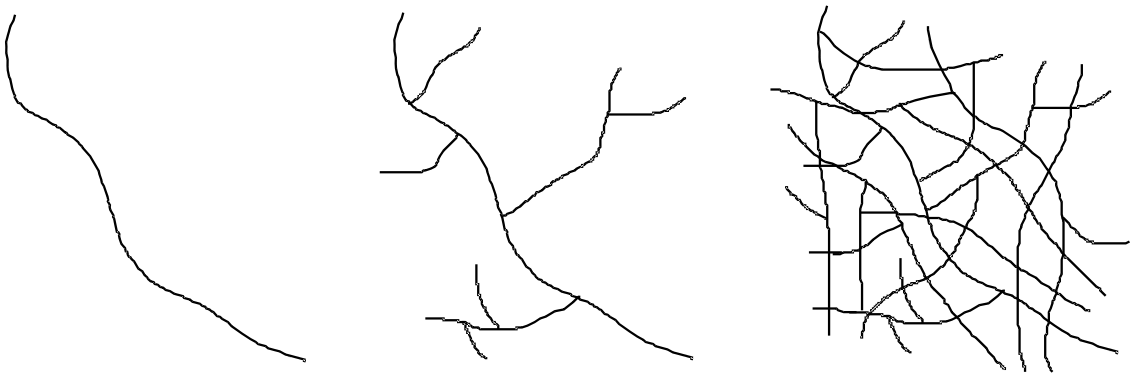


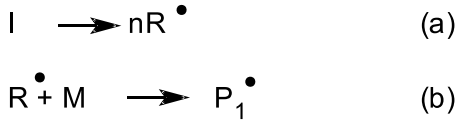
Figure 1-1: Different types of polymers: linear, branched and network (Young & Lovell, 1991a):

1.3 Free radical polymerisation

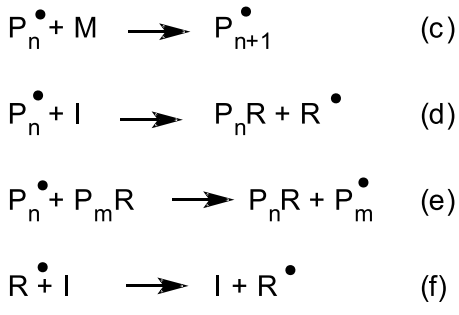
There are several ways to create a polymer from a monomer but at this point the free-radical polymerisation will be introduced; it will be the first step for more advanced techniques that will be presented later. In an old method of

classification (Svec & Fréchet, 1996) free-radical polymerisation is an addition polymerisation, as the polymers created have repeated units which have identical molecular formulae to those of the monomers from which they are formed and there is no generation of by-products created when monomer molecules are bonded to the growing chain. The chemical composition of the final chain is the result of addition of the chemical compositions of its constituent monomers.

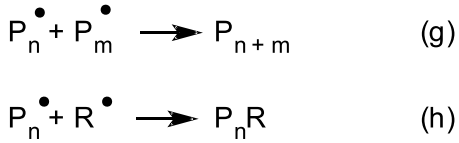
Initation



Propagation



Termination



Scheme 1-2: The three stages of the free radical polymerisation process

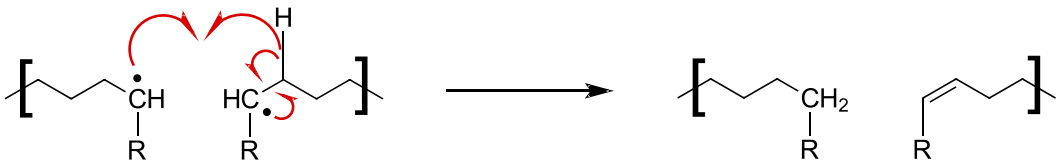
A better basis for classification is provided by considering the underlying polymerisation mechanism. In this particular case the process is known as chain-growth polymerisation because the polymer chain grows only by reaction of monomer with a terminal free-radical reactive site on the growing chain

(**Scheme 1-2**). Once the process is finished the partially polymerised mixture will consist of high molar mass polymer and unchanged monomer. This process usually requires an initial reaction between the monomer and an initiator to start the growth of the chain. After every addition of monomer the active centre is transferred to the newly-created chain end. The reaction can be divided into three distinct stages: initiation, propagation and termination (Young & Lovell, 1991a):

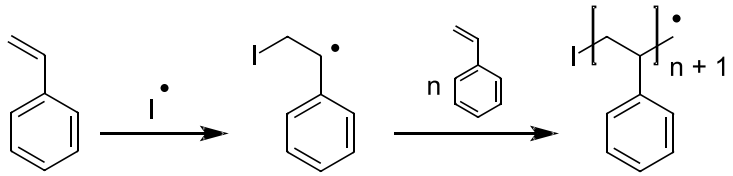
- The initiation, reaction **a** in the **Scheme 1-2**, involves the creation of the free-radical active centre and usually occurs in two steps. The first is the formation of the free radicals, $\mathbf{R}^{\bullet}$, derived from the decomposition of a low-molecular weight compound called the initiator, **I**, and the second is the addition of one of these free radicals to a molecule of monomer, **M**, reaction **b**. An active centre is created when a free radical attacks a molecule of monomer but not all the radicals formed from the initiator are destined to react with molecules of monomers; some of them are lost in side reactions such as recombination or reactions with the solvents leading to the formation of stable compounds. Side reactions of this sort reduce the rate of polymerisation because the concentration of active centres is decreased.
- The propagation involves growth of the polymer chain by rapid sequential addition of monomer to the active centre. The time required for each monomer addition typically is of the order of a millisecond thus several thousand additions can take place within a few seconds. Although the reactions **d** and **e** contribute to the propagation step, they result in termination of growth of a polymerising chain. They are more exactly called chain transfer reactions because the chain radical, $\mathbf{P_n}^{\bullet}$, abstracts a hydrogen atom or a group of atoms, **R**, from another molecule (initiator, solvent, polymer chain) to yield a macromolecule without the capacity to grow, $\mathbf{P_nR}$, and a new radical which can react with a molecule of monomer to initiate the growth of a new chain, $\mathbf{R}^{\bullet}$ & $\mathbf{P_n}$. The nature of the new radicals depends whether the chain transfer reaction includes a molecule of initiator **I**, solvent or a polymer chain, $\mathbf{P_mR}$. If the chain

transfer is to an initiator, polymer chain will be shorter than expected; if it is to a solvent, the polymer chain will have a different end group than the other chains; if it is to a polymer chain it could result in the formation of branched polymer molecules. The chain transfer reactions often are responsible for a significant fraction of the chain ends in the polymer and, if this is seen as undesirable, solvents, initiators and secondary molecules must be chosen that have low or negligible chain transfer constants. Compounds with high transfer constants (such as mercaptans, sulphur based molecules (Frank *et al.*, 1948)) cannot be used as initiators or solvents for polymerisation but could be employed as regulators at low concentrations to control the polymerisation reaction by lowering the molar mass of the polymer product.

- Termination describes processes that lead to the destruction of active centres resulting in cessation of growth of the polymer chain. The most typical termination mechanism is the bimolecular reaction **g** between two growing chains, giving rise to a single polymer molecule (radical recombination). A related mechanism is primary radical termination **h** in which the chain radical reacts with a free radical from one molecule of initiator, $\mathbf{R^{\bullet}}$. There is another process included in the termination, the disproportionation, in which a hydrogen atom from one growing chain can be abstracted by another growing chain. Two polymeric chains are created, one with a saturated end and the other with a double bond. Both terminations occur depending on the conditions of the polymerisation they will have different extents.



Scheme 1-3: Disproportionation, a hydrogen atom from one growing chain is abstracted by another growing chain



Scheme 1-4: Synthesis of polystyrene from styrene by addition of an initiating radical (R•)

The general chemistry associated with each stage of the free radical polymerisation is well described by considering vinyl polymerisation. In vinyl polymerisation the process starts by opening the double bond using the radicals derived from the decomposition of an initiator molecule and the whole process occurs without the elimination of any part of the molecule (Mishra & Yagci, 1998). An example of this is represented in the following **Scheme 1-4**, in which the molecules of styrene are joined together until the polymer is created. The level of thermally activated polymerisation of styrene without an initiator below 100°C is negligible compared with that performed using an initiator (Wünchs, 2000).

$$x = \frac{M}{M_0}$$

Equation 1-1: Degree of Polymerisation

1.4 Size of the polymers

As it is virtually impossible that every chain formed will have the same number of repeat units or monomers, the polymer will have groups of macromolecules of different size, therefore of different molar mass, hence the concept of *average molar mass*. The molar mass (M) of a polymer is the mass of 1 mole of the material and is quoted in units of g•mol-1. The degree of polymerisation (x, **Equation 1-1)**)(Young & Lovell, 1991b) is related to the molar mass of

homopolymers because it is the number of repeat units in an average polymer chain. M_0 is the molar mass of the repeat unit. The groups of macromolecules of different size will have different molar masses, therefore there will be a distribution of molar mass (**Figure 1-2**) in a typical sample of a polymer and the term average molar mass will be used.

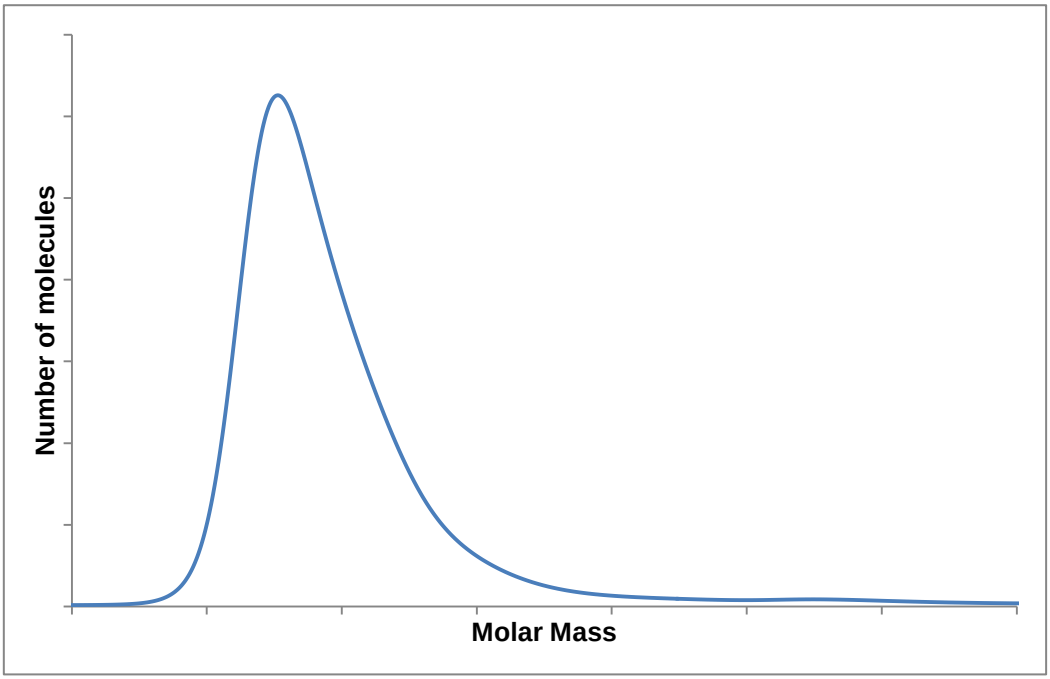


Figure 1-2: Typical molar mass distribution curve from the analysis of a polymeric mixture

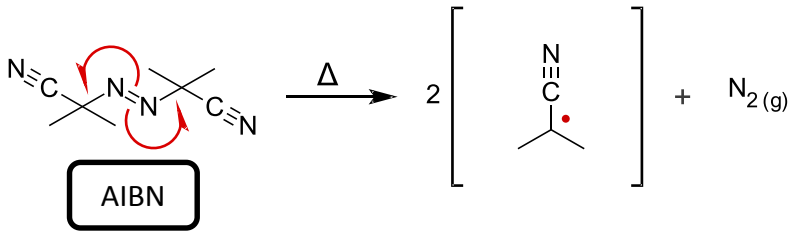
1.5 Degree of cross-linking

The degree of cross-linking (DC) is a measure of how rigid the polymer network is and is defined as the number of junction points per monomer in the polymer (Young & Lovell, 1991c).

1.6 Initiators

Radical initiators are molecules with one or more weak bonds with bond dissociation energies around 100-200 KJ•mol-1 (Denisov *et al.*, 2003). When

the temperature is high enough, the initiator decomposes with homolysis of the weakest bond (reaction a in the **Scheme 1-2**) and produces free radicals that can initiate a polymerisation. One of the most typical sorts of initiators is the azo compounds and within this family of compounds, the 2.2'-azobisisobutyronitrile (AIBN) (**Scheme 1-4**) is a typical example. The azo linkages in this molecule undergo thermolysis in the convenient temperature range of 50-100ºC (Young & Lovell, 1991d) forming alkyl radicals by homolytic scission and liberating nitrogen (**Scheme 1-5**). It can also serve as a photoinitiator under the influence of near UV radiation which is absorbed leading to the same dissociation into radicals as in the thermolysis.



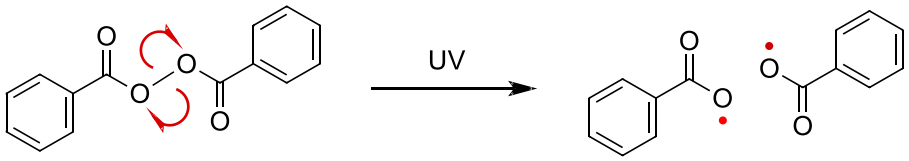
Scheme 1-5: Thermal decomposition of the initiator 2.2'-azobisisobutyronitrile (AIBN) generating two 2-cyanopropyl radicals and nitrogen gas (Young & Lovell, 1991d)

1.6.1 Photoinitiators

The photopolymerisation is a process in which a monomer is polymerised by a free radical reaction initiated by electromagnetic radiation. The absorption of photon energy from electromagnetic radiation by the initiator leads to an excited state of the molecule: the outermost electron orbitals gain energy and electrons are elevated from their lowest energy state to a higher state (Osburn & Morris, 2003). Therefore, several physical and chemical reactions will occur to release this excess energy and return the species to its ground state; one such process being bond cleavage generating free radicals (**Scheme 1-6**) that will initiate polymerisation of the monomer.

The essential molecule for photopolymerisation is the photoinitiator: a compound that absorbs energy from photons to form reactive species: free radicals. It is essential that the molecule of photoinitiator possesses a bond with dissociation energy lower than the excitation energy of the reactive excited state, on one hand, and sufficiently high, on the other hand, to provide thermal stability (Gruber, 1992).

The use of light, rather than heat, to drive the reactions could lead to a variety of advantages, including solvent-free reactions, high reaction rates at low temperatures, low energy input, and chemical versatility since a wide variety of polymers can be polymerised photochemically.



Scheme 1-6: Photochemical decomposition of the photoinitiator benzoyl peroxide generating two radicals; the mechanism continues generating two phenyl radicals and two molecules carbon dioxide (Rabek, 1995)

The reaction vessel in photochemical reactions is an important issue. Borosilicate glass could be a fairly good choice since transmits more of the UV light than the ordinary glass. A 5-mm thickness transmits about 30 per cent of the incident 320-nm and about 5 per cent of 300-nm light (Demis, 1994).

1.7 Radicals

The radicals were already discussed in the section about initiators (see **Section 1.6**) and, although initiation of polymerisation is their main role in polymer chemistry, they can also be important in other areas.

Radicals are very unstable and highly reactive molecular fragments with unpaired electron/s. They will react with any atom nearby to gain some stability

so they are not selective in their reactions. The radicals are formed upon homolytic cleavage of a covalent bond between two atoms (**Scheme 1-7**) and that cleavage requires certain amount energy, as was stated above (see **Section 1.6**).

Scheme 1-7: Homolytic cleavage of chlorine molecule to generate two chlorine radicals

They are used widely in catalysed process, especially when metal species are involved (Q.-Y. Chen *et al.*, 1988; Ryu *et al.*, 2002; Ford & Jahn, 2009), and also in synthesis (K. Chen *et al.*, 2008). Because of the problems derived from their high reactivity, some attempts to control them were performed (Quiclet-Sire & Zard, 1997).

1.7.1 Dormant radicals

Not all the radicals are extremely reactive, there is a group of molecular fragments that contain a radical and that can be considered stable. The existence of the first stable radical, the triphenylmethyl radical (**Figure 1-3**), was reported by Gomberg in 1900 and that event is considered as the starting point of organic free radical chemistry (Gomberg, 1900). The compound reacted with several species in solution so the definition of stable was suggested to be changed for persistent (Hicks, 2007).

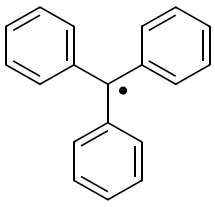


Figure 1-3: Triphenylmethyl radical, a persistent radicalary structure

The triphenylmethyl radical has the characteristic of having one carbon atom that only uses 3 of the 4 valences, and the fourth one is not shared with any other atom so the valence remains dormant (Gomberg, 1932). After the synthesis of the triphenylmethyl radical, several derivatives of that structure were synthesised (Bowden *et al.*, 1939), including different functionalities to the aromatic rings, and those compounds were analysed with no other purpose than explore in the nature and stability of those species. The stable free radical field did not receive much attention for almost 30 years. In the 1960's, with compounds like (2,2,6,6-Tetramethylpiperidin-1-yl)oxyl (TEMPO) (**Figure 1-4**), the free radicals started to gain the attention that they had before. TEMPO is probably the best known nitroxide dormant radical and its stability is due the nitrogen which donates part of its electron density in the p-orbitals to the free radical (oxygen atom)(Al-Malaika, 1997).

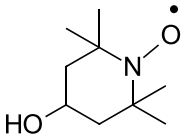


Figure 1-4: Another persistent radical: (2,2,6,6-Tetramethylpiperidin-1-yl)oxyl, also called TEMPO

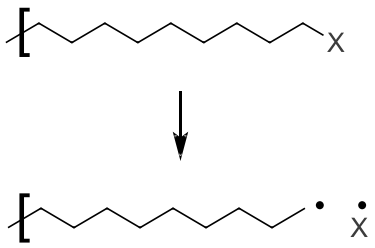
TEMPO was widely used for its redox capabilities in organic-based battery applications (Kunz & Wolf, 2011), as a radical-trap in process like radical cascade reactions (Barriga, 2001), and as a catalyst in the oxidation of several functionalities (Bolm & Fey, 1999).

TEMPO also gained a role within the polymerisation process that began to be called “living” radical polymerisation (Craig J. Hawker, 1997). The great importance of “living” radical polymerisations lies in their advantages over classic polymerisation protocols. Polymer chemists started to look for new molecules that could act as agents in “living” radical polymerisations and more

substances that could generate dormant radicals were discovered, e.g. dithiocarbamates.

1.8 “Living” radical polymerisation

Free radical polymerisation is a very useful method for the preparation of large-scale polymers, although this process still has some problems that remain to be resolved. The control of the structure of the polymer created is lost due the fact that the radicals are very reactive species; they will react with each other creating a stable covalent bond that cannot be broken thus the growth of the chain is completely stopped. That is the reason why the synthesis of polymers through the “living” radical polymerisation has gained special importance, because the formation of reacting centres is kept under control. Although the termination reaction between radicals also happens in this case, the process is reversible and some of the created bonds between them can be broken (**Scheme 1-8**), again generating two radicals, therefore the ability of the growing polymer chain to terminate has been removed from the system (Otsu, 2000).



Scheme 1-8: Deprotection of active site in the polymer chain

The chain termination reaction is almost absent in this type of polymerisation; it could be said that there is no termination and there is instead a protection and deprotection of the active sites of the growing chain. Also the rate of chain initiation is also much larger than the rate of chain propagation. It can be decided, by selecting the initiator concentration and the time of reaction, what the average molar mass of the synthesised polymer will be. Thus the necessary

control over the design the structure of the polymers is achieved and it is possible to prevent the synthesis of polymers with broad molar mass distributions. The “living” radical polymerisation has a great versatility with a wide range of monomers (Chiefari *et al.*, 1998), apart from control of the molar mass and the low polydispersities of the resulting polymers, it has a great potential in the preparation of tailor-made polymer products.

1.9 Iniferters

Iniferters are molecules designed to act as initiators, transfer agents and terminators in “living” radical polymerisations (Otsu, 2000). Initially they were created to work as photo-initiators and had very specific structures, e.g. tetraethylthiuram disulphide (TETD) or dibenzoyl sulphide (Krzysztof, 2005)(**Figure 1-5**), but more recently a wider variety of different molecules have been reported that function as either thermal or photochemical iniferters (T. Sato *et al*., 1983; Reghunadhan Nair & Clouet, 1990; Otsu, 2000). The most important factor is that those molecules are initiators that have very high reactivity for the chain transfer reaction to the initiators and/or primary radical termination, avoiding ordinary bimolecular terminations that made the polymerisation process uncontrolled.

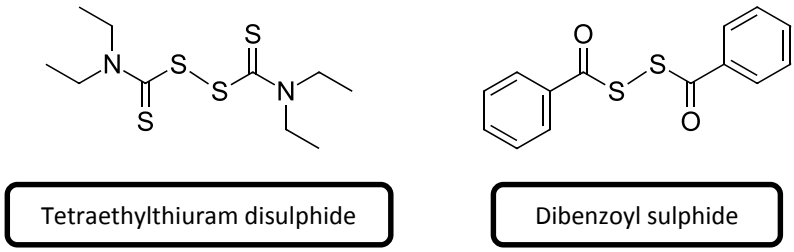


Figure 1-5: Tetraethylthiuram disulphide and dibenzoyl sulphide, typical photo-iniferters

Although the iniferter reaction demonstrates some of the characteristics of a “living” polymerisation there are also a number of deficiencies. The reaction lacked the true living character that was expected and also some possible side

reactions that affected the living character (Lambrinos *et al.*, 1990). Furthermore the photoiniferters are very slow at initiating new chains throughout the course of the reaction (Lambrinos *et al.*, 1990), so the polydispersities are relatively large.

1.9.1 Dithiocarbamates as iniferters

The dithiocarbamates (DTCs) like Benzyl-N,N-diethyldithiocarbamate (BDD)(**Figure 1-6**) have been widely used in “living” free radical polymerisation (Otsu, 2000).

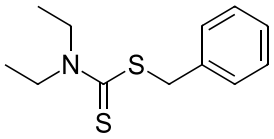
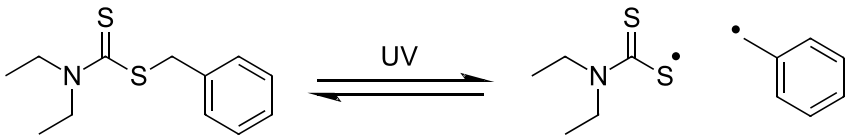


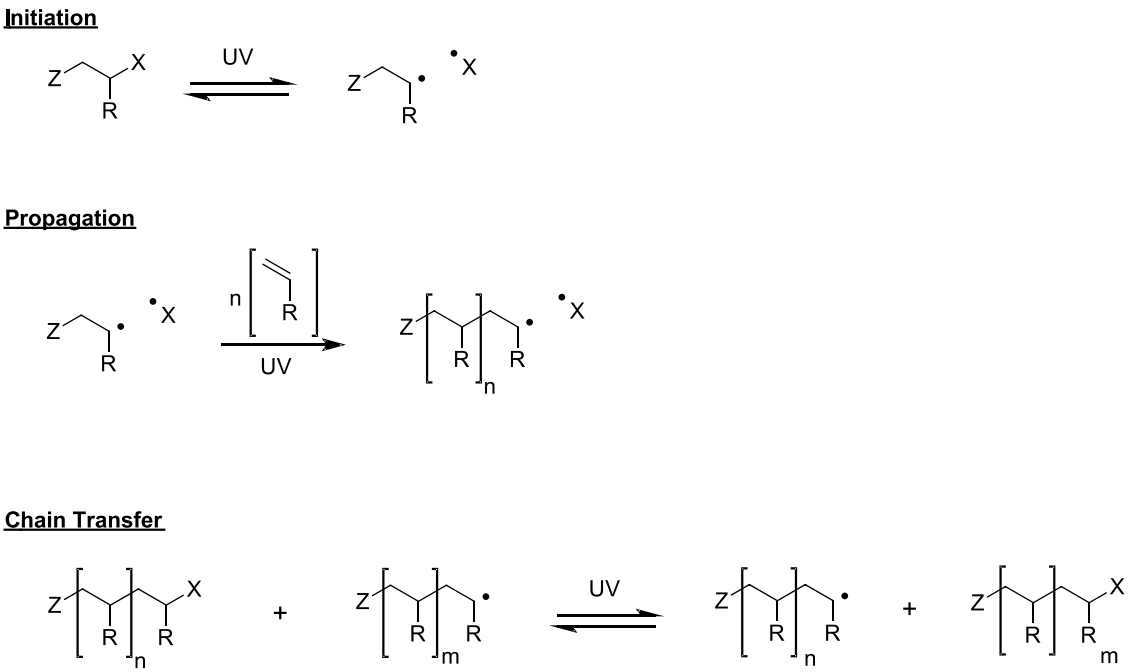
Figure 1-6: Benzyl-N,N-diethyldithiocarbamate (BDD), a dithiocarbamate and an iniferter

Iniferter polymerisations using dithiocarbamate esters are significantly different from and slower than conventional radical polymerisations; the mechanism is shown in **Scheme 1-10**. The iniferter absorbs UV light and the C–S bond is homolytically cleaved (**Scheme 1-9**) to generate a carbon-centred radical and a sulphur-based dithiocarbamyl radical (Dika Manga *et al.*, 1998). That dissociation seems to be reversible in molecules of similar structure (Nichols & Grant, 1983) because the radical concentration was found to be much lower than that of undissociated iniferter. The carbon radicals produced are extremely reactive and initiate the polymerisation by reacting with a monomer, while the dithiocarbamyl radical is relatively less reactive and does not participate significantly in initiating polymerisation (Otsu *et al*., 1995).



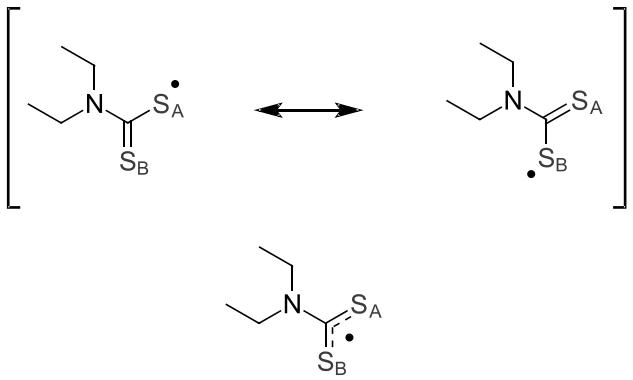
Scheme 1-9: Irradiation and generation of radicals in dithiocarbamates, a sulphur based radical and a carbon based radical are created

The unreactivity of the dithiocarbamyl radical relative to the carbon radical suggest a longer life for the former. That stability arises from the possibility of the resonance effects due the ability of the unpaired electron to delocalise onto both sulphur atoms (**Scheme 1-11**) (Nichols & Grant, 1983). Propagation occurs by addition of the double bonds of the monomers to the active centres. In the iniferter polymerisations, the carbon radicals constitute the active centres because the dithiocarbamyl radical is stable and relatively unreactive to propagation (Otsu *et al*., 1995).



Scheme 1-10: Free radical iniferter process ((X represents the dithiocarbamyl part of the molecule)

The dithiocarbamyl radicals are mainly radical terminators and propagation by these radicals is negligible (Lambrinos *et al.*, 1990) and they do not initiate polymerisation, so can be considered unreactive (dormant) relative to the carbon radicals (S. R. Turner & Blevins, 1990). The carbon-carbon radical termination rate constant (k_{tc}) drops to a value lower than the carbon dithiocarbamyl radical termination rate constant (k_{ts}) (Kannurpatti *et al.*, 1996). The dithiocarbamyl radical is a non-reactive small radical which does not initiate, but readily undergoes a primary radical termination with a carbon radical to give the identical C–S with an “n” number of molecules of monomer inside. Since the chain transfer reaction of the carbon macroradical to the C–S bond would also give a similar carbon macroradical and C–S bond, this reaction does not affect this model. Therefore, if the polymerisation proceeds via the repetition of dissociation at the C–S bond, addition of the monomers to the carbon macroradical and primary radical termination with dithiocarbamyl radical and/or chain transfer reaction of the carbon macroradical to one C–S bond, such polymerisation may proceed via a “living” radical mechanism and the process is controlled. The process could be interpreted as the insertion of monomers into the C–S bond.



Scheme 1-11: Delocalisation of the unpaired electron onto sulphur atoms

If the end groups of polymers obtained by radical polymerisation using iniferters still have an iniferter function, the radical polymerisation is expected to proceed

via a “living” radical mechanism; the macroradical formed is as effective as the carbon-centred radical derived from the iniferter at propagating polymerisation (S. R. Turner & Blevins, 1990) so the process will continue as long the irradiation continues and the polymerisation is therefore controlled. Details of the mechanism were proposed elsewhere (Kannurpatti *et al.*, 1996).

1.9.2 A different kind of iniferters: inimers.

The typical iniferter with the structure is represented by BDD (**Figure 1-6**). There is one type of iniferter that, apart from their functionality that could undergo photochemical cleavage of a bond to generate radicals, it also has a site capable of participating in a polymerisation. One example can be found in the compound 4-vinylbenzyl N,N-diethyldithiocarbamate (VBDC) (Otsu *et al.*, 1986)(**Figure 1-7**).

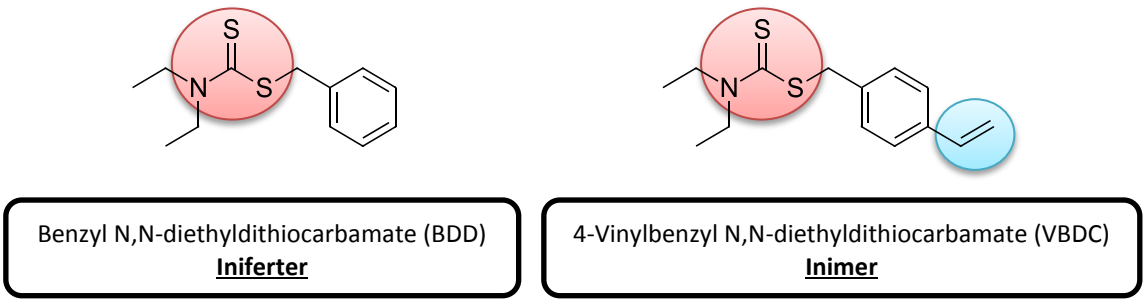
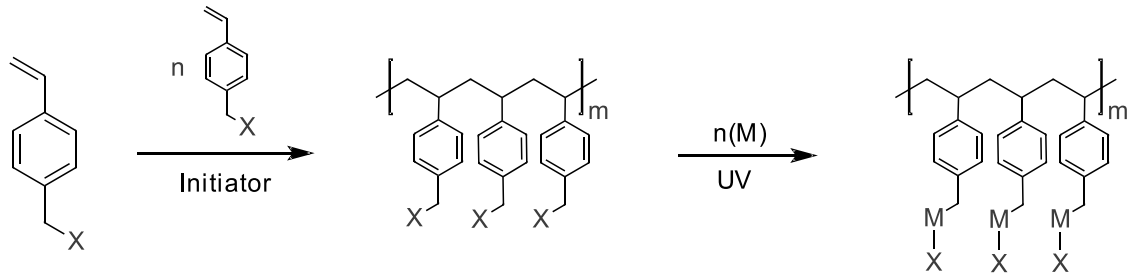


Figure 1-7: Iniferter with dithiocarbamate group (left, red circle) and inimer with dithiocarbamate group (right, red circle) plus double bond (right, blue circle)

This molecule was called an initiator-monomer or inimer because it has iniferter and monomer properties due to the presence of both dithiocarbamate ester functionality and a polymerisable double bond in its structure. These molecules are used successively as both monomer and components of macro-iniferters (macromolecules with iniferter abilities) and they were used to obtain graft polymers as shown in the **Scheme 1-12** (X represents the dithiocarbamyl part of the molecule).

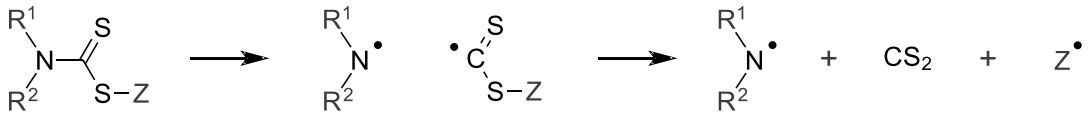


Scheme 1-12: Graft polymerisation of monomer M to poly(VBDC)

The important aspect of this approach is that the homopolymer, copolymer and macro-iniferter were found to act as excellent photoiniferters of living radical polymerisation in a homogeneous system to give graft copolymers. The possibilities for these sorts of compounds are numerous due to the availability of the (Yamase *et al.*, 1970) double bond, allowing attachment to surfaces or to other molecules and with the dithiocarbamate groups acting as iniferters in further polymerisation processes.

1.9.3 Limitations of dithiocarbamates as iniferters/inimers

In this process there is one disadvantage: a decomposition of the DTC occurs during the photo-initiation process with loss of the living nature of the chain end. This decomposition seems to increase linearly with the exposure time and the rate depends strongly upon the monomer used. For instance, TETD is expected to have a half-life of 20 days in the near UV (United States Environmental Protection Agency, 2001). A photochemical cleavage of the thiocarbonyl-nitrogen bond and subsequent elimination of CS_2 as the decomposition pathway (**Scheme 1-13**) were proposed (S. R. Turner & Blevins, 1990; Yamase *et al*., 1970). In another study (Valentine *et al.*, 1995) it was shown that diethyldithiocarbamates in neutral aqueous solution decompose to give CS_2 and the parent amine. In water, at pH7, TETD is expected to have a half-life of 2 days and in more alkaline solution hydrolysis would occur in a matter of hours (United States Environmental Protection Agency, 2001).



Scheme 1-13: Decomposition of the dithiocarbamate

The proposed mechanism for decomposition is through unimolecular cleavage once the DTC has captured a hydrogen atom via its sulphur atom radical (Joris *et al.*, 1970), the limiting step being the transfer of that hydrogen from sulphur to nitrogen (**Figure 1-8**).

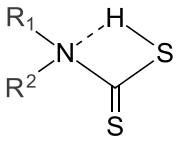


Figure 1-8: Interaction between nitrogen and hydrogen

1.9.4 General applications and toxicity of the dithiocarbamates

The DTCs and polymers containing DTC groups have many applications in a variety of fields. They have been studied because of their biological activities, such as TETD, known commercially as disulfiram, which is used in aversion therapy against chronic alcoholism (Bower *et al.*, 2005) and with a potential use in cancer therapies (D. Chen *et al.*, 2006). The common uses of the DTCs and DTC polymers in this field are as antiviral agents (Schreck *et al*., 1992; Krenn *et al*., 2005; Si *et al*., 2005), spin traps (Timoshin *et al.*, 2008), in the improvement of herbicides (Rogachev *et al.*, 1998), bactericides and antimicrobial agents (Chakraborty *et al.*, 1984; Baikenova *et al.*, 2004; Kaplancikli *et al.*, 2004), antitumor drugs (Scozzafava *et al.*, 2000), use of the antioxidant properties of these molecules against cancer cells (Moriyama-Gonda *et al.*, 2003) or as therapeutic agents for metal toxicity due to their great capability for chelating metals (Leyden & Luttrell, 1975; Tiwari & Bajpai, 2005). For their main

application, the DTCs have an important role in agriculture, being widely used as fungicides (e.g. propineb, zineb, maneb, mancozeb, ziram, thiram) because of their efficacy against a broad spectrum of fungi and their associated plant diseases. These compounds are also used in industry as lubricants (Lee *et al.*, 1999), antioxidants (Al-Malaiaka *et al.*, 1987; Hu *et al.*, 2007; Chakraborty & Scott, 1986; Chakraborty *et al.*, 1984) an oil-soluble catalyst for hydroprocessing heavy oils (Iwata *et al.*, 2001), up-grading heavy petroleum and in the liquefaction of coal (Watanabe *et al.*, 2002), decreasing the toxicity of PVC materials (Lakshmi & Jayakrishnan, 1998) as accelerators of the vulcanization process of rubber materials (Pudovik *et al*., 1988; Nieuwenhuizen *et al*., 1999) and as antimicrobial disinfectant (Arvanitis *et al.*, 2004). Because of their chelating properties, they are also used as scavengers in waste-water treatment (Wen *et al*., 1999; Garcia & Humeres, 2002; Todorovi *et al*., 2002), for the separation and purification of metal ions (Pişkin *et al.*, 1996), for preventing the corrosion due to water in steel structures (Schreck *et al.*, 1992), for analytical procedures as excellent reagents for the analysis of trace metals (Brenner *et al.*, 1997) and many other applications.

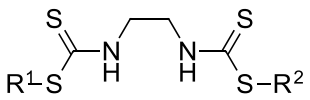


Figure 1-9: Generic structure for the ethylenebisdithiocarbamates (DADCs)

DTC fungicides are used worldwide (e.g. propineb, zineb, maneb, mancozeb, ziram, thiram) mainly due to their relatively low acute mammalian toxicity but that low toxicity could be questioned. The toxicological significance of the DTCs arises from the metabolite or degradation products (Various, 1988), known to be carcinogenic and teratogenic in laboratory animals although the studies in humans sometimes are contradictory (Houeto *et al.*, 1995; Struble *et al.*, 1999; Segovia *et al.*, 2002; K. Kimura *et al.*, 2005; Clementi *et al.*, 2007; Yokoyama, 2007). These main products of degradation for the dialkyldithiocarbamates

(DADCs) are carbon disulphide, dialkylthiocarbamic acid being formed as a free acid or as S-glucuronide conjugate, formaldehyde, sulphate, and dialkyl amine (Various, 1988). On the other hand the ethylenebisdithiocarbamates (EBDCs) (**Figure 1-9**) metabolize via different mechanisms, giving as the main products carbon disulphide, a few ethylene bisthiuram disulphides, hydrogen sulphide, ethylene bisthiocyanate, 1,2-diaminoethane, and ethylenethiourea (Houeto *et al.*, 1995; Cary *et al.*, 1999).

The mainly reason of the toxicity of the DTCs seems to be their high water solubility and their ability to release CS_2. The effects of the DTCs are disturbances of the nervous systems (Segovia *et al.*, 2002), mutagenic capacity (Agrawal *et al.*, 1997), affecting pregnancy outcome (Stoker *et al.*, 1996), and having a potential human genotoxicity and possible carcinogenicity (Tinkler *et al.*, 1998). On the other hand DTCs are suitable for the removal of metals from organisms but they also are able to alter redistribution, resulting in increased toxicity (Stefan *et al.*, 1995).

The conclusion is that although some experiments shows contradictorily results, it could be assured that the DTC-based compounds have demonstrated toxicity and must be manipulated with caution. That fact must be bore in mind when the use of these DTC based materials are directed to health care applications.

1.9.5 Synthesis of dithiocarbamates and thiuram disulphides

The synthesis of the DTCs is relatively simple and the most commonly used method involves the reaction of carbon disulphide with a large range of primary and secondary amines in the presence of an alkali metal hydroxide to generate the corresponding dithiocarbamate salt (Rudorf, 2007). However Najmedin Azizi (Azizi *et al*., 2006) created several dithiocarbamates in a “one-pot” reaction at room temperature, without solvent and in a relatively short period of time. There are more references to the synthesis of dithiocarbamate esters, involving the initial generation of the dithiocarbamate salt, its stabilisation and finally fixing the molecule by reaction with an alkyl halide, but they are very tedious, needing different reagents and solvents (Salvatore, Sahab, *et al*., 2001; Chaturvedi & Ray, 2006).

There is also the possibility of the synthesis of symmetrical dithiocarbamates (**Figure 1-10**) requiring heat and slow addition of reagents (Z. Yan *et al*., 2007) for their preparation.

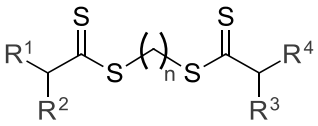


Figure 1-10: A dithiocarbamate with a symmetrical structure

Regarding the synthesis of the thiurams (**Figure 1-11**) the beginning of the procedure is similar to the synthesis of the DTC but once that specie is formed an oxidation is necessary to create the disulphide bond; that oxidation can be done with a different range of oxidants (Neelakantan, 1958; Song *et al.*, 2003; Akhond *et al.*, 2006). However the synthesis can be done in the same efficient, easy and one-pot way as in the synthesis of DTC esters (A. Patel & Mequanint, 2008). Although the use of iodine as oxidant in the synthesis of a thiuram disulphide-inimer could affect the polymerisable double bonds it was found that the iodine addition is not normally thermodynamically favourable (Vollhardt & Schore, 2002).

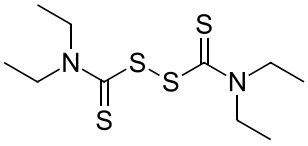
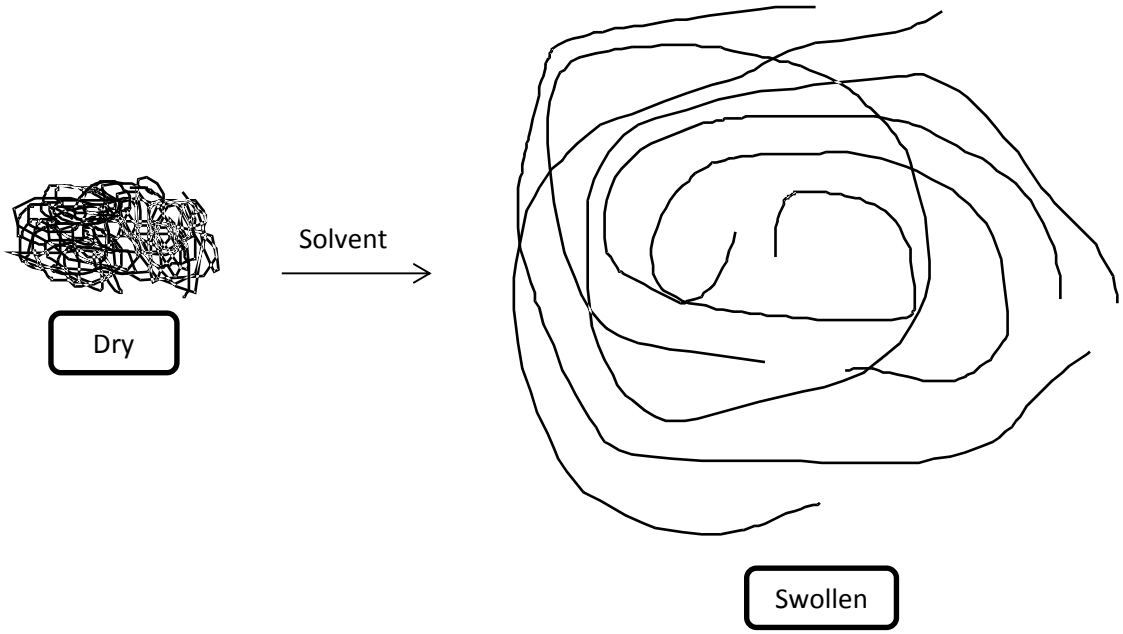


Figure 1-11: Tetraethylthiuram disulphide, a well-known thiuram

1.10 Swelling of polymers

The process of dissolving a polymer in a solvent is more complex than the solubilisation of a small molecule. It usually takes longer, it strongly depends on

the thermodynamics and on the chemical nature of the polymer (Kurata, 1982). First the macromolecules that comprise the polymer are in the form of an entanglement (Teegarden, 2004). To dissolve the polymer the solvent molecules should penetrate through the polymer and surround the macromolecules. At this stage the polymer swells. The mobility of the macromolecules will increase until the chains start to detach from the swollen polymer (Labarre *et al*., 2010).



Scheme 1-14: The mobility of the polymer chains increase when they are surrounded by molecules of solvent

That process only happens if the polymer is linear, but if the polymer is cross-linked and is forming a network, the chains are not able to gain enough mobility and the polymer will swell to a degree dictated by the thermodynamic interactions and the force exerted by distension of the network (Ferry, 1980). The swelling properties of polymers have found practical applications in the field of hygiene, being used as an adsorbent material in nappies, incontinence pads and in sanitary napkins. The use of polymers that swell many times their weight

with water allows these items to be made much thinner than those using cotton or paper as the adsorbent material. Another application is in agriculture, adding superabsorbent polymers to the soil so it can retain more water and favouring the growth of plants (Vancotthem *et al.*, 1991). These kind of polymers are also being used to coat cables and insulate them more effectively from water (Chatterjee & Gupta, 2002). Some polymers are able to change their ability to swell when the temperature or pH is modified. This can be used to induce movement that can be used in the preparation of “artificial muscles” (American chemical Society, 1994) and also has applications in therapeutic drug release (Jones, 2004).

1.11 Reactions housed by polymers

There is an interest in organic reactions in the solid phase, especially when one of the reactants is a macromolecule. These are termed polymer-supported reactions and they offer some advantages in comparison to traditional reaction systems. The main advantage is the easy separation of the products, particularly when the polymer is in the form of beads or it is a cross-linked polymer, since such materials are insoluble in all solvents (Parker, 1997). If the polymer is soluble it can be still be separated relatively easy using precipitation and filtration techniques, although those techniques will affect the purity of the products. For economic reasons another advantage is when polymers are used in heterogeneous catalysis, the solid support can be reused (Lindström, 2007).

1.12 Macrocycles

There is a growing interest in methods for making macrocyclic oligomers of commercially important polymers (Koji Ishizu & Kanno, 1996; Kubo *et al*., 1998; Kubo *et al*., 2002; Lepoittevin & Hémery, 2002), because these macrocyclic oligomers can be used for various processing technologies where the physical and chemical properties of the macrocyclic oligomers have advantages over the corresponding linear polymers. For instance it has been observed that the solubility of the macrocycles is higher than the linear polymers (Wood *et al.*, 1997; Bryant & Semlyen, 1997).

The synthesis of these species is not trivial. According to the Ruggli-Ziegler dilution principle, in the case of cyclization reactions, the intramolecular reaction is favoured over the intermolecular reaction by high dilution with an inert solvent (Reichardt & Welton, 2011). According to that principle, the dilution increases the chances of cyclization in step-growth polymerisation (Fawcett *et al.*, 1995) but the very diluted solutions allow the synthesis of only very small amounts of products.

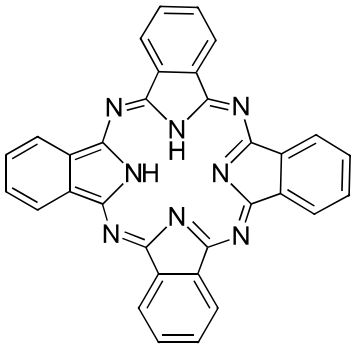


Figure 1-12: Phthalocyanine, a macrocyclic compound used widely as a dye

The macrocycles have been in use for several decades as dyes. Analogues of porphyrins such as the phthalocyanines (**Figure 1-12**) have been used as dyes and pigments since 1928 (Jiang *et al.*, 2010). There have many other uses, as for example the removal heavy metals from solutions (M Izatt *et al.*, 2011) and also as a part of rotaxanes, molecular architectures formed by a macrocycle captured in a dumbbell shaped molecule (Balzani *et al.*, 2000). These rotaxanes can be used, amongst other things, as molecular switches because the macrocycle can move across the dumbbell shaped molecule generating several stable structures. Different macrocycles have been also used as sensors, especially in anion recognition (Beer & Gale, 2001).

1.13 Hyper-branched polymers

The hyper-branched polymers are a type of polymer in which the branching is denser, with an intrinsic globular structure and with a high number of terminal

functional groups (England & Rimmer, 2010). Hyper-branched polymers have different behaviours to their linear or cross-linked counterparts made with the same monomers, and show properties typical of nanoparticles (K Ishizu & Mori, 2000) or micelles (Y. H. O. Kim & O. W. Webster, 1990). These hyper-branched polymers have an unexpected solubility, even compared with the linear analogues, because the hyper-branched structures (**Figure 1-13**) offer open and accessible cavities between branches where the solvent can be accommodated (Y. H. Kim, 1998).

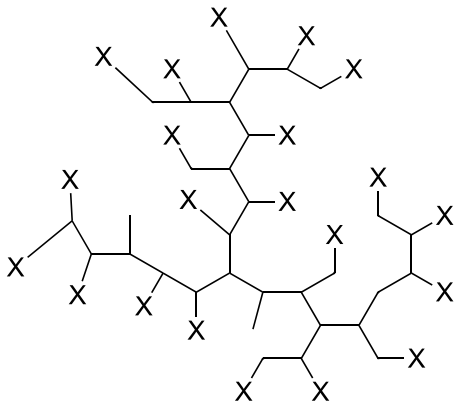
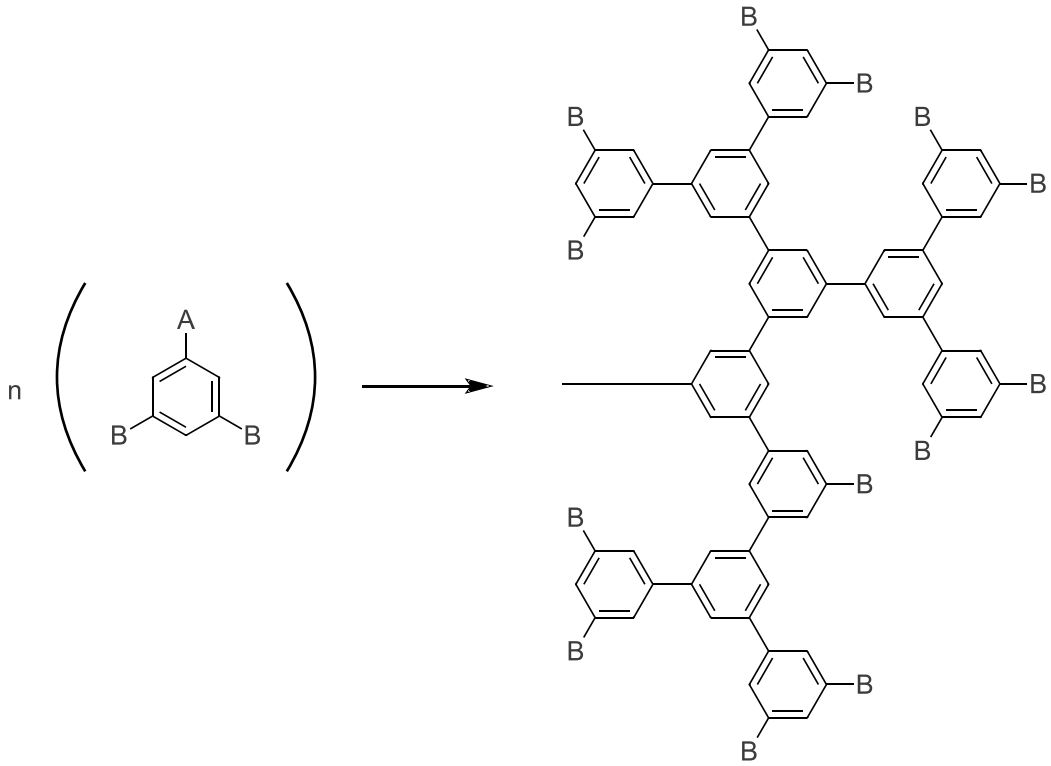


Figure 1-13: Hyper-branched polymer, with X as terminal groups

The size of these polymers is also an issue, hyperbranched polymers with molecular weights 5000-35000 were synthesised but these molecular weights determined by gel permeation chromatography (GPC) were found by Kim (Y. H. Kim, 1998) to be non-reproducible. These hyper-branched polymers have a random branched structure compared with dendrimers (Gao & D. Yan, 2004). One important advantage of these macromolecules is that they could be prepared rapidly and economically: in the early stages of the research of these materials the synthesis were just polycondensations (**Scheme 1-15**) of monomers with AB_x functionality where the A group of one molecule reacts with the B group of another molecule (Y. H. Kim, 1998) but soon new monomers (K Ishizu & Mori, 2000) and new ways of polymerisation, like a solid-supported

polymerisation (Bharathi & Moore, 1997), photopolymerisation (K Ishizu & Mori, 2000), or copolymerisation (K Ishizu & Mori, 2001; K Ishizu & Mori, 2002), were introduced.



Scheme 1-15: Polycondensation in the synthesis of a hyperbranched polymer

Regarding the applications, the large number of terminal functional groups (B in **Scheme 1-15**) allows the use of hyper-branched polymers as macroinitiators (Y. H. O. Kim & O. W. Webster, 1992). They are also used as a core for other polymers (F. Wang *et al.*, 1997), to increase the toughness in composites (Hedrick *et al*., 1997; K Ishizu & Ochi, 2006) and as drug-delivery systems (Roovers & Charleux, 1999).

1.13.1 Dithiocarbamates used in the synthesis of hyper-branched polymers

The possibility of synthesising hyper-branched polymers from dithiocarbamate based “inimers” has been studied since Otsu accidentally synthesised a hyper-branched polymer trying to produce a macromer (Otsu *et al*., 1986) from the inimer 4-vinylbenzyl N,N’-diethyldithiocarbamate (VBDC) (**Figure 1-14**).

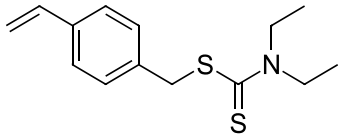
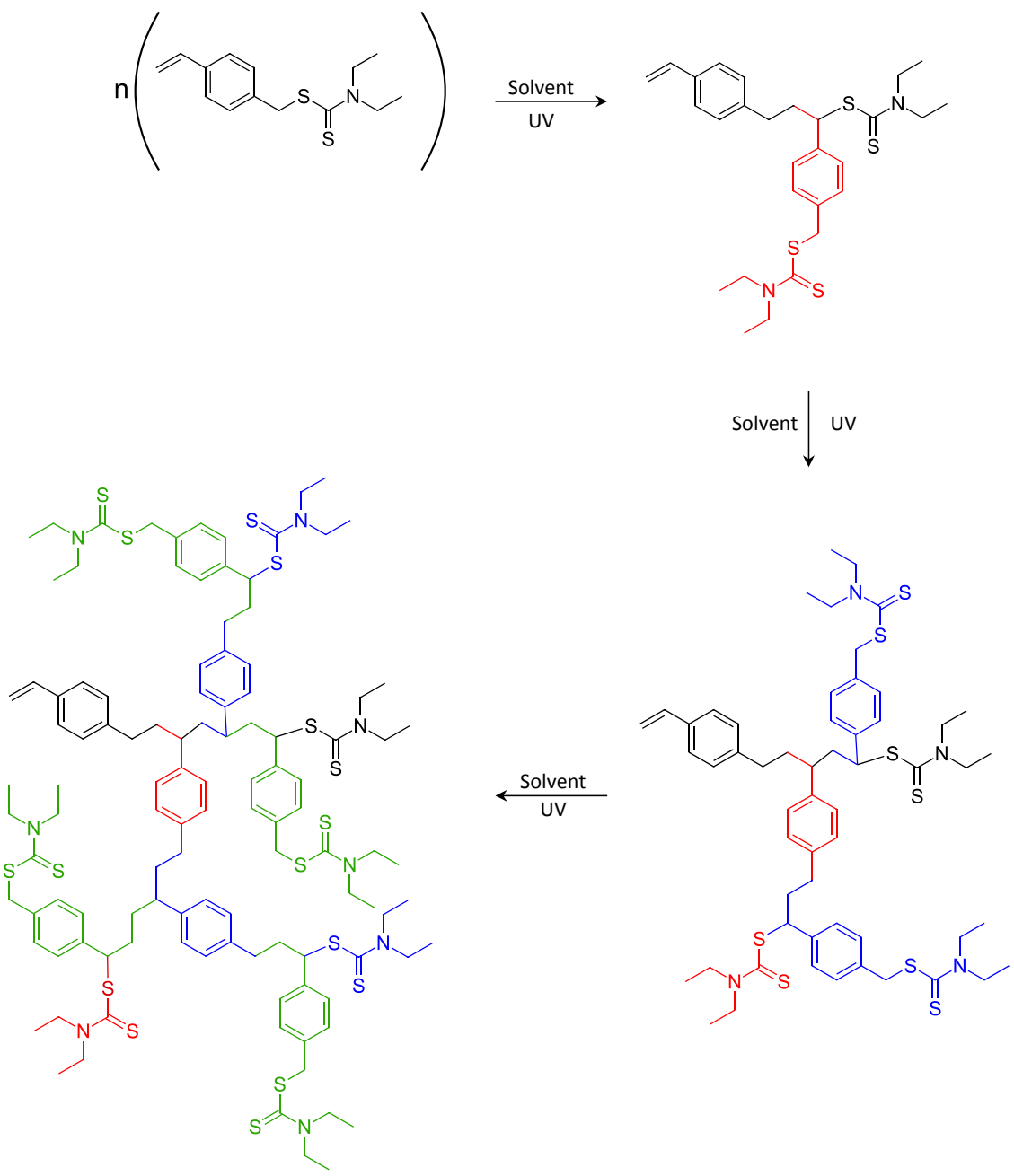


Figure 1-14: 4-vinylbenzyl N,N-diethyldithiocarbamate (VBDC), an inimer that can generate hyper-branched polymers

Since then, it many efforts have been made in this field to produce a large series of hyperbranched polymers from the inimer synthesised by Otsu (K Ishizu & Mori, 2000; K Ishizu & Mori, 2001; K Ishizu, Kojima, *et al.*, 2004; K Ishizu *et al.*, 2006) or a modified form of this inimer one (K Ishizu *et al.*, 2003; K Ishizu, Park, *et al.*, 2004) with different monomers (Lee *et al*., 1999)(K Ishizu & Mori, 2001; K Ishizu & Mori, 2002; Nakayama *et al.*, 2002; K Ishizu, Kojima, *et al.*, 2004; K Ishizu & Ochi, 2006; K Ishizu *et al.*, 2007; K Ishizu *et al.*, 2006).

The process using the inimer synthesised by Otsu is a self-condensing vinyl polymerization (SCVP) and it follows a specific pathway (Gao & D. Yan, 2004) (**Scheme 1-16**):

1. The dithiocarbamate functionality is activated by UV irradiation generating activated sites that initiate the propagation of the vinyl part in another molecule.
2. In that situation there is a dimer structure with a double bond, a growth site and a initiating site.
3. This dimer is an inimer itself and following reactions in its three sites will generate a hyperbranched macromolecules.



Scheme 1-16: Synthesis of a hyper-branched polymer from the inimer synthesised by Otsu (Otsu *et al*., 1986)

One disadvantage of this method is the different reactivity of the growth sites and the initiation sites, leading to lower degrees of branching (Gao & D. Yan, 2004) and showing a bimodal distribution (K Ishizu & Mori, 2000) suggesting that indeed two different process are taking place in these polymerisations. That

system elaborated by Otsu has the peculiarity of have a styrene part as an active radical and a dithiocarbamate part as a dormant radical. So, for instance, when a self-addition polymerisation of the inimer (K Ishizu & Mori, 2000) or a copolymerisation of the inimer with styrene (K Ishizu & Mori, 2001) is performed, a polystyrene hyperbranched polymer with dithiocarbamate functionalities in the surface (**Figure 1-15**) is obtained. Those hyperbranched structures are so compact that have spherical shape even in a good solvent so they behave as nanospheres in solution (K Ishizu & Mori, 2001; K Ishizu & Mori, 2002). Besides, because they have the photofunctional groups on their surface, different sort of polymers could be grafted changing the properties of the material (K Ishizu & Mori, 2002). Not only photoinduced polymerisations were carried out: for instance emulsion polymerisation was used to synthesise hyperbranched polystyrene polymers from styrene, divinylbencene and the inimer VBDC Those polymers could act as macroinitiators due they have terminal DTC groups so different structures could be photo-induced (K Ishizu *et al.*, 2007).

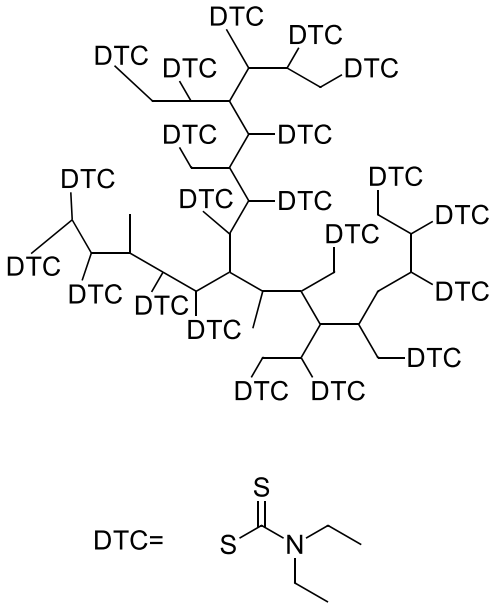


Figure 1-15: Polystyrene core with terminal dithiocarbamate groups

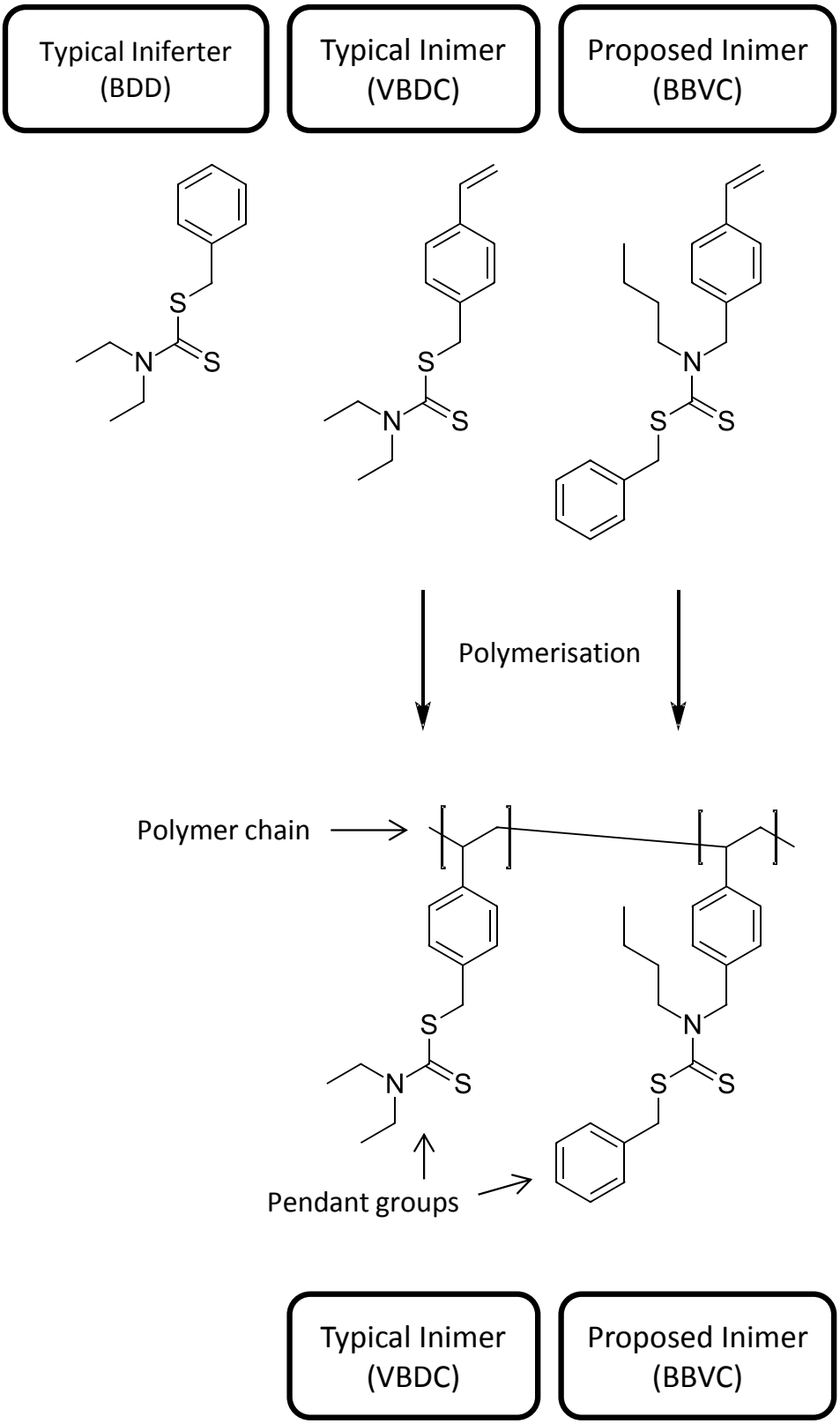
1.14 Aims and objectives

The principal aim of this project was to study in depth the dormant radicals: species containing free radical structures that have longer lifetimes and greater stability than radicals in general. Many studies were found regarding the use of these systems to perform controlled polymerisations, but apart from that, the possibilities of the dormant radicals in uses like catalysis and separations have not been exploited adequately.

In this study, the intrinsic nature of the dormant radicals was investigated, their behaviour inside molecules and macromolecules, and also their interactions with other systems in order to use those radicals in a range of applications that could improve substantially the existent methods.

To accomplish those aims, the objectives in this research were the creation, development and study of polymeric systems capable of producing dormant free radicals. A stable solid polymeric supports, that contained dormant radicals generated under controlled conditions, could be created. These solid supports are quite convenient since a big amount of material could be easily synthesised and also could be easily manipulable.

Within the available systems that generate dormant radicals the dithiocarbamate functionality was chosen due the large bibliography about its synthesis and uses in “living” radical polymerisations and also because there were not investigated enough in the subject that matters in this discussion. An approach which involved the synthesis of monomer-initiators (inimers) to create several polymers very different in nature was used. The proposed approach however have differed slightly from the previous ones (Otsu *et al*., 1986) because the proposed inimers will have the styryl double bond attached to one of the N-substituents (**Scheme 1-17**). In this way the dormant radical will be attached to the polymer “main chain” and not in the leaving group. In this way, the synthesised species, apart from their potential for use in “living” radical polymerisations, will give rise to dormant radical-based polymers.



Scheme 1-17: Structures of the typical iniferter (BDD), typical inimer (VBDC), and proposed inimer (BBVC); different spatial conformation of the inimers upon polymerisation of the styryl part

The following list summarise the most important topics in this study (**Scheme 1-18**):

- Synthesis of monomers (inimers) with dithiocarbamate or thiuram disulphide functionalities.
- Polymerization of the monomers to generate polymers containing the dithiocarbamate or thiuram functionalities.
- Testing of the polymers in different applications such as separation, catalyst ...

These dormant radicals (radical structures that have longer life-times and greater stability than radicals in general) could be used in a range of existing devices. The synthesised polymers were tested for several applications and that study could suggest new and revolutionary approaches to the solution of a range of problems. The main innovative idea of this study is using the dormant radicals for different applications than the generally used in the “living” radical polymerisation.

1.15 Summary of the experiments and results

In the following chapters, the different experiments that were performed will be explained and the results obtained from the study of these materials will be discussed. The connecting thread in this thesis will be the applications for which the polymers were synthesised (**Scheme 1-18**), therefore each chapter is dedicated to one potential application that one or more polymers were tested in. As can be seen in the **Scheme 1-18**, all the pathways to potential applications start with an initiator-monomer (inimer). The inimers can be polymerised in different ways to produce homopolymers and copolymers: linear, cross-linked and hyperbranched. The inimers described have different structures, bearing groups that can contribute distinct functionalities to their polymers. These polymers will possess features and functionalities according to the structure of the constituent inimers, therefore many different structures can be produced, leading to a great range of possible materials and applications.

The list of applications included in this chapter are summarised below (**Scheme 1-18**):

- **Chapter 2: Recycling of materials**

  A linear polymer [poly(BBVC)] was transformed into a cross-linked polymer [auto-poly(BBVC)] which was transformed back into another linear polymer [de-cross-auto-poly(BBVC)]. In a more practical context that conversion would mean a very elegant approach to recycle hard polymeric materials that could not be thermally moulded due to their cross-linked nature.

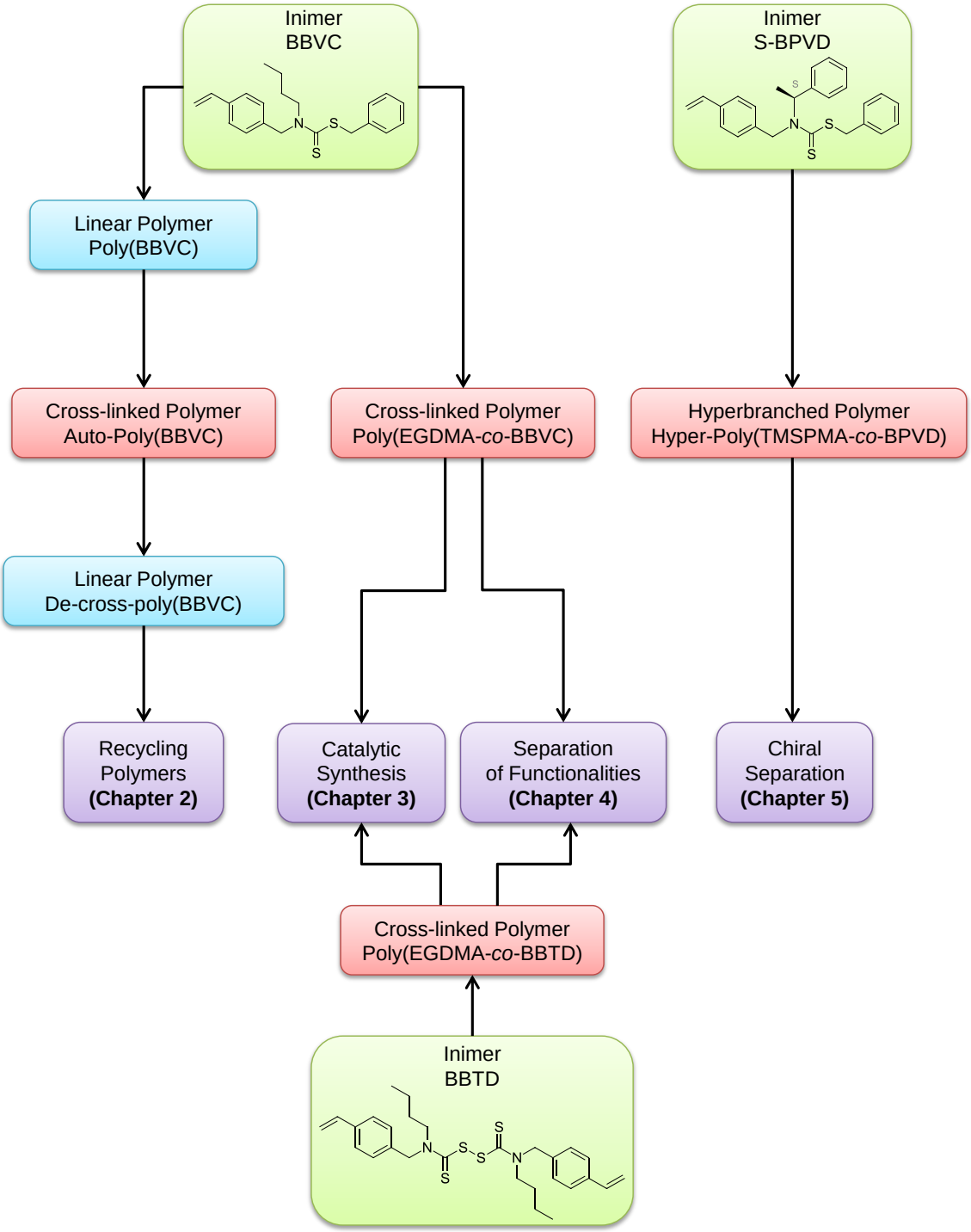
  The last linear polymer was very similar in structure to the first one, thus achieving a cycle of transformations. The ability of recombination of the dithiocarbamate radicals was tested.

- **Chapter 3: Catalytic synthesis**

  Two cross-linked polymers [Poly(EGDMA-*co*-BBTD) and Poly(EGDMA-*co*-BBVD)] were used to synthesise a macrocycle from typically commercially available monomers like Styrene, Methacrylic acid and Methyl Methacrylate. Since the mechanisms proposed involved catalytic reactions, the macrocycle generated would be a very interesting macromolecule composed only by molecules of monomer; theoretically no initiator residues could be found in the structure. Therefore, the dithiocarbamate radicals were tested for their ability to catalyse synthetic reactions.

- **Chapter 4: Separation of molecules with different functionalities**

  Two cross-linked polymers [Poly(EGDMA-*co*-BBTD) and Poly(EGDMA-*co*-BBVD)] were packed into columns in order to test their utility as chromatographic stationary phases for the separation of mixtures of compounds. It is barely impossible to predict how the dithiocarbamate dormant radicals would interact with different functionalities; therefore those interactions were tested, investigating the potential of the columns to separate mixtures of compounds with different functionalities.



Scheme 1-18: Synthetic and application pathways: relationships between the different monomers (inimers) (yellow), linear polymers (blue), cross-linked polymers (red) and applications (magenta)

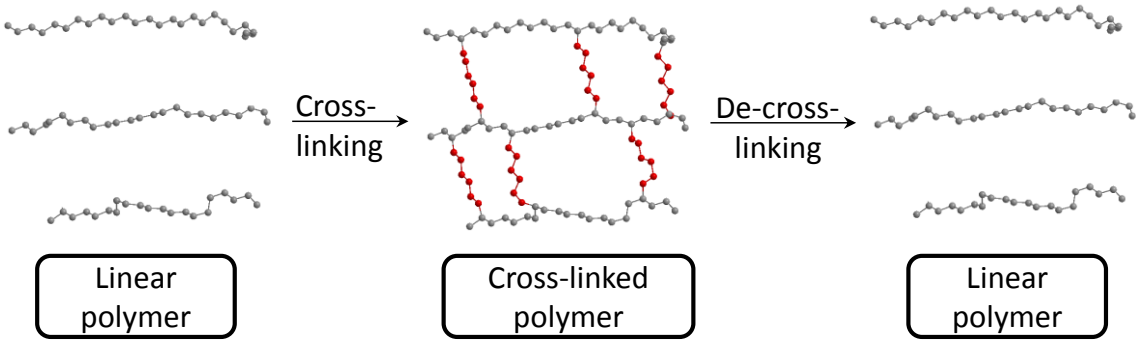
- **Chapter 5: Enantiomeric separation**

  A chiral hyper-branched polymer supported in glass beads [Hyper Poly(TMSPMA-*co*-BPVD)] was used as a column packing to separate racemic mixtures. Since the polymer would have a high density of chiral centres, it was theorised that, within a pair of enantiomers, one isomer would interact strongly with those centres than the other isomer, achieving the so important chiral resolution. In order to create the chiral polymeric material, it was tested the ability of specific dithiocarbamate systems to generate hyper-branched polymers containing chiral centres.

2 Recycling polymers: De-cross-linking of a cross-linked polymer

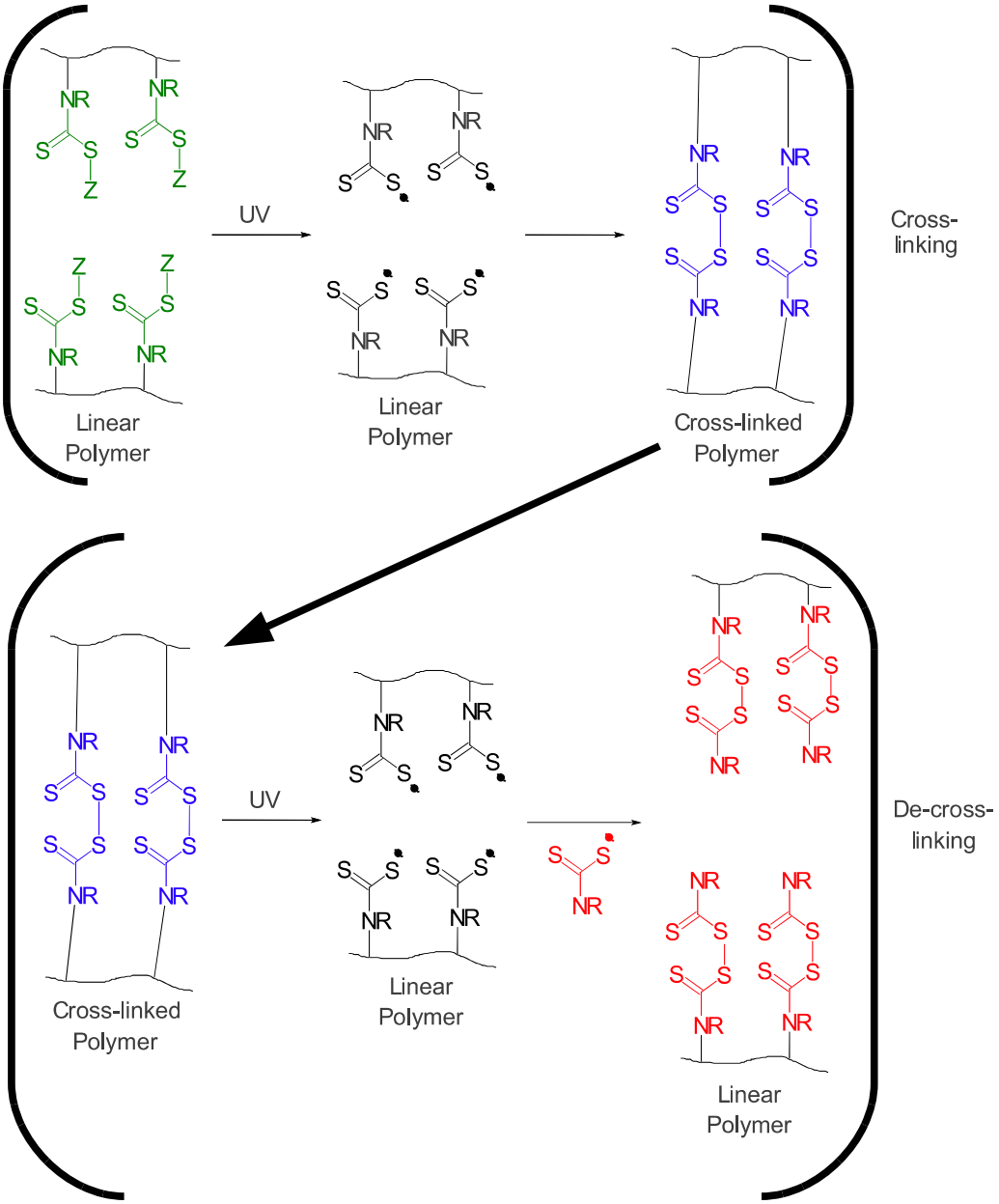
2.1 Introduction

The aim of this experiment was the synthesis of a polymeric material that could be transformed reversibly between its linear (uncross-linked) and cross-linked state through the formation of reversible cross-links (marked in red in **Scheme 2-1**). In this way a polymeric material can be rendered insoluble under mild conditions and converted back into a linear polymer that is soluble in common laboratory solvents by a similarly mild transformation. The process would also change the structure of the polymers in a controlled way.



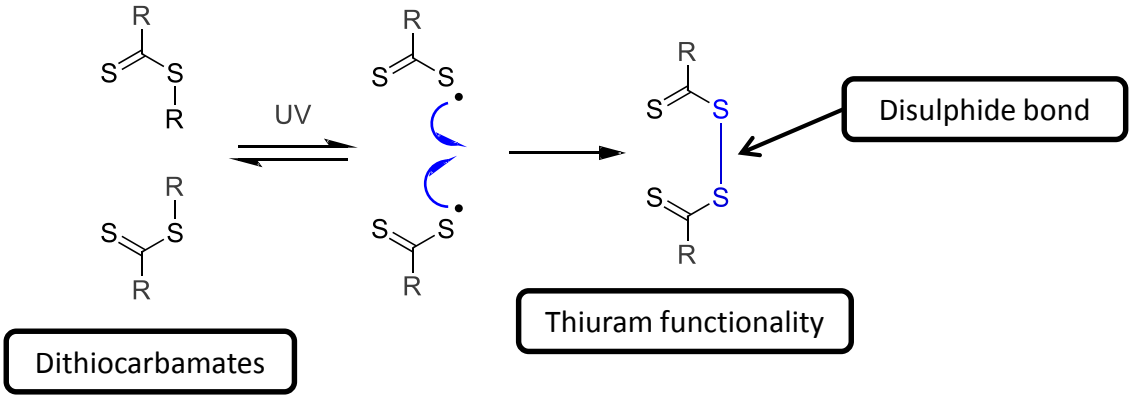
Scheme 2-1: Simplified view of the cross-linking / de-cross-linking process

The idea at the heart of the process is the creation of disulphide bonds between polymeric chains, which can produce cross-links (in blue in fragment in **Scheme 2-2**). The dithiocarbamate ester functionalities are able to generate sulphur-centred radicals when irradiated at the appropriate wavelength of UV light and, if they are allowed, they are able to reorganise by the creation of disulphide bonds and generating thiuram functionalities (**Scheme 2-3**).



Scheme 2-2: Cross-linking and de-cross-linking schematic process

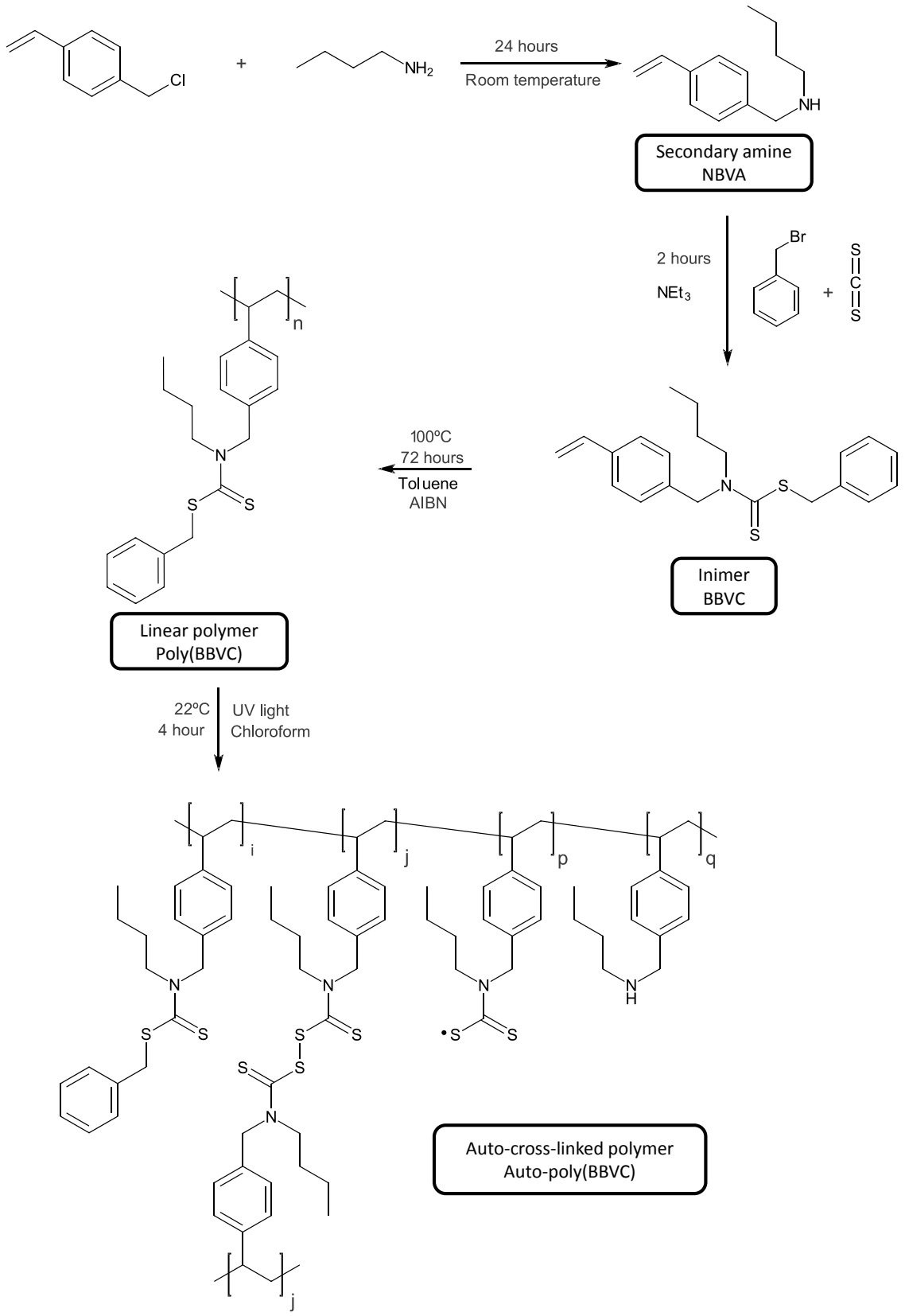
It would be possible to create a cross-linked polymer without the use of a cross-linker, just with a linear polymer with pendant dithiocarbamate ester functionalities (green fragments in **Scheme 2-2**). Irradiating the linear polymer, pendant dithiocarbamate radicals would be generated (black fragments in **Scheme 2-2**).



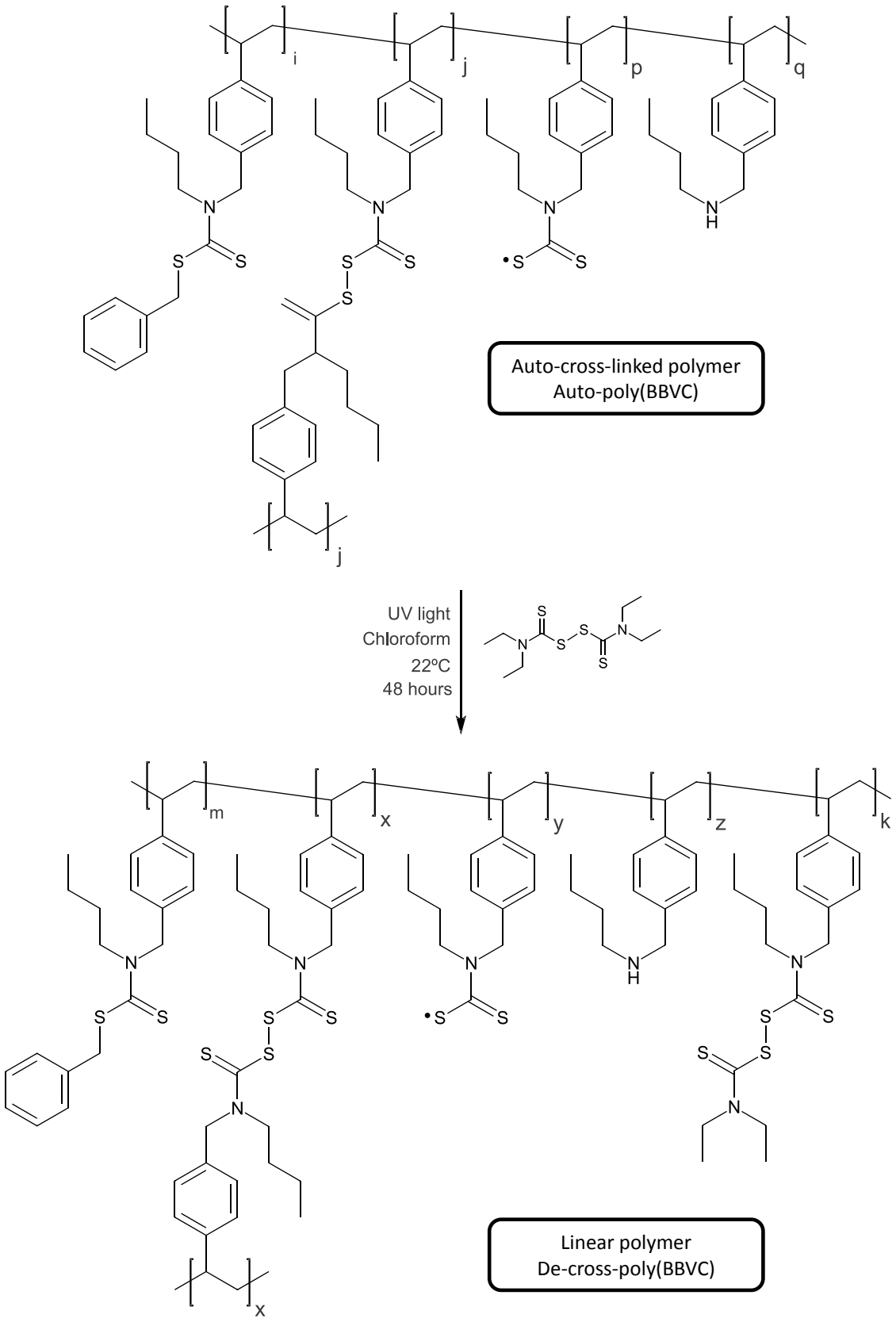
Scheme 2-3: Generating thiuram functionality with disulphide bonds irradiating two dithiocarbamates and allowing the formed radicals to cross-react

These dithiocarbamate radicals would be able to reorganise and create disulphide bonds (thiuram functionalities) between adjacent linear polymer chains (blue fragments in **Scheme 2-2**). Since the thiuram groups are themselves photo-labile it would be possible to break those cross-links with continued irradiation and regenerate linear polymers chains with pendant dithiocarbamate radicals (black fragments in the de-cross-linking process in **Scheme 2-2**). If an excess of another low molecular weight dithiocarbamate radical was introduced, recombination could lead to the creation of different thiuram functionalities by cross-coupling (blue fragments in the de-cross-linking process in **Scheme 2-2**). The last polymer created would be then a linear polymer bearing thiuram groups in the side-chain.

As can be seen in **Scheme 2-4**, the process starts with the synthesis of an inimer (BBVC). The next step is the polymerisation of that inimer, BBVC, to create a linear polymer (poly(BBVC)). The next step is a cross-linking process to generate a cross-linked polymer (auto-poly(BBVC)). And the final step is a de-cross-linking process in which the bonds between chains would be broken in order to again obtain a linear polymer (de-cross-poly(BBVC))(**Scheme 2-5**). However this linear polymer de-cross-poly(BBVC) would be substantially different from the previous poly(BBVC) due to some differences in its structure.



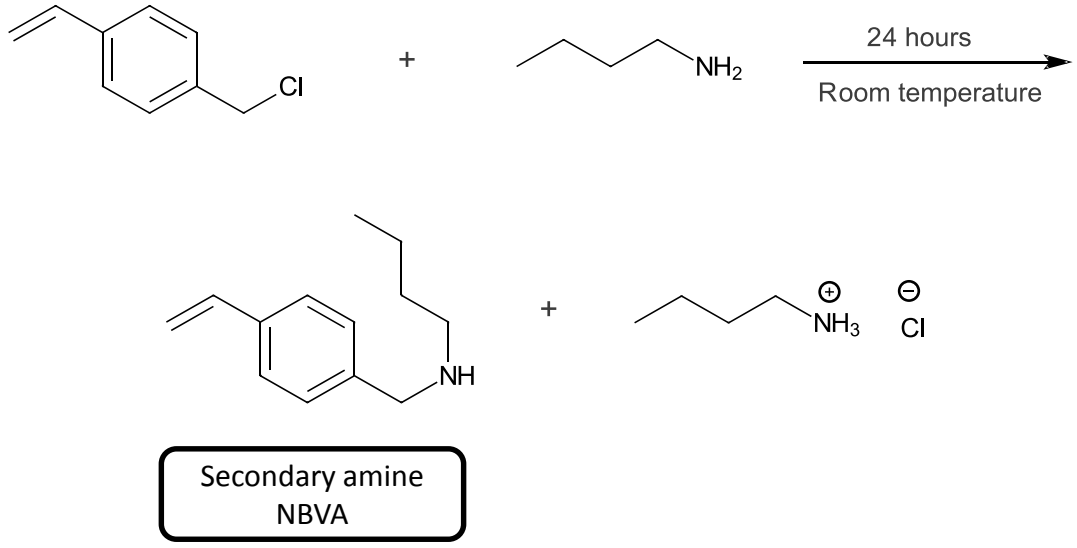
Scheme 2-4: Pathway to synthesise the auto-cross-linked polymer



Scheme 2-5: De-cross-linking process of the auto-cross-linking polymer

2.2 Synthesis of the secondary amine: N-(4-vinylbenzyl)butan-1-amine [NVBA]

The first step of the process is the synthesis of a secondary amine (**Scheme 2-6**). It was necessary for the secondary amine to have only one polymerisable group, hence an amine bearing a styryl (4-vinylbenzyl) group and an alkyl group (butyl) was prepared. The requirement for a secondary amine was to generate a tertiary dithiocarbamate, since the primary and secondary dithiocarbamates are much less susceptible to photo-dissociation (Graeme Moad & Solomon, 2006).



Scheme 2-6: Synthesis of the amine NVBA

The synthetic pathway start with the synthesis of the secondary amine (**Scheme 2-6**) in which the Hofmann alkylation procedure (Salvatore, Yoon, *et al.*, 2001) was followed. In that protocol a haloalkane is mixed with a primary amine in a large excess of the later. This is wasteful in terms of amine (especially if it is expensive) but it is the most efficient procedure (M. Smith & March, 2007) particularly if the excess of primary amine can be recovered when the synthesis is finished. The primary amine used in this synthesis, n-butylamine (NBA), was perfectly affordable, so it was then added in large

excess to act as a solvent for the reaction, as a reagent in the substitution reaction, and to neutralize the hydrochloric acid formed as a by-product.

In the Fourier transform infrared spectroscopy (FTIR) spectrum (**Figure 2-2**) the bands for the N–H stretching vibration, N–H bending vibrations, C=C and C–N stretching vibration can be found at 3315 cm^{-1}(only band since it is secondary amine, the primary amines have two weak bands), 1515 cm^{-1}, 1629 cm^{-1} and 1120 cm^{-1} respectively. Those bands were easy to assign as they are very well documented in the literature (Silverstein *et al.*, 2005).

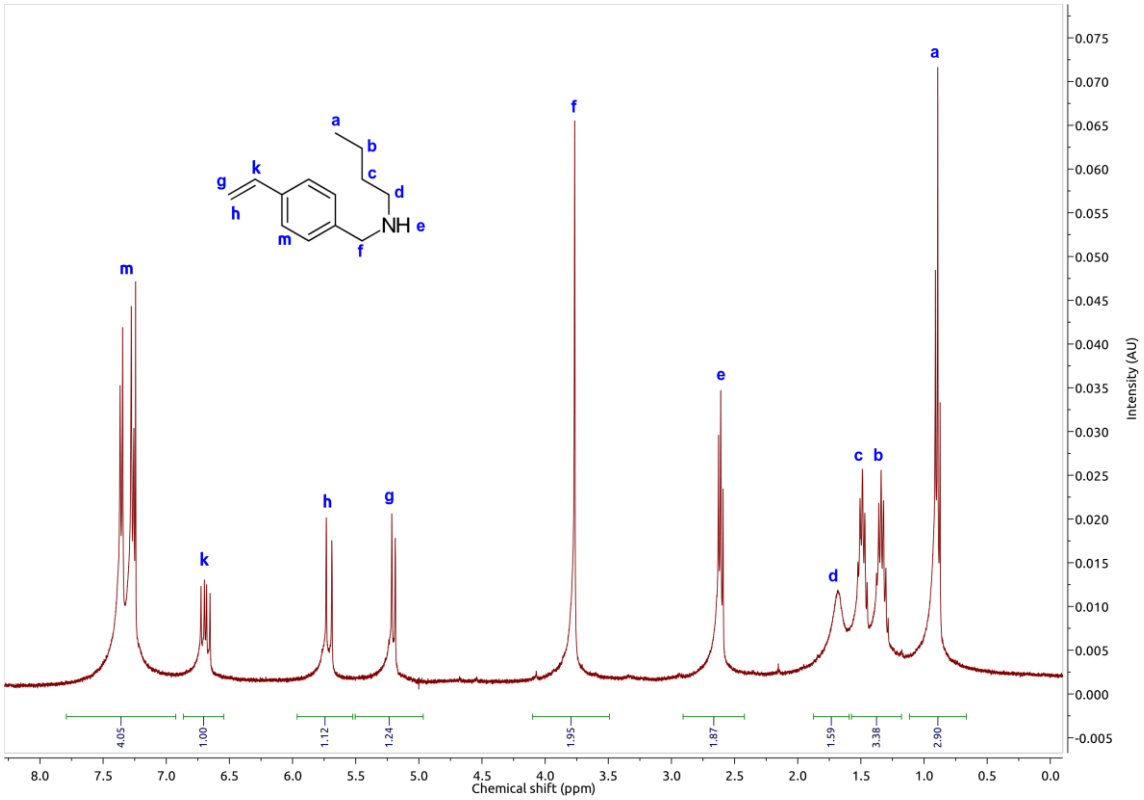


Figure 2-1: ^{1}H NMR of the secondary amine

All the protons in the structure of the secondary amine were uniquely assigned in the Nuclear Magnetic Resonance spectroscopy (NMR) spectrum (**Figure 2-1**).

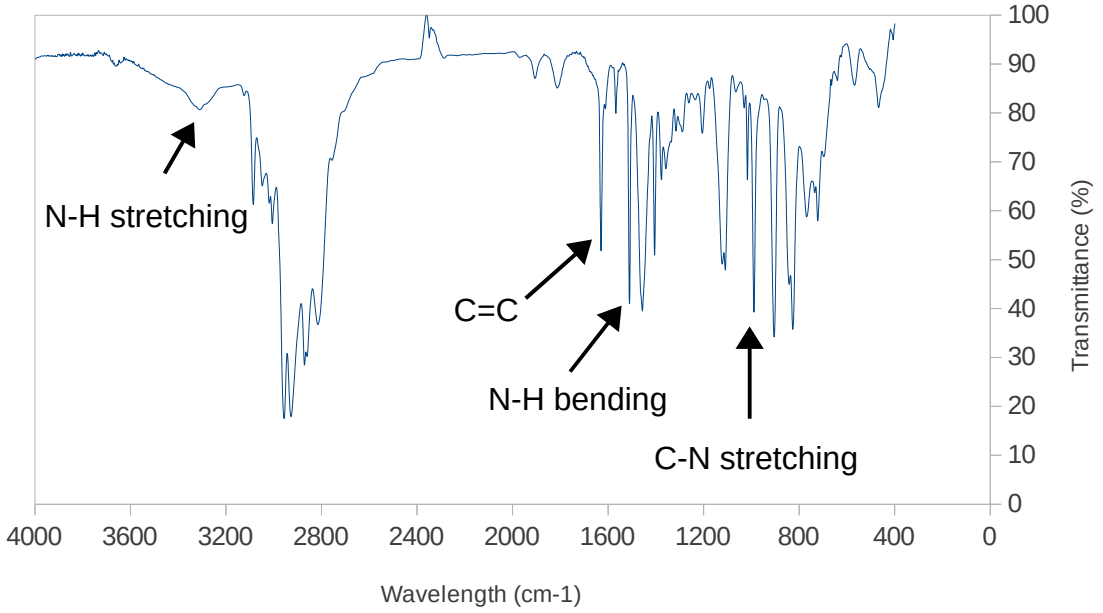
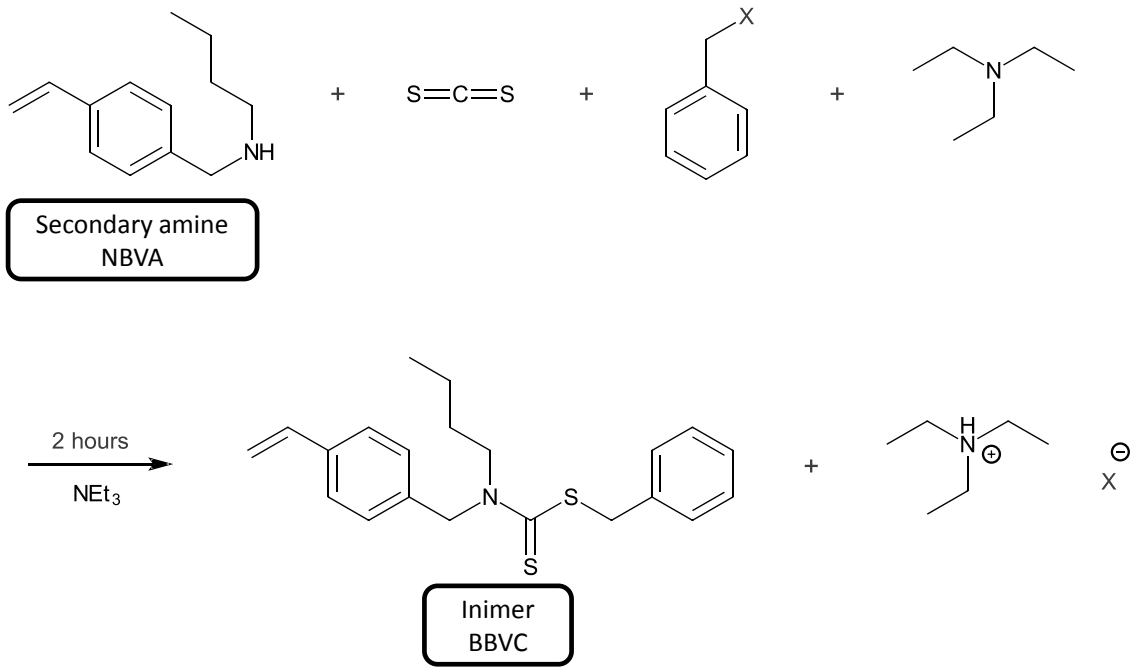


Figure 2-2: FTIR of the secondary amine NBVA

2.3 Synthesis of the inimer with dithiocarbamate functionality: Benzyl N-butyl-N-(4-vinylbenzyl)dithiocarbamate [BBVC]

The synthesis of the inimer BBVC (**Scheme 2-7**) was based in the work of Najmedin Azizi (Azizi *et al.*, 2006); this protocol was preferred as there was no requirement to reflux the reaction mixture which will help to avoid the risk of premature polymerisation of the styryl part in the secondary amine (the double bond will be required later to synthesise the linear polymer) and because the dithiocarbamic acid is so unstable, so it is better to perform the reaction in situ (Rudorf, 2007). The synthesis of the proposed inimer (**Scheme 2-7**) differed in one aspect with respect to the protocol established by Azizi: triethylamine was added to neutralize the hydrogen halide generated in the coupling process; if the triethylamine was not added the benzyl halide would consume part of the secondary amine, decreasing the yield of the reaction. As an amine was needed it was more convenient to add a cheap external base than consuming the previously synthesised secondary amine. The use of triethylamine in the synthesis of dithiocarbamates was previously reported by other authors but only in two step dithiocarbamate synthesis (Ottenbrite, 1972) so the novelty was

including it in the one-pot process. The amount of the triethylamine and also of the CS_2 was double that calculated to match the stoichiometry of the other reagents in order to ensure that: the former can function both as a base and as a solvent and to account for the high reactivity of the latter.



Scheme 2-7: Synthesis of the inimer BBVC from the secondary amine NBVA

Because of the light-sensitive features of the molecule the synthesis and purification were performed while trying to exclude ambient light as much as possible in order to maintain the integrity of the dithiocarbamate ester groups and to avoid undesirable polymerisation.

In the synthesis of this inimer two different vinylbenzyl halides were tried. The first one was vinylbenzyl chloride, which gave good yields, but the vinylbenzyl bromide gave even better results and its toxicity it is much lower, so it was rapidly adopted as the definitive reagent for the synthesis. The yellow solution formed by mixing the starting materials became dark red. It was found that the red coloration was something common and very noticeable in the synthesis of

the different synthesised dithiocarbamates along the study. It was suspected that the coloration suggested interesting aspects of the mechanism of the reaction but since the yield of the reaction was acceptable, the phenomenon was noted for possible future study. The final product was purified by flash column chromatography and the resultant oil freed from solvent using a rotary vacuum pump since an attempt to purify the inimer by distillation resulted in polymerisation.

Table 2-1: Elemental analysis of the inimer BBVC

Inimer	C	H	N	S
Theory	70.94	7.09	3.94	18.03
Experimental	70.46	7.35	4.03	17.78

The values found in the elemental analysis of the compound were very close to the theoretical ones (**Table 2-1**).

Comparing the FTIR spectrum of the inimer with that of the secondary amine (**Figure 2-3**): the bands for the C═C vibrations at 1629 cm^{-1} were common to both compounds; however the band at 3315 cm^{-1} (N-H vibration) was not present in the dithiocarbamate ester, proving that the secondary amine structure was absent. Additional bands for the C─N and C─N─C bond vibrations were found at 1475 cm^{-1} (Cervantes *et al*., 1997; A. Patel & Mequanint, 2008). The assignation of the bands in the area of 1200-700 cm^{-1} was difficult as bands from both the N─C═S and the new aromatic ring should appear in the same region of the spectrum. In any case, the incorporation of both fragments was surmised by the appearance of these bands.

The ^{1}H NMR spectra of the inimer in DMSO-d_6 at 30ºC (**Figure 2-4**) were not clear enough to assign all peaks with matching integral values. This observation was taken as evidence that this molecule has a different behaviour to the precursor (secondary amine NBVA).

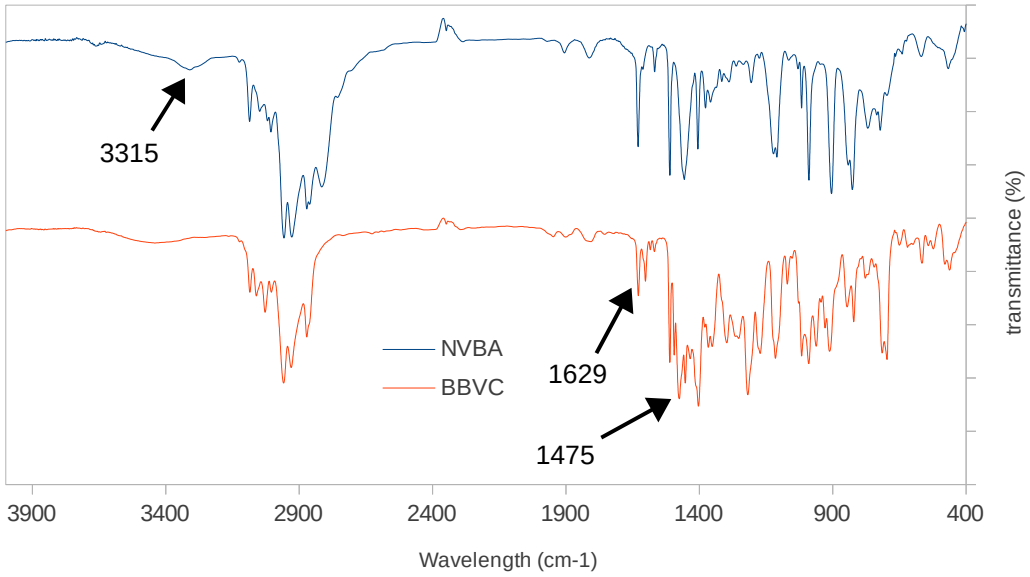


Figure 2-3: Comparison of the FTIR from the secondary amine NVBA and the inimer BBVC

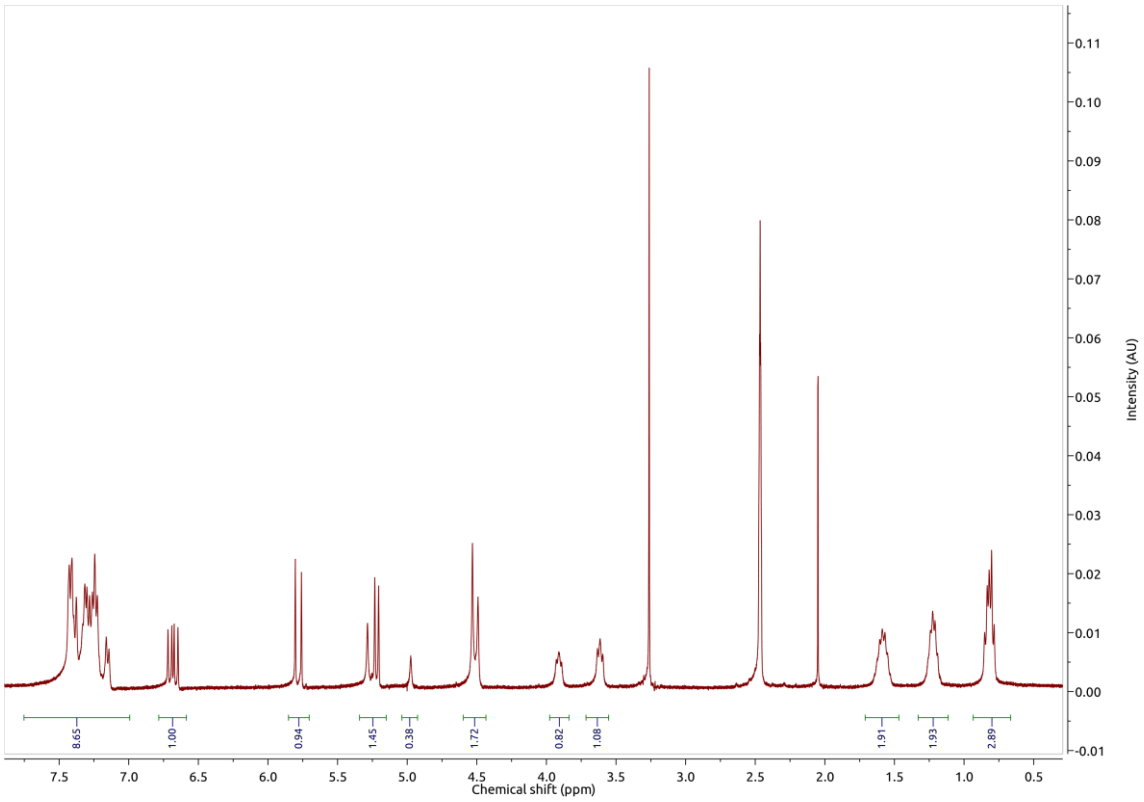
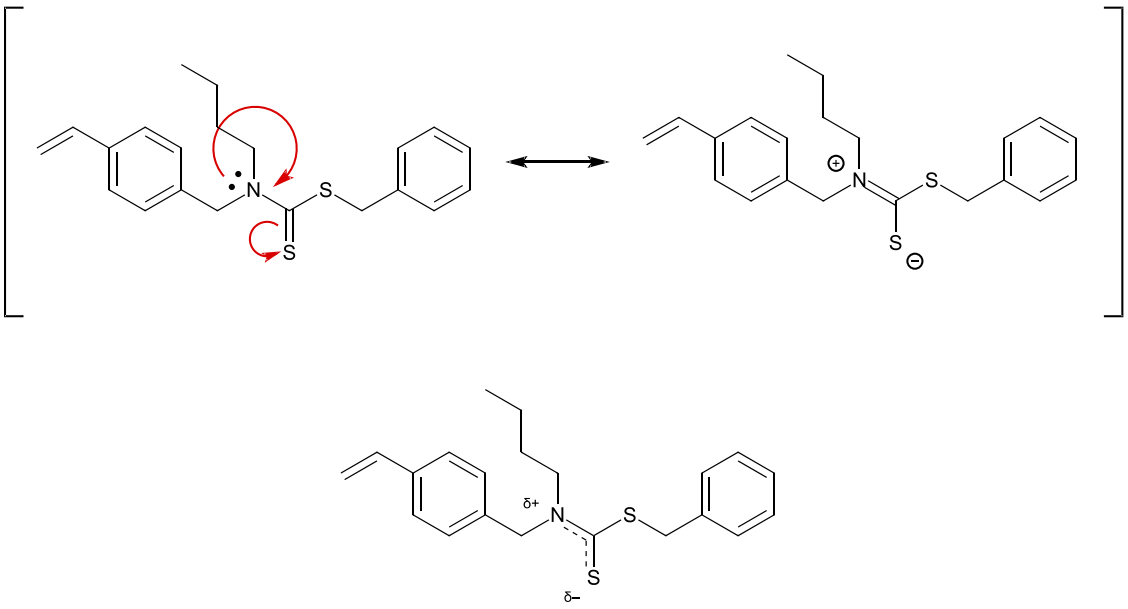


Figure 2-4: ^{1}H NMR in DMSO-d_6 of the inimer at 30ºC

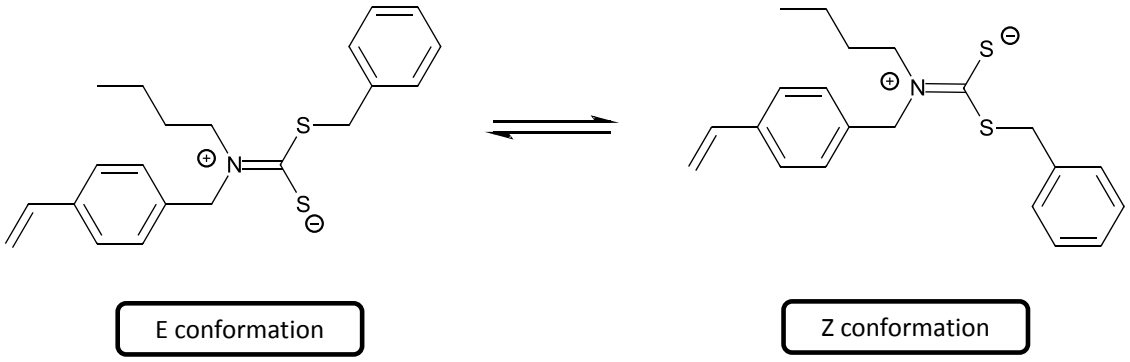
Some signals were split in two with a broad appearance and the integrals did not match with the theoretical values for the number of hydrogen atoms attached to each carbon atom. These effects were specially remarkable in the carbons close to the nitrogen atom, giving us a clue that hindered movement around a bond with a significant activation energy for a torsional barrier, causing bond to be slow on the NMR timescale, could explain these features of the NMR spectrum (Holloway & Gitlitz, 1967; Sandström, 1967; Devi *et al.*, 1981). The delocalisation of electrons from the lone pair on nitrogen to the C–N bond was responsible for introducing a high degree of double character in it. This behaviour is reinforced by movement of electrons from the C=S bond to the sulphur atom (**Scheme 2-8**), creating partial charges in the system.



Scheme 2-8: Electron movement inside the inimer, canonical forms and resonance structure

A good explanation for those unexpected signals in the NMR spectra could be that the polar canonical form in which C-N double bonding occurs contributes considerably to the structure (Cavell *et al.*, 1979), as it can be seen in the resonance form, which more closely resembles the real molecule. Thus the C-N

bond has a clear double bond character (K Ishizu & Mori, 2001) due to the delocalisation of the lone pair of electrons on the nitrogen atom, giving two possible conformational isomers: *Z* and *E* (**Scheme 2-9**).



Scheme 2-9: E and Z conformations (flip around the double bond)

There is evidence for this explanation in several crystal structures from "The United Kingdom Chemical Database Service" (Fletcher *et al.*, 1996). It could be found C-N-C angles closer to 120º (**Figure 2-5**) in the structure of some dithiocarbamate molecules (**Figure 2-6**) that suggest a planar conformation, instead the ~110º expected for a pyramidal arrangement of bonds. That also proves the double bond character of this structure.

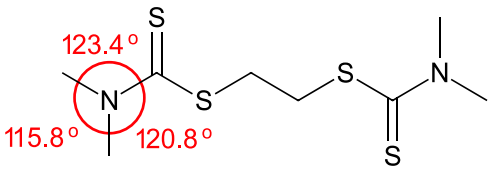


Figure 2-5: C-N-C angles in the ethylene bis(dimethyldithiocarbamate) from the published crystal structure (Fletcher *et al*. 1996)

Based on this hindered rotation, the most favoured form at a low temperature would be the E isomer. That difference can be calculated using the integral of

the peaks that split in two in the NMR spectra, for instance the CH2 of the butyl group closer to the nitrogen bond suggests that at 30ºC the proportion of the E form is 57%.

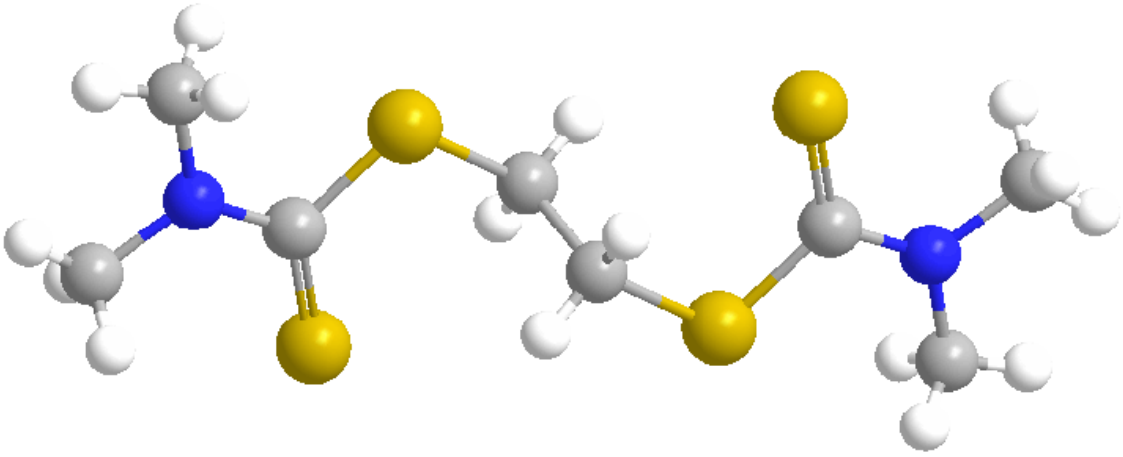
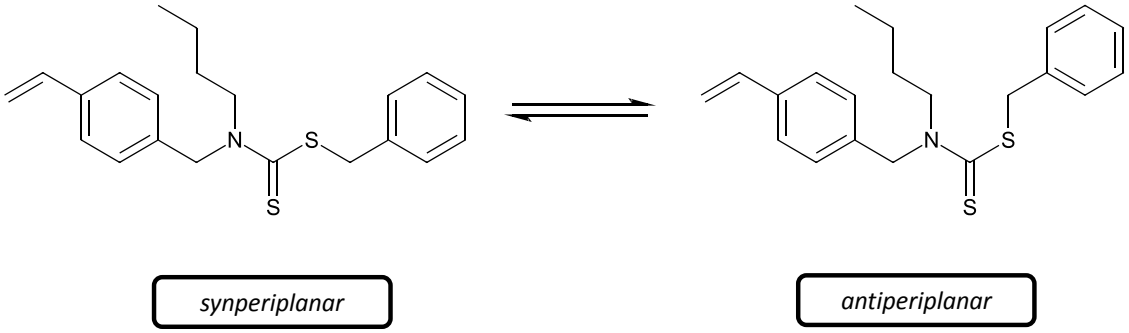


Figure 2-6: 3D structure of ethylene bis(dimethyldithiocarbamate)

When the temperature used in the analysis of the inimer is increased to 80ºC, coalescence of the signals can be seen and the peaks appeared to become sharper (**Figure 2-7**). The highest temperature studied in ^{1}H NMR analysis of the inimer BBVC was 150ºC (**Figure 2-8**), where peak averaging allowed full assignment and integration.



Scheme 2-10: Synperiplanar and antiperiplanar conformations of the dithiocarbamate

Apart from the E and Z conformations in the dithiocarbamate other conformations have been found in such molecules related to the group bond to the sulphur respect the C=S bond: synperiplanar (*sp*) and antiperiplanar (*ap*) (**Scheme 2-10**).

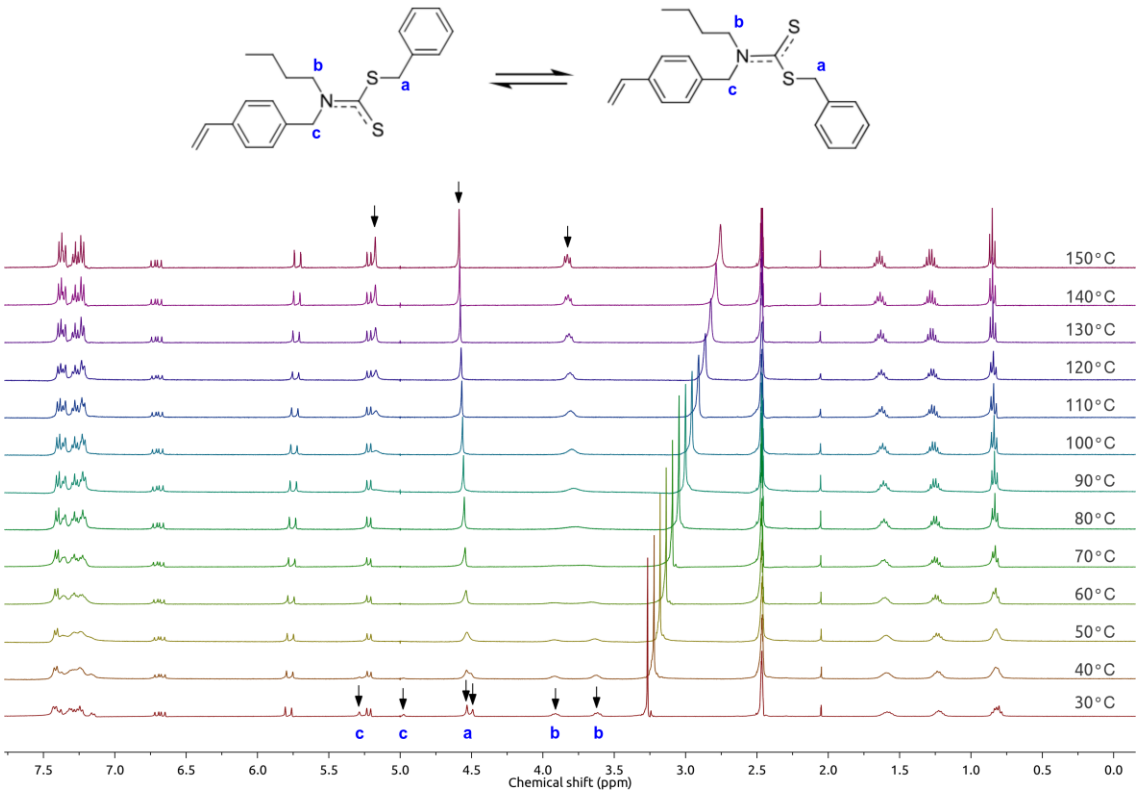


Figure 2-7: ^{1}H NMR of the inimer in DMSO-d_6 with temperature gradient and assignation of the peaks

The factors affecting these conformations are the C-N and S-C dipole interactions and the repulsion between the lone pair of electrons on ester sulphur and nitrogen which results in the stabilization of the *ap* with respect to the *sp* conformations in primary and secondary dithiocarbamates (Oki & Nakanishi, 1971; Devi *et al.*, 1981). This phenomenon is not quite clear in tertiary dithiocarbamates (Oki & Nakanishi, 1971) and it could be due to steric repulsion between the S-alkyl groups and the N-alkyl groups compared with the

repulsion between the S-alkyl groups and the C-S bond. This effect seemed to be less important than the partial double bond character discussed above.

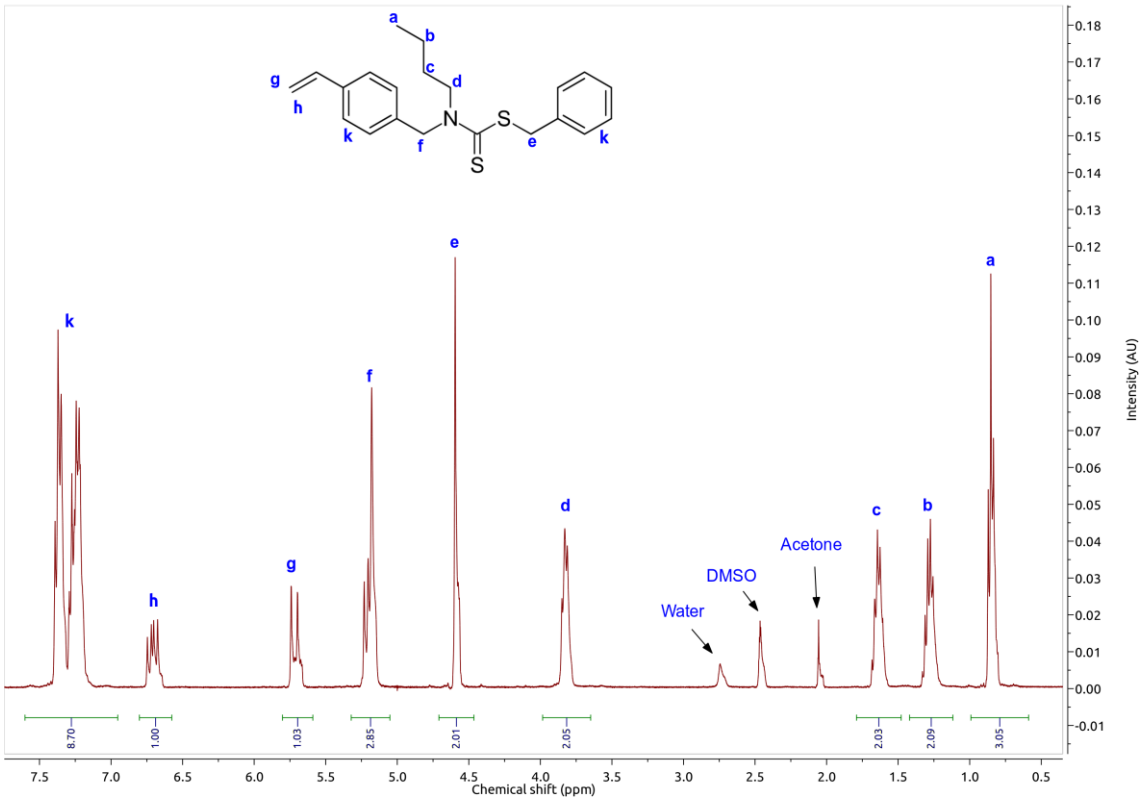


Figure 2-8: ^{1}H NMR of the inimer in DMSO-d_6 at 150ºC

The kinetics of radical formation during UV irradiation of the inimer (**Figure 2-9**) was investigated by Electron Paramagnetic Resonance (EPR). The DTC ester group is intact at the start of the experiment. The intensity of the EPR signal was seen to increase linearly as a function of irradiation time over the first 2000s, starting from zero intensity at time t = 0s. This is a characteristic of a system in which the formation of active species is fast compared to other processes (such as polymer propagation) and where the rate of termination can be considered to be negligible until relatively high conversions (Merna *et al.*, 2005).

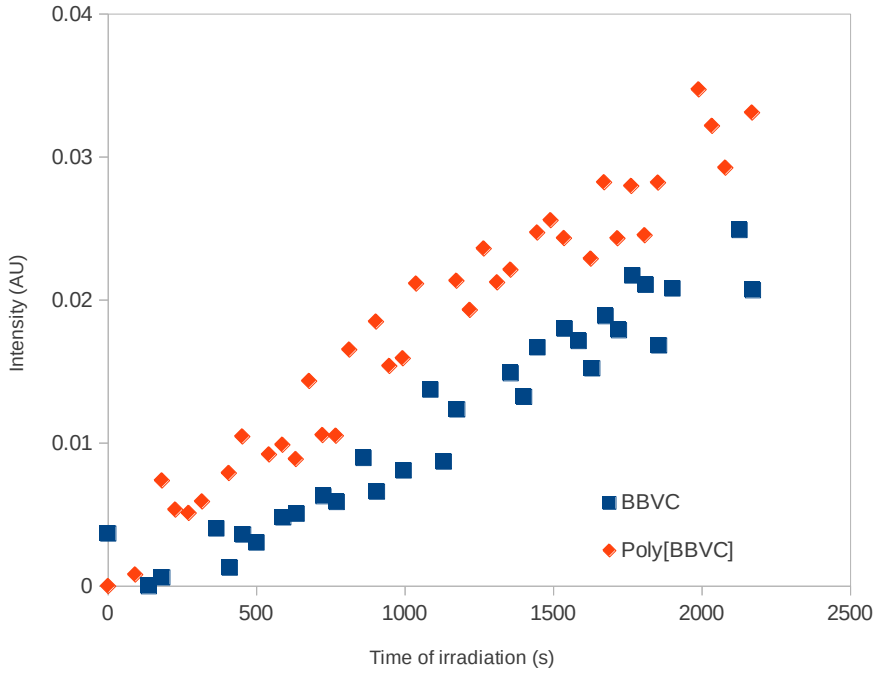
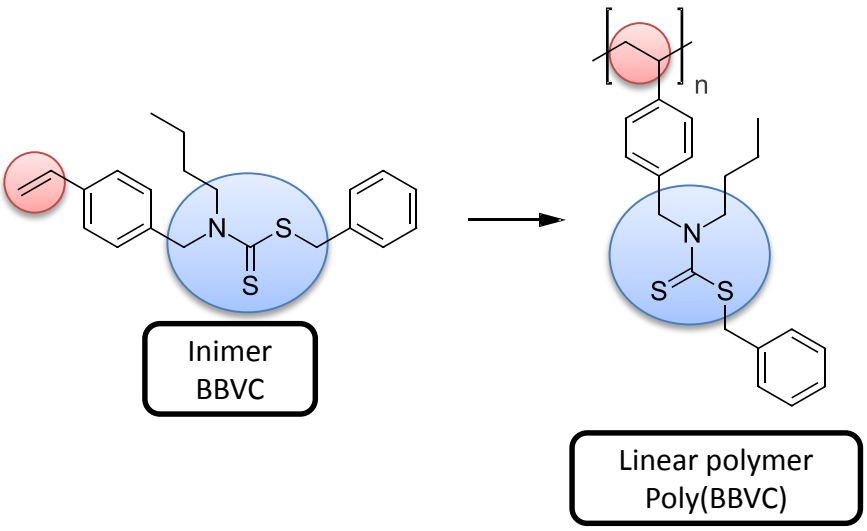


Figure 2-9: Comparison of the averaged EPR signal intensity from the inimer BBVC and the linear polymer poly[BBVC], both increase linearly as a function of UV irradiation time

2.4 Synthesis of the linear polymer with dithiocarbamate functionality: Poly(benzyl N-butyl-N-(4-vinylbenzyl)dithiocarbamate) [Poly(BBVC)]

The next step in the pathway was the synthesis of a linear polymer from the inimer, BBVC. The inimer has two functionalities that can participate in polymerisation reactions: one is the double bond of the styryl group and the second is a photochemically-activated initiator (dithiocarbamate ester functionality). To accomplish the synthesis of the required linear polymer it was necessary to selectively polymerise the styryl part using thermal, rather than photochemical initiation **(Scheme 2-11**) to preserve the integrity of the side-chain. The resultant polymer is a macroiniferter and can be used in a “living” radical polymerisation process to graft additional polymers to the side-chain,

although it would not be used this ability in order to achieve the proposed objectives.



Scheme 2-11: In the synthesis of the linear polymer poly(BBVC) from the inimer BBVC the double bond reacts and the dithiocarbamate functionality is kept intact

After testing different solvents, toluene was the best one to be used. This polymerisation was performed in an inert atmosphere and in the absence of light to avoid photolysis of the C-S bond (Otsu *et al*., 1986). UV-activation of the dithiocarbamate ester group would have resulted in the formation of hyper-branched polymers (see **Section 1.13.1**).

In the synthesis of this linear polymer the conversion increased to a very small extent beyond 24 hours of reaction so the reaction time was kept under that value.

In this process the monomer concentration does not seem to be a critical factor to achieving a high molar mass polymer or to obtain a good conversion in the synthesis. The concentration of the inimer in solution is subject to its solubility in the solvent and also the solubility of the initiator. So variations in those parameters were limited; they were used values of monomer concentration of

between 0.01-1.0 g / mL and the results do not change to a great extent. In this synthesis it was used toluene as solvent, because it was found to be the only common solvent for the inimer, initiator and polymer product. Furthermore, due to its high boiling point (111ºC), it was possible to achieve the 100ºC necessary for obtaining the best yield found in this particular polymerisation. However it is known that the DTCs in the acid form can decompose at temperatures between 50-110°C giving CS_2 and the starting amine (Gergaly, 1985). The NMR evidence suggested that the dithiocarbamate ester function in the structure of BBVC had good thermal stability, however since polymerisation involves prolonged heating, attempts were made to synthesise this polymer at lower temperatures (>60°C to <100°C) as a precaution against decomposition, but all were unsuccessful. The requirement for high temperatures during polymerisation could be related to the structure of the inimer, making it less reactive towards polymerisation.

The polymer was precipitated into methanol and purified by re-precipitation using the system toluene / acetone. Acetone was used as non-solvent instead of methanol on account of the negligible solubility of inimer in the methanol. That issue complicated the purification process as the linear polymer produced a gel in acetone. That gel was difficult to filter because it easily blocked the pores of the filter making the purification process slow. The obtained solid was dried using a rotary vacuum pump to produce a yellow solid.

Table 2-2: Elemental analysis of the linear polymer Poly(BBVC)

Linear Polymer	C	H	N	S
Theory	70.94	7.09	3.94	18.03
Experimental	70.93	7.53	4.00	20.38

The elemental analysis of the linear polymer (**Table 2-2**) shows some variation from the predicted amount of sulphur. The N / S ratio shows that the amount of sulphur in the sample is slightly higher with respect to the theoretical value. The

C / N ratios suggest that a certain number of benzyl groups may have been lost due to C–S cleavage.

The FTIR of the polymer looks virtually identical to the FTIR of the monomer (**Figure 2-10**) with the exception of the band for the C=C bond, which is missing in the spectrum of the linear polymer, indicating that the double bonds of the inimer have disappeared during the polymerisation.

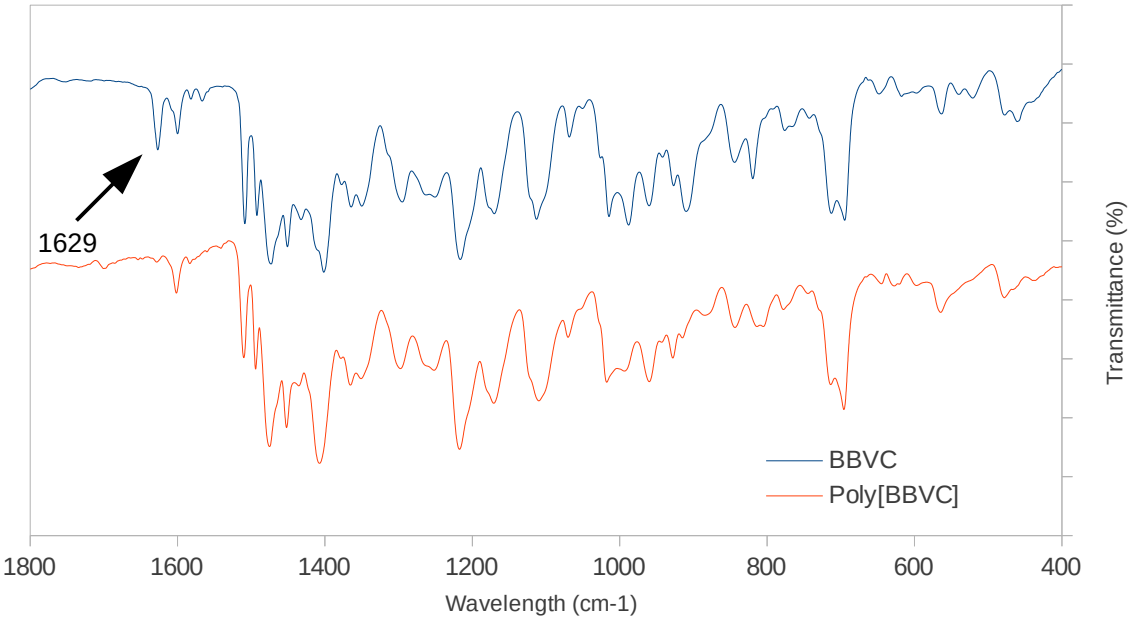


Figure 2-10: FTIR of the linear polymer compared to the spectrum of the monomer, the peak corresponding to the double bond has virtually disappeared

To record a clear ^{1}H NMR spectrum of the linear polymer (**Figure 2-11**) it was necessary to heat the sample to minimise conformational effects. The linear polymer was not soluble in DMSO-d_6 so toluene-d_8 was used, however the boiling point of this solvent (110ºC) was not high enough to fully resolve the spectrum as was obtained for the inimer in DMSO-d_6. A clear enough spectrum was obtained to allow assignment of chemical shifts and to show that the signals of the double bond had disappeared.

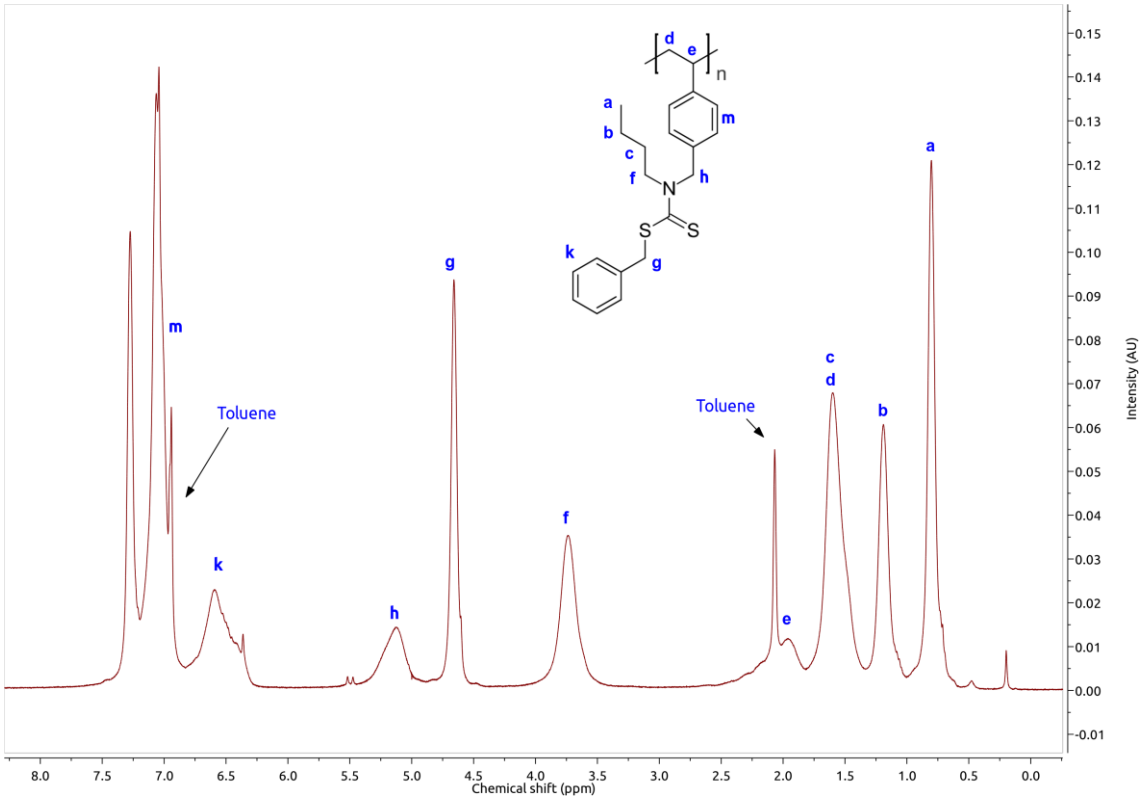


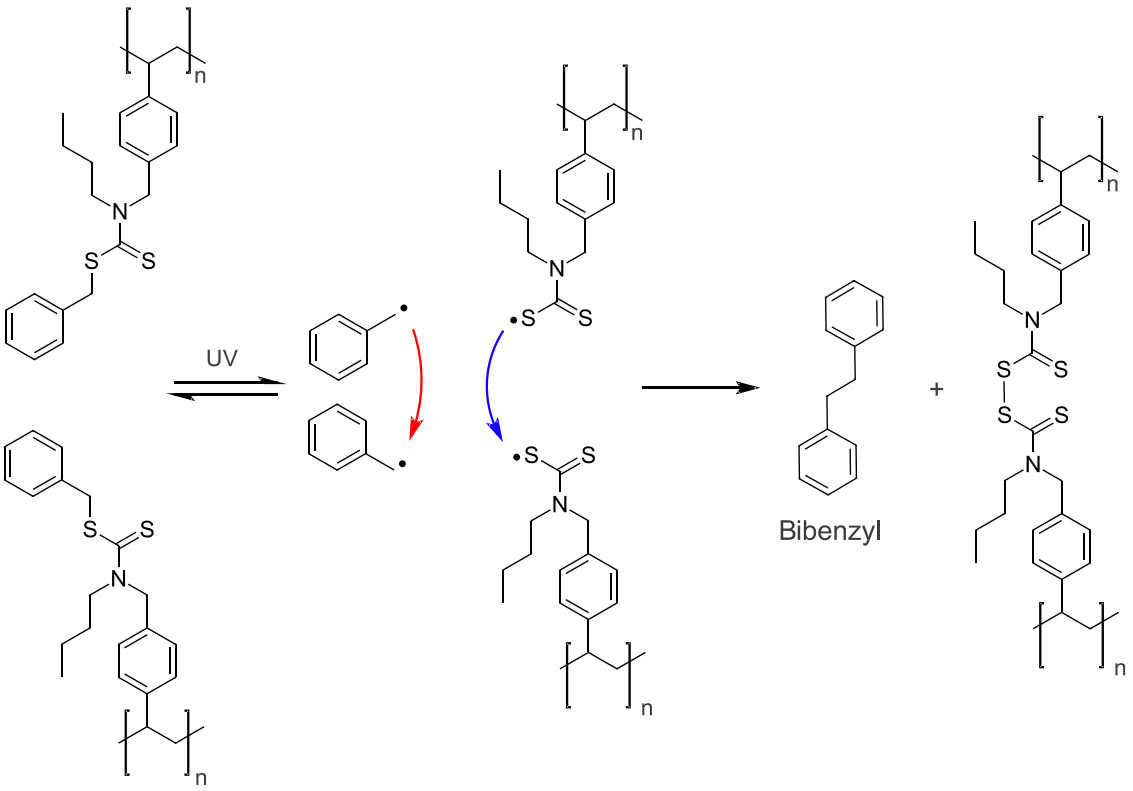
Figure 2-11: ^{1}H NMR of the linear polymer in toluene-d_8 at 100ºC

The analysis with gel permeation chromatography (GPC) of the linear polymer (**Figure 2-14**) showed the creation of high molar mass polymer. In the GPC analysis the presence of a small quantity of unreacted inimer was evident in the polymer. The trace amounts of inimer remaining were considered unlikely to affect later processes involving the polymer and it was considered not worthwhile to attempt to completely eliminate it as further purification attempts would be time-consuming and lead to unacceptable losses of polymer.

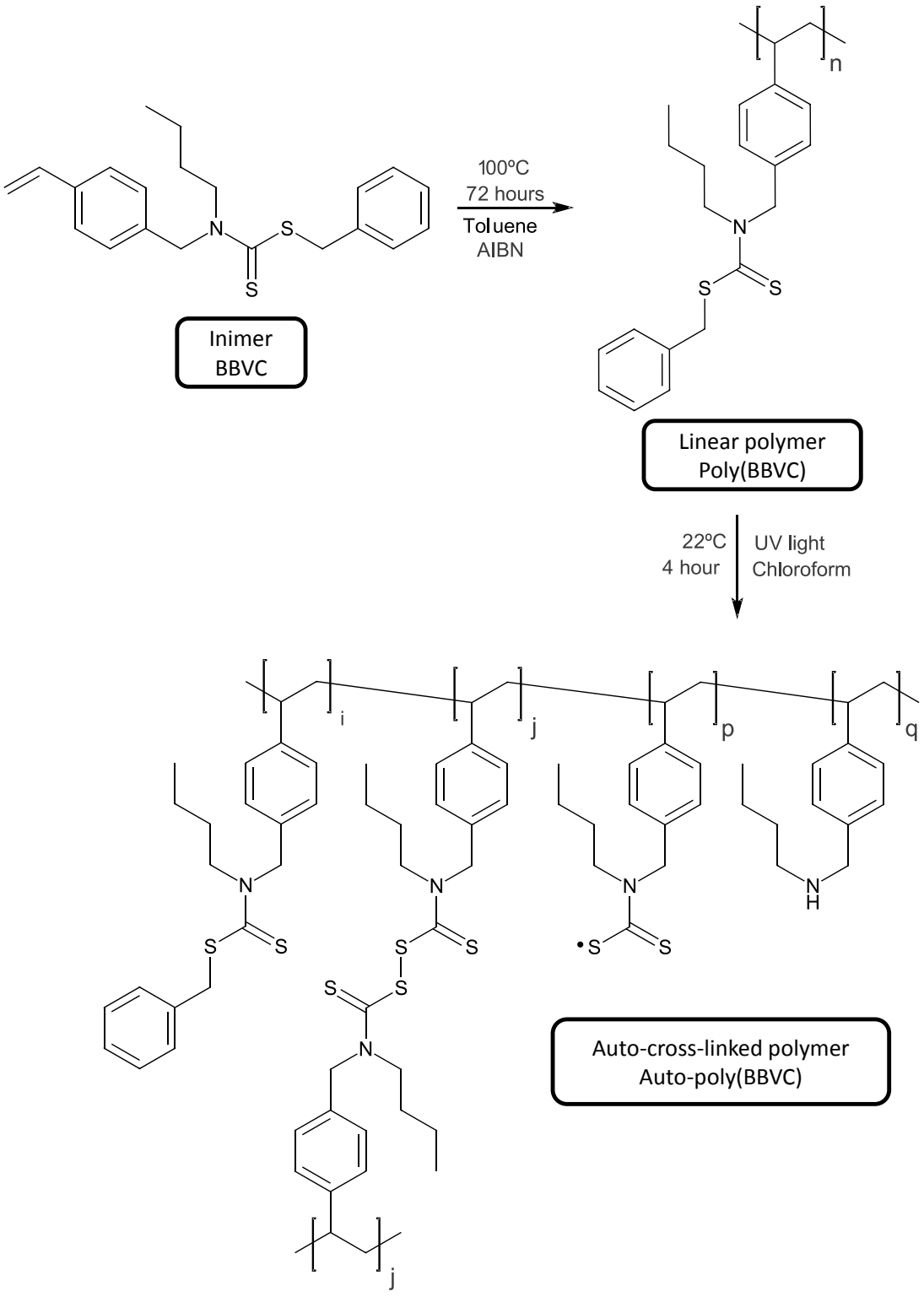
Regarding the kinetics of radical formation during irradiation, the linear polymer showed the same behaviour as the inimer: the intensity of the EPR signal was seen to increase linearly as a function of irradiation time (**Figure 2-9**).

2.5 Synthesis of the auto-cross-linked polymer: Auto-poly(benzyl N-butyl-N-(4-vinylbenzyl)dithiocarbamate) [Auto-Poly(BBVC)]

The following step in the synthetic pathway was the creation of a cross-linked polymer from the linear polymer poly(BBVC) (**Scheme 2-13**). This linear polymer is a macroiniferter that can be irradiated with a UV source in the absence of monomers, creating soluble benzyl radicals and sulphur radicals attached to the polymer backbone. In the normal case of irradiating a dithiocarbamate ester-based iniferter, the radical products formed will recombine to reform the original structure, however when there is a high concentration of radicals forming, as will be the case of irradiating the linear polymer, other reactions become more likely.

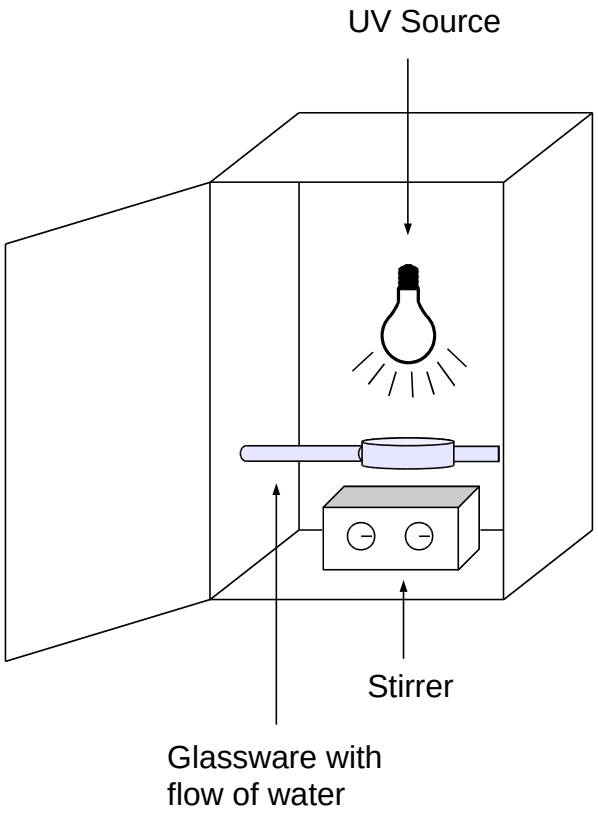


Scheme 2-12: The irradiation of the linear polymer poly(BBVC) generates the photodissociation and the cross-over reaction of radicals, creating a cross-linked polymer and bibenzyl as subproduct



Scheme 2-13: Synthesis of the auto-cross-linked polymer by cross-over radical recombination; secondary amines, dithiocarbamate radicals and unreacted dithiocarbamate have place in the structure since the restricted motion of the polymer chains prevents recombination

One such reaction involves the cross-over reaction where two sulphur-centred radicals recombine to form a dithiuram linkage and two benzyl radicals recombine to form bibenzyl (**Scheme 2-12**). The creation of bibenzyl is irreversible since this molecule is expected to be photostable (Palau *et al.*, 2011). Although the thiuram cross-links can still being rearranged (since the thiuram linkage is photolabile) the number of this links will increase with the time of irradiation and the loss of bibenzyl molecules. The result will be an increase in the average molecular weight of the polymer (or network formation) due to cross-linking and a reduction in the mass of the polymer fraction due to loss of bibenzyl and possibly of other by-product of photodegradation.



Scheme 2-14: Irradiation system, it is a photochemical safety cabinet with glassware that supports the reaction vessel and maintains the temperature with a flow of water (S. I. Patel *et al.*, 2004)

As in the synthesis of the linear polymer, in this synthesis it was used a non-polar solvent: chloroform. Although the chloroform is known to be unstable under UV irradiation (M. E. Simonsen and E. G. Soegaard, 2008) it is another solvent in which the linear polymer is completely soluble and toluene was not necessary because the reaction is performed at room temperature. Another advantage in using chloroform instead of toluene is its low boiling point; making is easy to remove at the end of the photocross-linking reaction. A further benefit of using this solvent is that it does not have a chromophore at the irradiation wavelength (>320 nm), so the solvent does not act as a UV filter during the reaction.

The vessel was placed in a glass water-circulation jacket (**Scheme 2-14**) to control the temperature and the solution was then irradiated for a period using a UV light source placed at a fixed distance from the reaction vessel. The whole irradiation system was covered with reflecting walls to protect the operator and passers-by from exposure to the irradiation from the 300W UV lamp.

Table 2-3: Elemental analysis of the photochemically auto-cross-linked polymer Auto-cross-poly(BBVC)

Photochemically auto-cross-linked polymer	C	H	N	S
Theory(considering 100% of cross-linking)	64.70	7.24	5.03	23.03
Experimental	65.54	7.01	4.11	19.75

Observing the elemental analysis of the photochemically auto-cross-linked polymer (**Table 2-3**) there is a clear decrease in the amount of carbon and hydrogen, probably due the loss of bibenzyl groups in its synthesis (**Scheme 2-12**). The calculations based in that data showed a cross-linking degree of up to 16% in this polymer (**Appendix A**), it is not a high value but big enough to change the properties of the material with respect to the linear polymer.

There was no possibility to record a ^{1}H NMR of the auto-cross-linked polymer in solution due to its insolubility in general solvents. However, the solvent used in

the photopolymerisation and also the supernatant obtained from the precipitations were evaporated and the obtained material analysed by ^{1}H NMR. In both samples the signals of bibenzyl were found in (**Figure 2-12** and **Figure 2-13**) confirming the radical cross-over.

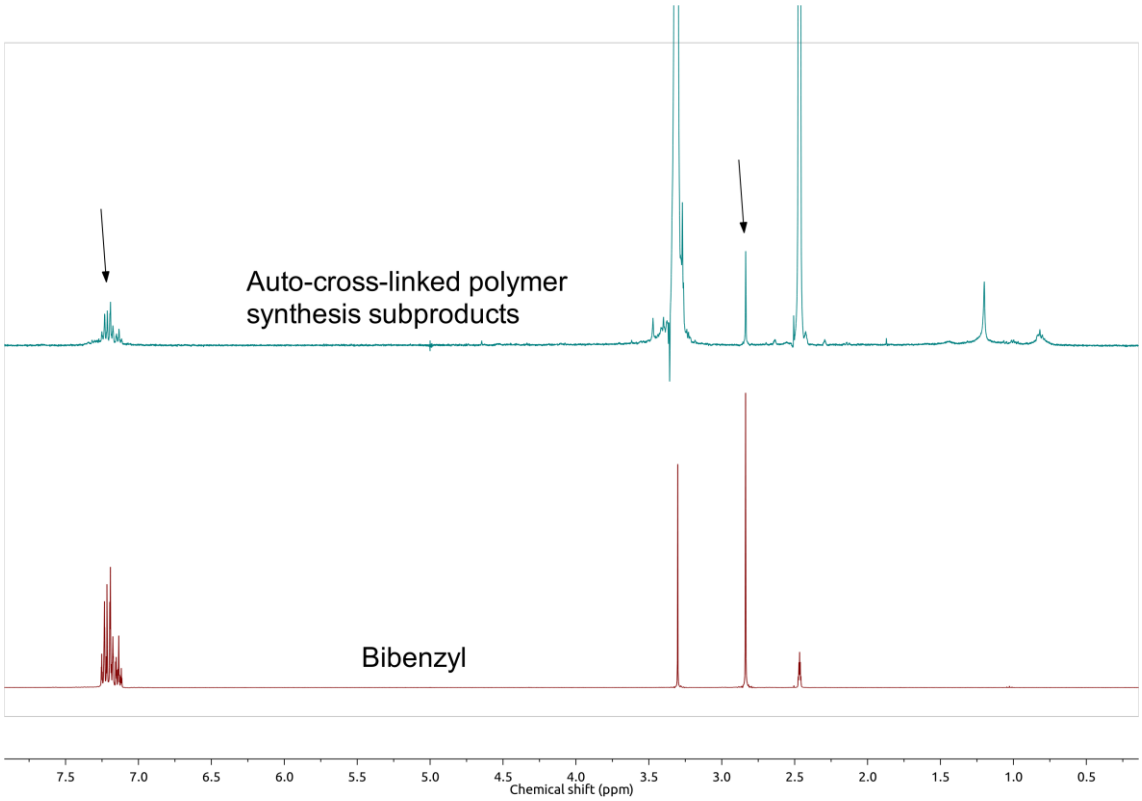


Figure 2-12: Comparison of the ^{1}H NMR from the auto-cross-linked polymer synthesis byproducts with the ^{1}H NMR from an authentic sample of bibenzyl in DMSO-d_6 at 30ºC, the peaks corresponding to the bibenzyl are marked with arrows

Regarding the GPC analysis, the auto-cross-linked polymer was not soluble in tetrahydrofuran (the solvent used for the analysis), only a small fraction of low cross-linked chains could be dissolved in that solvent. Even in this fraction, the formation of new peaks due to high molar mass molecules as well as new signals for low molar mass compounds could be seen (**Figure 2-14**). This

confirmed the creation of cross-links between chains and the formation of the expected by-products of irradiation (e.g. bibenzyl; **Scheme 2-12**).

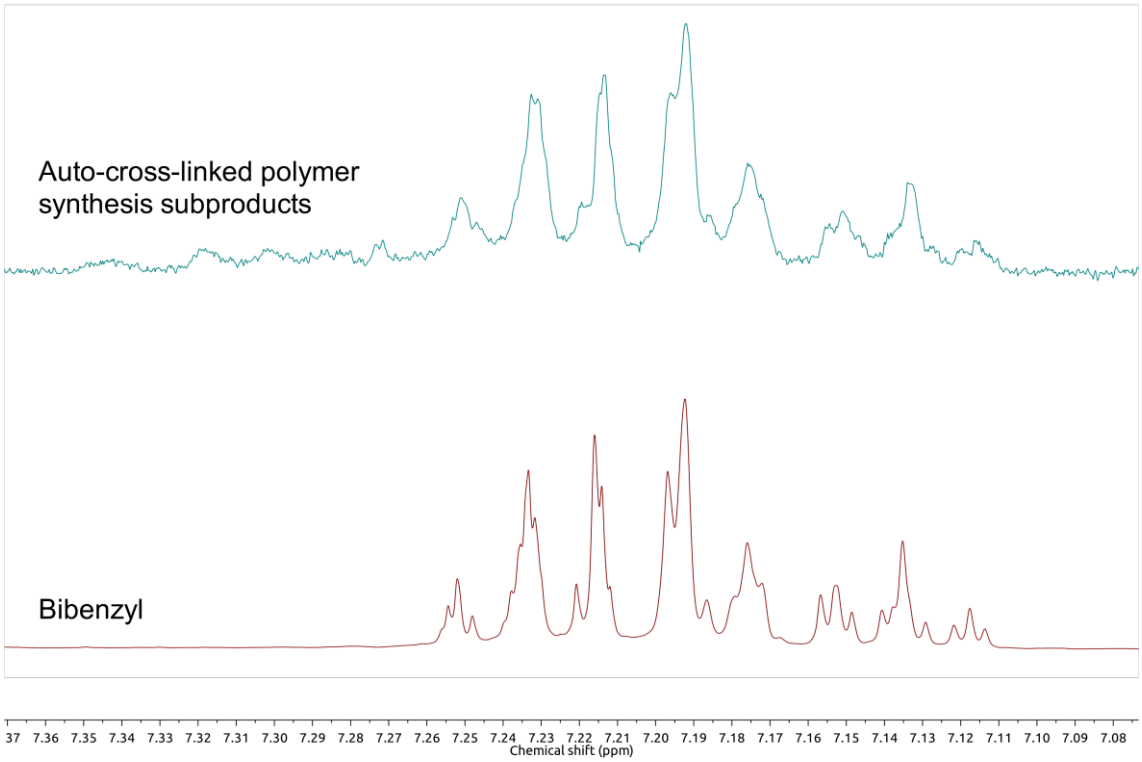


Figure 2-13: Comparison of the aromatic area of the ^{1}H NMR from the auto-cross-linked polymer synthesis subproducts with the ^{1}H NMR from the bibenzyl in DMSO-d_6 at 30ºC

In order to investigate the early stages of photochemical cross-linking, samples of the linear polymer were irradiated for 1, 3 and 5 minutes only and the solutions examined by GPC (**Figure 2-15**). It could be seen how upon irradiation the peak for the linear polymer is decreasing meanwhile new peaks corresponding to higher molar mass material are appearing on the left.

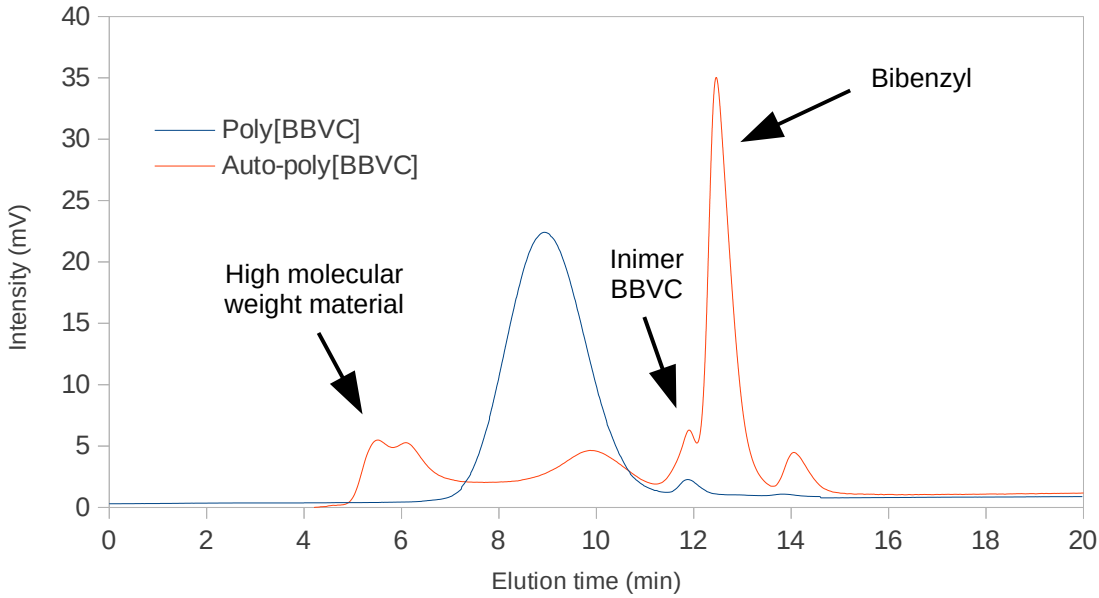


Figure 2-14: Comparison of the GPC from the linear polymer poly[BBVC] and the fraction of the cross-linked polymer auto-poly[BBVC] that was soluble in the eluent

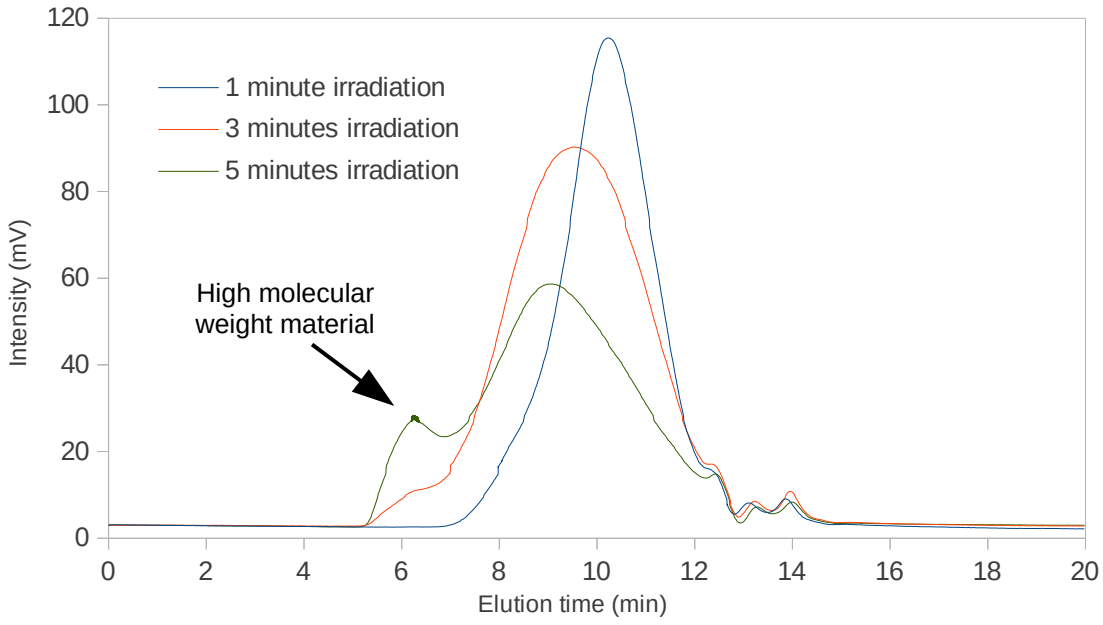


Figure 2-15: Irradiation of the linear polymer poly[BBVC, initial stages of photocross-linking process]

High molecular weight material started to appear after 5 minutes of irradiation, meaning that the process is quite fast in its early stages (**Figure 2-15**). The average molecular weight (polystyrene equivalents) of the polymeric fraction produced after 5 min irradiation was 20 kiloDalton (KDa) (highest peak in green plot in **Figure 2-15**) in contrast with the 14 KDa of the linear polymer (highest peak in blue plot in **Figure 2-15**). The solution also contained a growing fraction with a much higher molecular weight, estimated to be >150 KDa (second highest peak in green plot in **Figure 2-15**), which is most likely formed during the initial stages of gel formation.

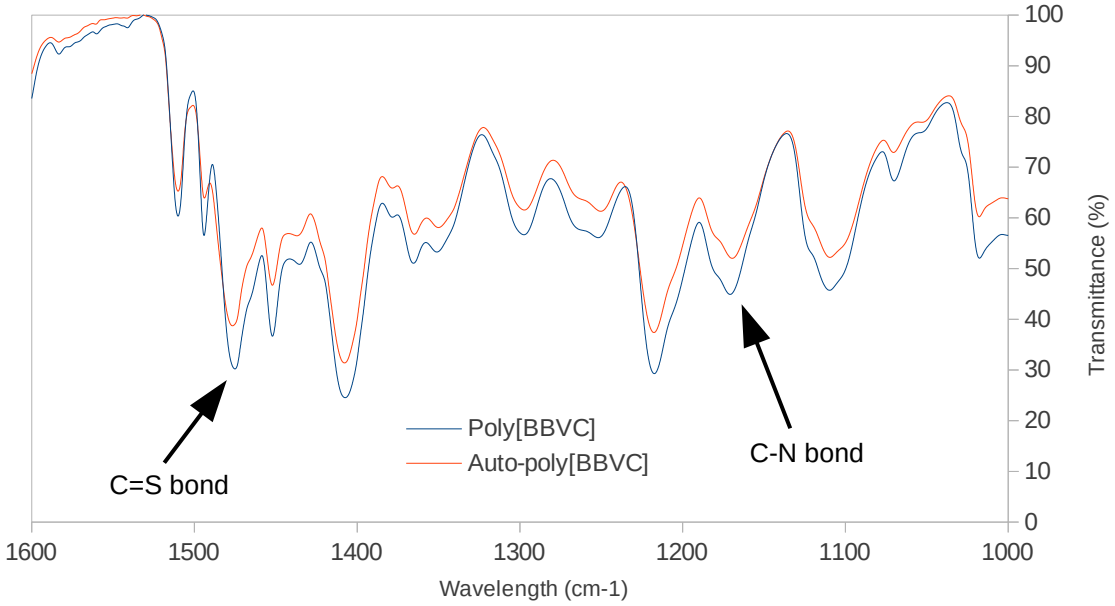


Figure 2-16: Comparison of the FTIR spectra of the linear and auto-cross-linked polymers

The best way to demonstrate the nature of the auto-cross-linked polymer by FTIR is finding the existence of the S-S bond. It was found that the S-S stretching showed a strong peak at 750 cm^{-1} in some compounds of a similar nature (A. Patel & Mequanint, 2008). This peak does not appear in the spectrum of the inimer or in that of the linear polymer, but only in the auto-cross-linked polymer (**Figure 2-17**). The auto-cross-linked polymer FTIR

spectrum (**Figure 2-16**) exhibits a peak at 1174 cm^{-1}, assigned to C=S stretching vibrations (A. Patel & Mequanint, 2008), and a strong absorption band at 1477 cm^{-1} confirming the partial double bond character of the C-N function (Cervantes *et al.*, 1997; Desai *et al.*, 2008; A. Patel & Mequanint, 2008)

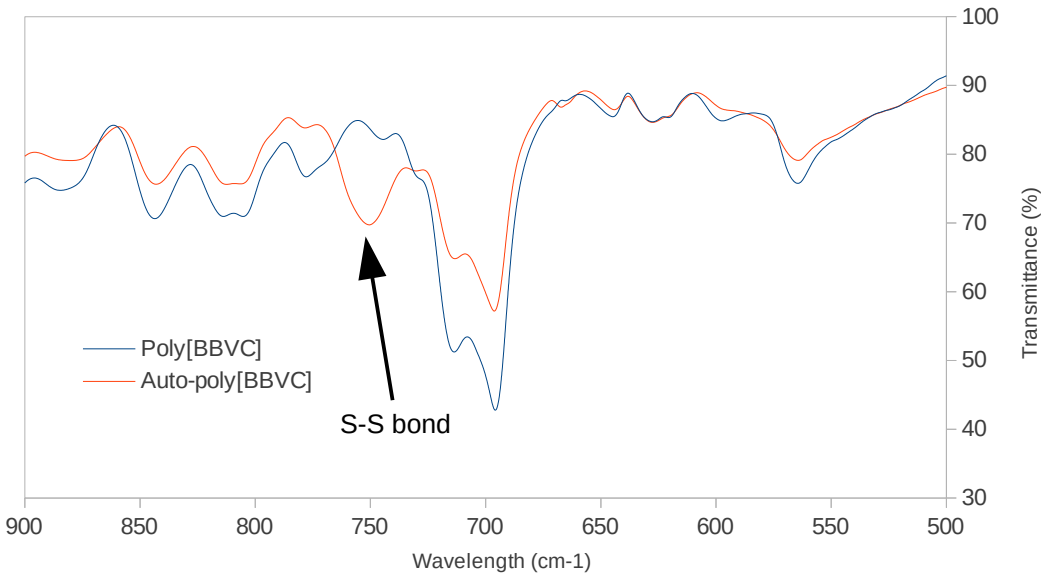


Figure 2-17: New FTIR signal for S-S bond in the auto-cross-linked polymer in comparison to the linear polymer

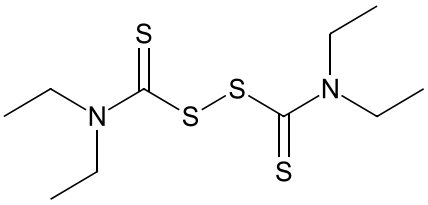


Figure 2-18: Tetraethylthiuram disulphide (TETD)

The FTIR spectrum of the auto-cross-linked polymer was compared with that of tetraethylthiuram disulphide (TETD) (**Figure 2-18**) since both species has thiuram functionality in their structures. It was found that the peak

corresponding to the S-S bond slightly shifted to 767 cm^{-1} in the TETD molecule (**Figure 2-19**).

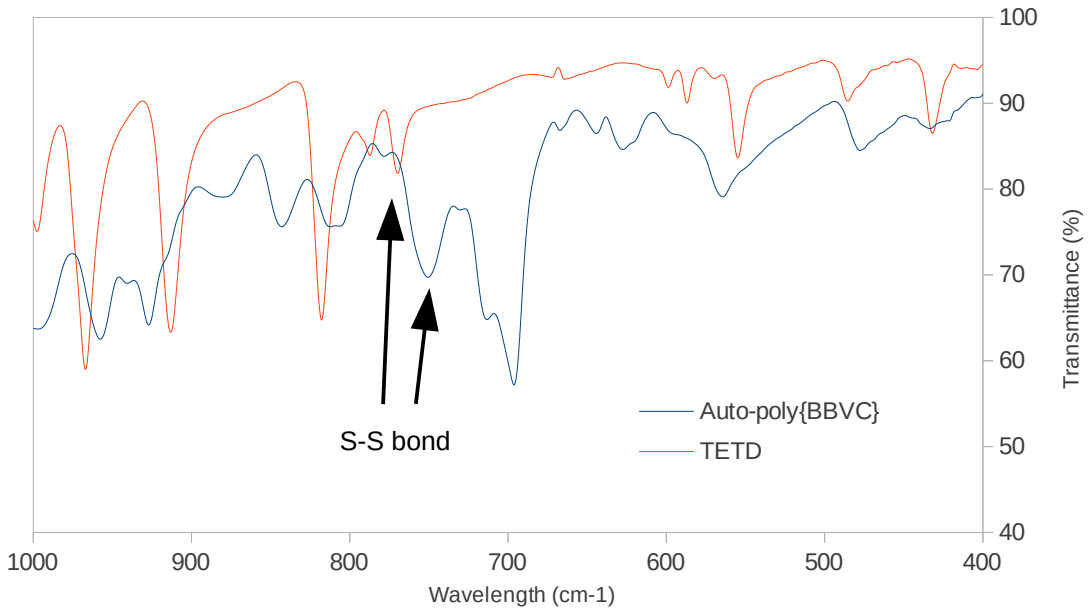


Figure 2-19: Peaks from S-S bond in tetraethylthiuram disulphide and the auto-cross-linked polymer

Regarding the kinetics of radical formation during irradiation, the auto-cross-linked polymer showed different behaviour to that shown by the inimer and linear polymer (**Figure 2-9**), possessing a significant EPR signal before irradiation due to the presence of isolated dormant radical species (**Figure 2-20**). Since this sample had been prepared more than 2 weeks previously, it shows the remarkable longevity of dormant radicals in this system. The generation of additional radical species is expected to occur as a result of dissociation of thiuram groups, present as cross-links between polymer chains. The rate of development of the EPR signal in the case of the auto-cross-linked polymer was not linear with time. The signal did not increase after ~1500s, suggesting that the rates of radical formation and loss were approximately equal.

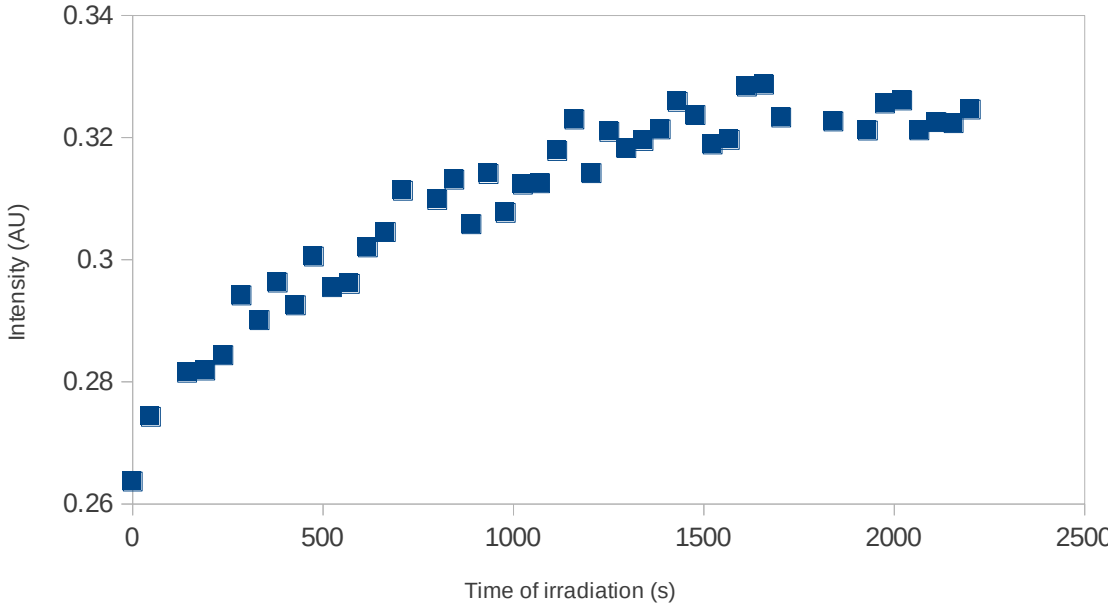


Figure 2-20: Average intensity of the EPR of the cross-linked polymer auto-poly[BBVC] against UV irradiation time

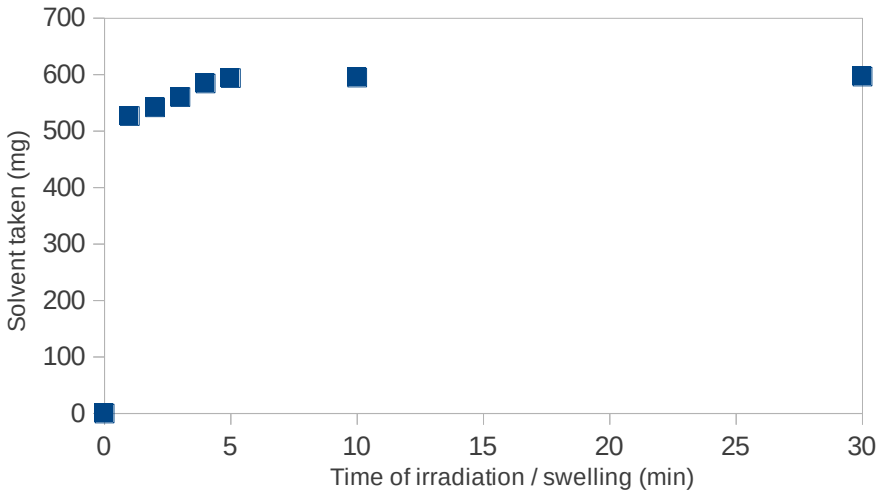


Figure 2-21: Swelling of auto-poly[BBVC] in chloroform without irradiation

The swelling properties of the auto-cross-linked polymer were analysed with a very simple but effective procedure. The experiment was divided in two parts, in the first one the polymer was placed in a graduated glass column and it was allowed to swell upon contact with a certain solvent, in this case the chloroform,

which happened to be the solvent in which the polymer swells to its greatest extent. In this first part of the swelling study the plot showed a 740 % swelling of the polymer without irradiation (**Figure 2-21**).

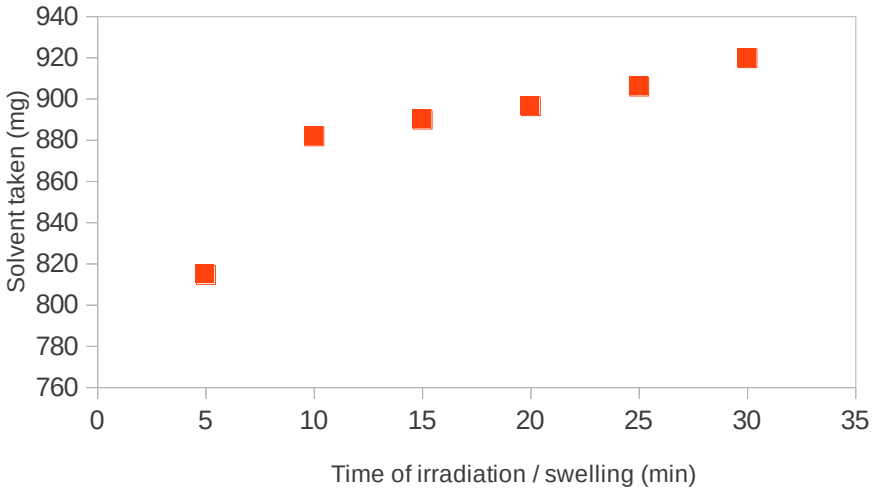


Figure 2-22: Swelling of auto-poly[BBVC] in chloroform with UV irradiation

In the second part of the swelling studies the auto-cross-linked polymer was suspended in $CHCl_3$ allowing the polymer to swell meanwhile the whole system was exposed to a UV light. The aim of the study was to find the differences in the swelling of the polymer upon irradiation. Observing the plot of the data from the second part of the swelling study (**Figure 2-22**) it was noticed an increase of the swelling abilities of the polymer compared with non-irradiated samples. The swelling of irradiated polymer was 920%, a great increase as compared with samples kept in the dark (**Figure 2-23**). The explanation could be that with UV irradiation the polymer cross-linking bonds are breaking, allowing the matrix to take up larger amounts of solvent.

Further studies of the swelling activities were carried out. The hypothesis was that this polymer would follow a cyclic swelling-deswelling process when the irradiation conditions were changed:

- Initially, in the dark the polymer would allow the solvent molecules to be accommodated into its matrix resulting in swelling.
- Then upon irradiation the cross-links would break allowing a greater volume of solvent to enter the matrix and the swelling would increase.
- Removing the irradiation source the radicals would regenerate the cross-links between chains and the swelling would be reduced to the initial value that obtained in the dark.
- When the polymer would be irradiated again its swelling would increase and so on.

Experiments were carried out to test this property in the polymer but this cycle swelling feature was not found, presumably because there is no restoring force to allow the further swollen polymer to contract to its original volume and new cross-links are formed that stabilise the more highly swollen state.

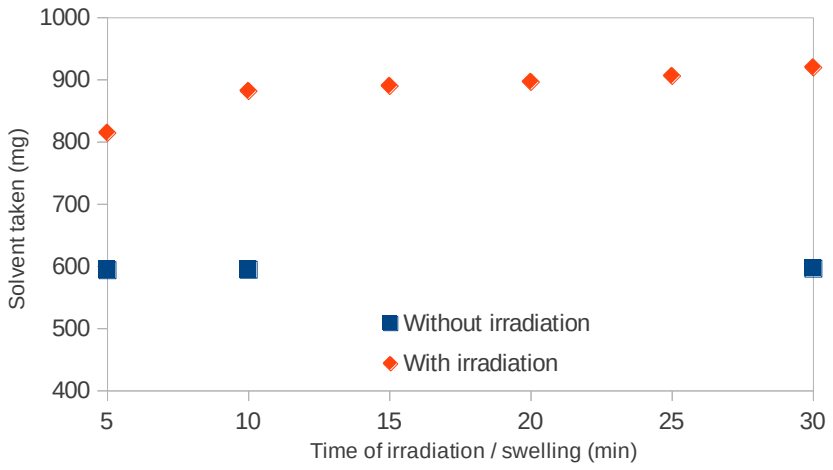
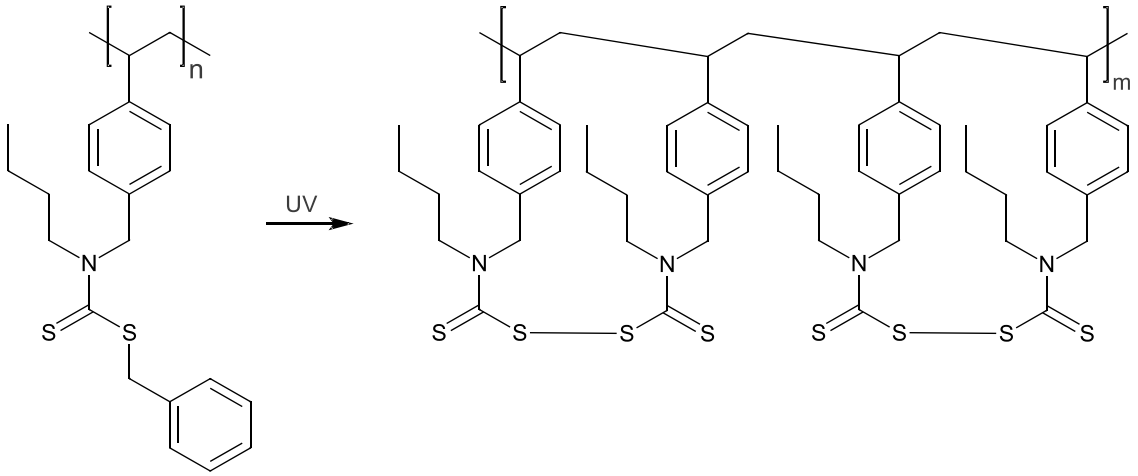


Figure 2-23: Comparison of swelling of auto-poly[BBVC] in chloroform with and without UV irradiation

2.6 Synthesis of the de-cross-linked polymer: De-cross-poly(BBVC)

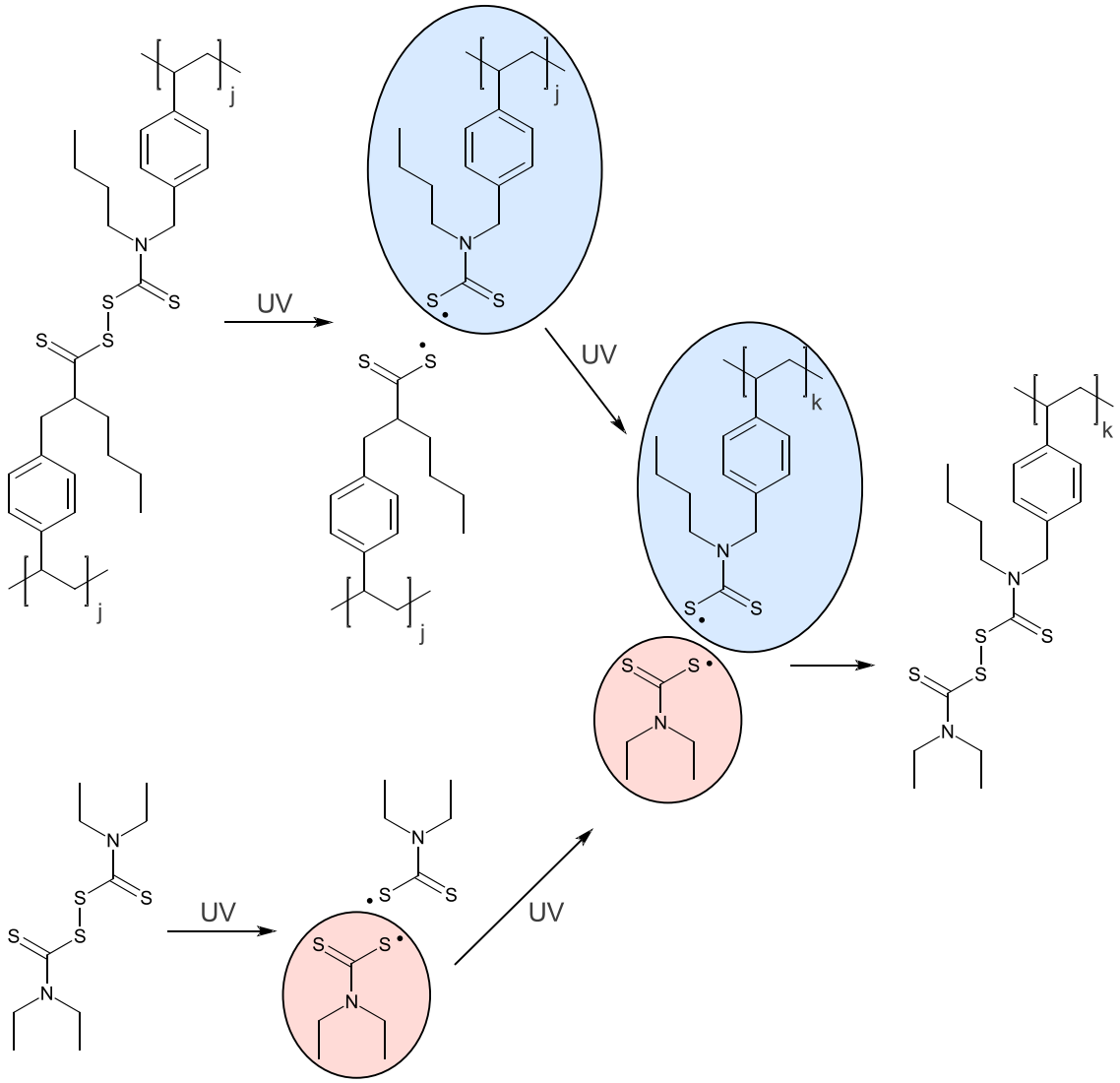
The last part of the process is the conversion of the auto-cross-linked polymer into another linear polymer via cleavage of the cross-links (**Scheme 2-17**). The hypothesis behind the idea is that if an excess of any free radical species is incorporated to the solution of the auto-cross-linked polymer, during UV irradiation in a suitable solvent recombination reactions would occur, eventually resulting in a steady-state situation according to the concentrations of the individual species and the reaction rates of the individual exchange processes. The system can then be allowed to return to a new stable state by removal of the source of UV light (**Scheme 2-16**).



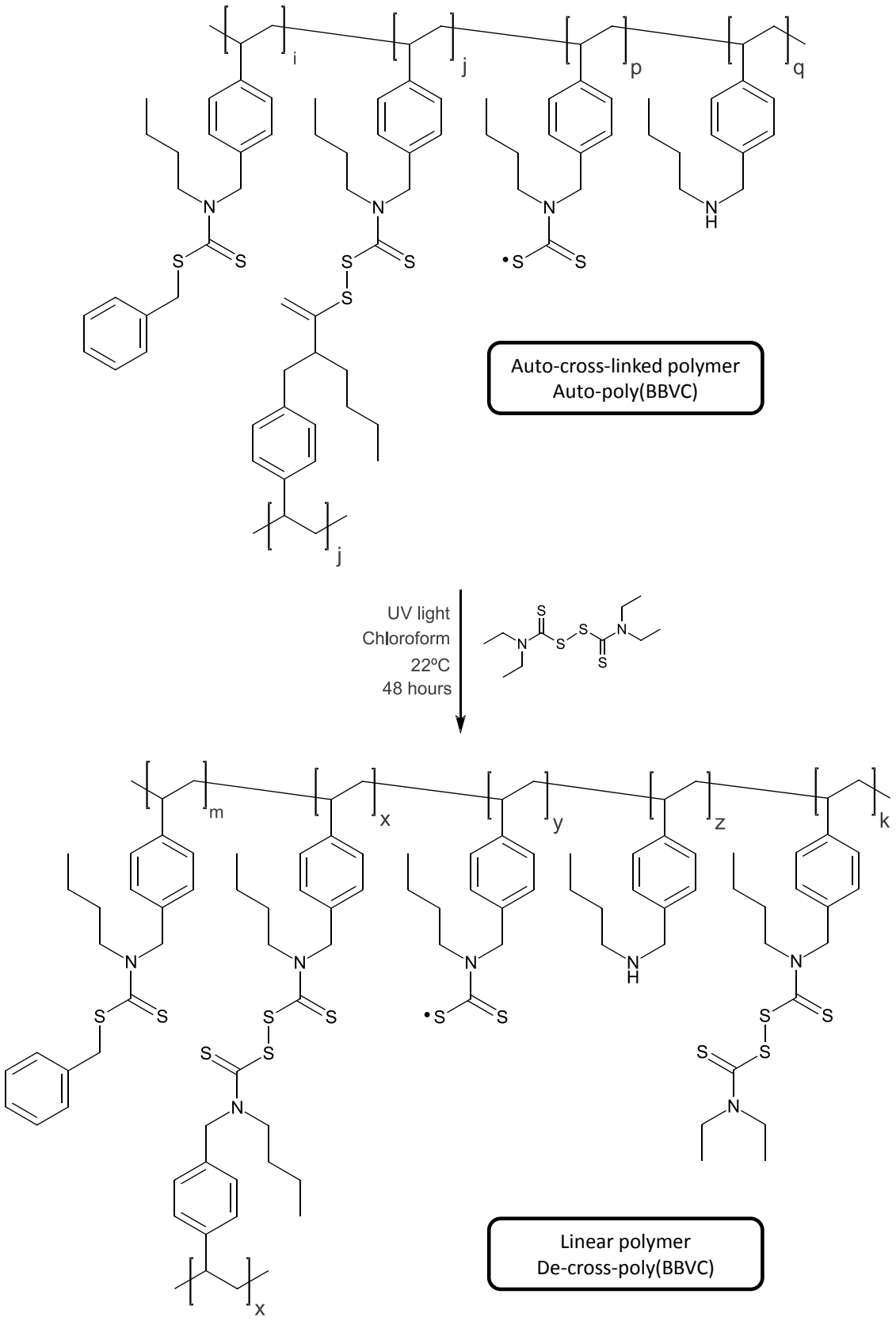
Scheme 2-15: Breakage of the disulphide bonds and intramolecular rearrangements

It is important to notice that the degree of cross-linking will not be zero; there will be some remaining cross-links in the structure, which is the reason why they are depicted in the **Scheme 2-17**. To check the possibility of the de-cross-linking process, a suspension of the auto-cross-linked polymer with an excess of tetraethylthiuram disulphide (TETD) was irradiated. After several hours of irradiation the solubility of the new polymeric material was not evident but after

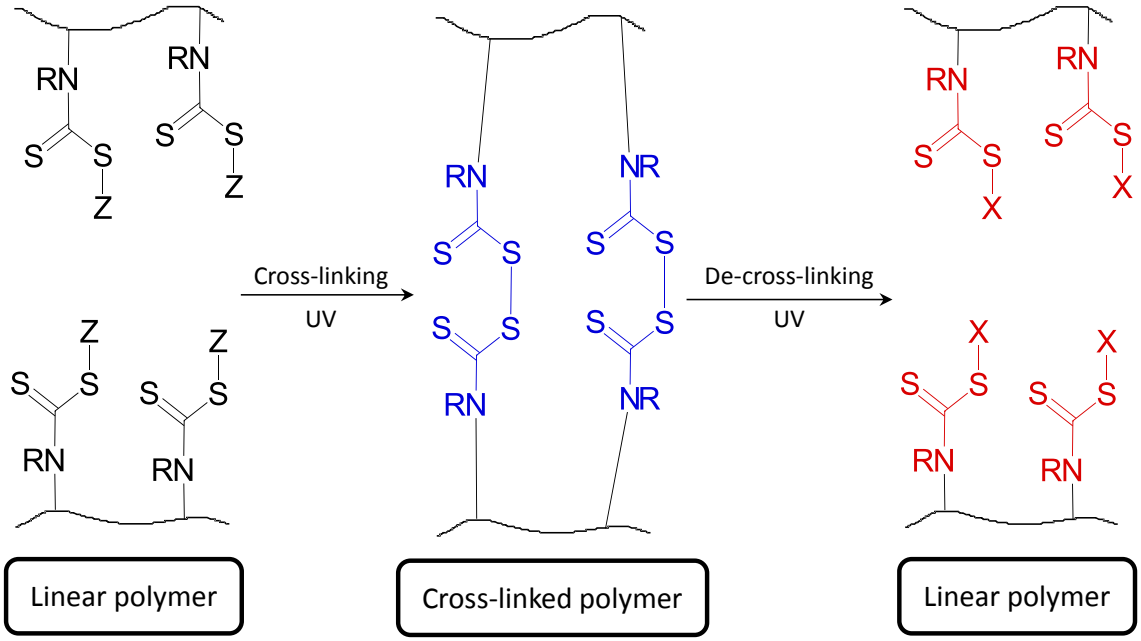
several hours standing in the dark the precipitate disappeared leaving a clear solution (**Scheme 2-18**). The auto-cross-linked polymer was found to be completely insoluble in chloroform regardless of how long it was left to stand. As a first observation the total solubility of the solution was a good sign of the success in the process.

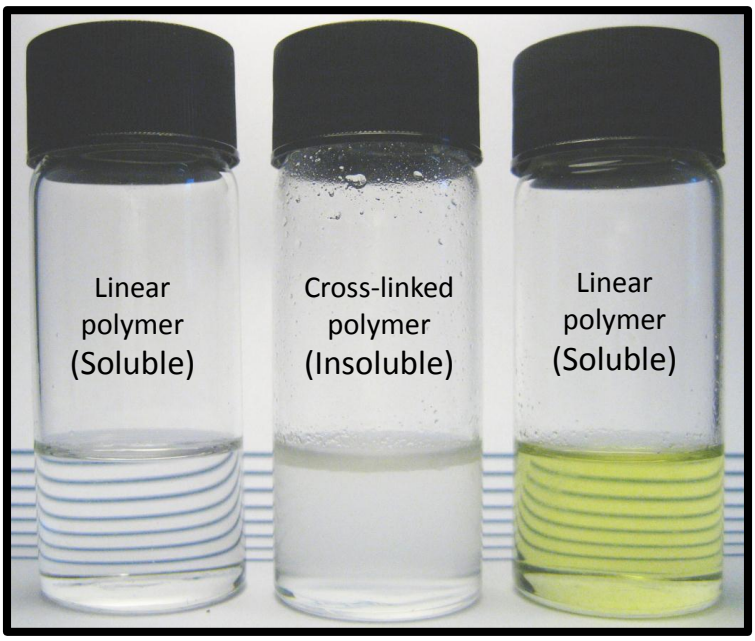


Scheme 2-16: Irradiation of the cross-linked poly(BBVC) in the presence of tetraethylthiuram disulphide



Scheme 2-17: De-cross-linking process of the auto-cross-linking polymer





Scheme 2-18: Conversion of the linear polymer into a cross-linked polymer and reconversion to a linear polymer (García-Con *et al.*, 2010)

That process would lead to the liberation of the polymer chains to the solution due a dramatic decrease of the cross-linking degree and a way to control the solubility of this cross-linked polymer. If the radical added to the solution has a dithiocarbamate nature the pendant groups in the chains will have the thiuram

disulphide structure (**Scheme 2-16**). There were some indications of the possibility of this process: In an early experiment to synthesise the auto-cross-linked polymer from the linear polymer it was possible to redissolve the precipitate gel formed at the beginning of the process. After 7 hours of irradiation the gel disappeared giving way to a compound similar to the linear polymer, but with longer chains. No higher molecular mass material was found. It could happen that the auto-cross-linked polymer was actually synthesised but the excessive time of irradiation allowed the breakage of the disulphide bonds and intramolecular rearrangements (**Scheme 2-15**). The experiment was initially considered as unsatisfactory and the material was not further investigated.

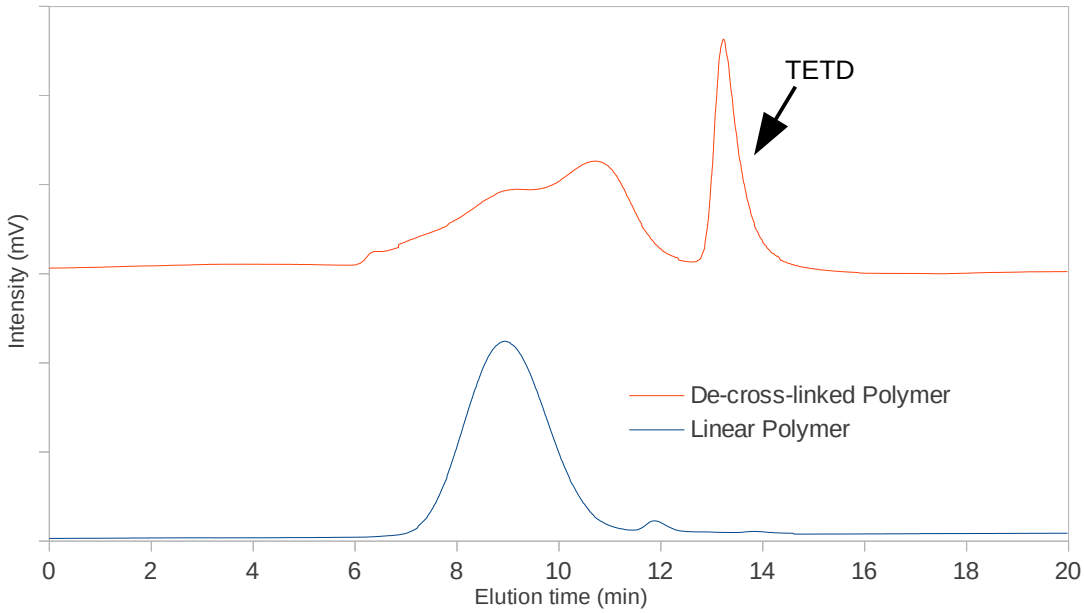


Figure 2-24: Comparison of the GPC of de-cross-poly(BBVC) and the linear polymer poly(BBVC)

The GPC was consistent with the change in the auto-cross-linked polymer (**Figure 2-24**). Analysis of the solution showed that the resulting polymeric material has a range of molecular masses closer to the linear poly(BBVC) polymer.

The ^{1}H NMR spectrum of the de-cross-linked polymer was compared with that of the linear polymer poly(BBVC) (**Figure 2-25**) since they have some similarities in structure. The integrals were normalised to the benzylic protons close to the nitrogen atom since those stays unaltered during the process. It was noticed a decrease in the aromatic protons, a decrease in the benzylic protons close to the sulphur atom and peaks corresponding to polymer-bound thiuram groups appeared. All these signs were consistent with the process and structures proposed.

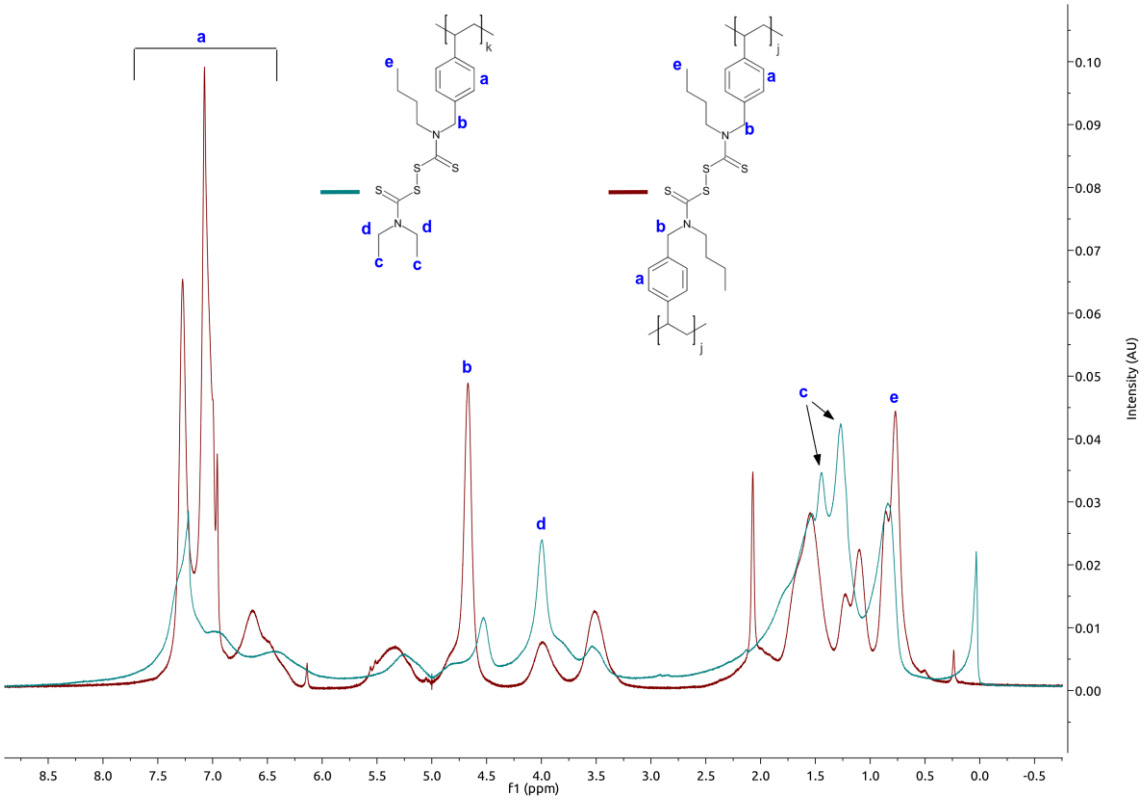


Figure 2-25: Comparison of the GPC of de-cross-poly(BBVC) and the linear polymer poly(BBVC)

2.7 Conclusions

A monomer-initiator (inimer) containing dithiocarbamate groups was synthesised with good yields using an easy protocol.

The inimer was polymerised to generate a linear polymer with pendant dithiocarbamate groups.

A cross-linked polymer was synthesised via photo-cross-linking of the dithiocarbamate groups from the linear polymer. This cross-linked polymer was created without the addition of external cross-linkers.

The cross-links of the cross-linked polymer were removed via photo-de-cross-linking process, yielding a linear polymer with pendant thiuram groups.

The swelling and photo-induced swelling of the cross-linked polymer were investigated. The polymer was able to house more solvent in its matrix when it was irradiated with UV light.

2.8 Future work

One disadvantage in the use of dithiocarbamate molecules is their toxicity, especially because they generate hazardous products upon decomposition. One challenge would be finding structures that would minimise the toxicity.

The temperature required to synthesise the linear polymer was higher than expected. That could affect some of the dithiocarbamate functionalities. The use of a co-monomer with higher reactivity could make the polymerisation temperature decrease, although the density of dithiocarbamate groups could also decrease.

The auto-cross-linked polymer is more a gel than a real polymer since its degree of cross-linking is quite low compared with highly cross-linked materials. It has advantages like its great swelling capabilities but it has also disadvantages. It is difficulty to manipulate, since it sticks to surfaces, and it is fragility compared to a proper cross-linked polymer. The disadvantages could be resolved if a cross-linker is added during the photo-cross-linking process. It would be interesting to try different cross-linkers in different proportions and test the materials synthesised. The proposed cyclic swelling-deswelling photo-process of the cross-linked polymer should be investigated deeply.

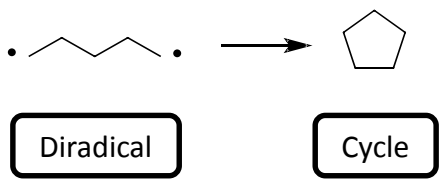
Since the control is one of the important topics in this experiment it is recommended to test this process with different thiurams and different dithiocarbamates in order to functionalise the polymers that were synthesised. The supposed unsuccessful experiment of irradiate for a long time the linear polymer poly(BBVC) should be repeated to study the material and see some similarities with the de-cross-linked polymer synthesised.

3 Synthesis of macrocycles using dormant radicals

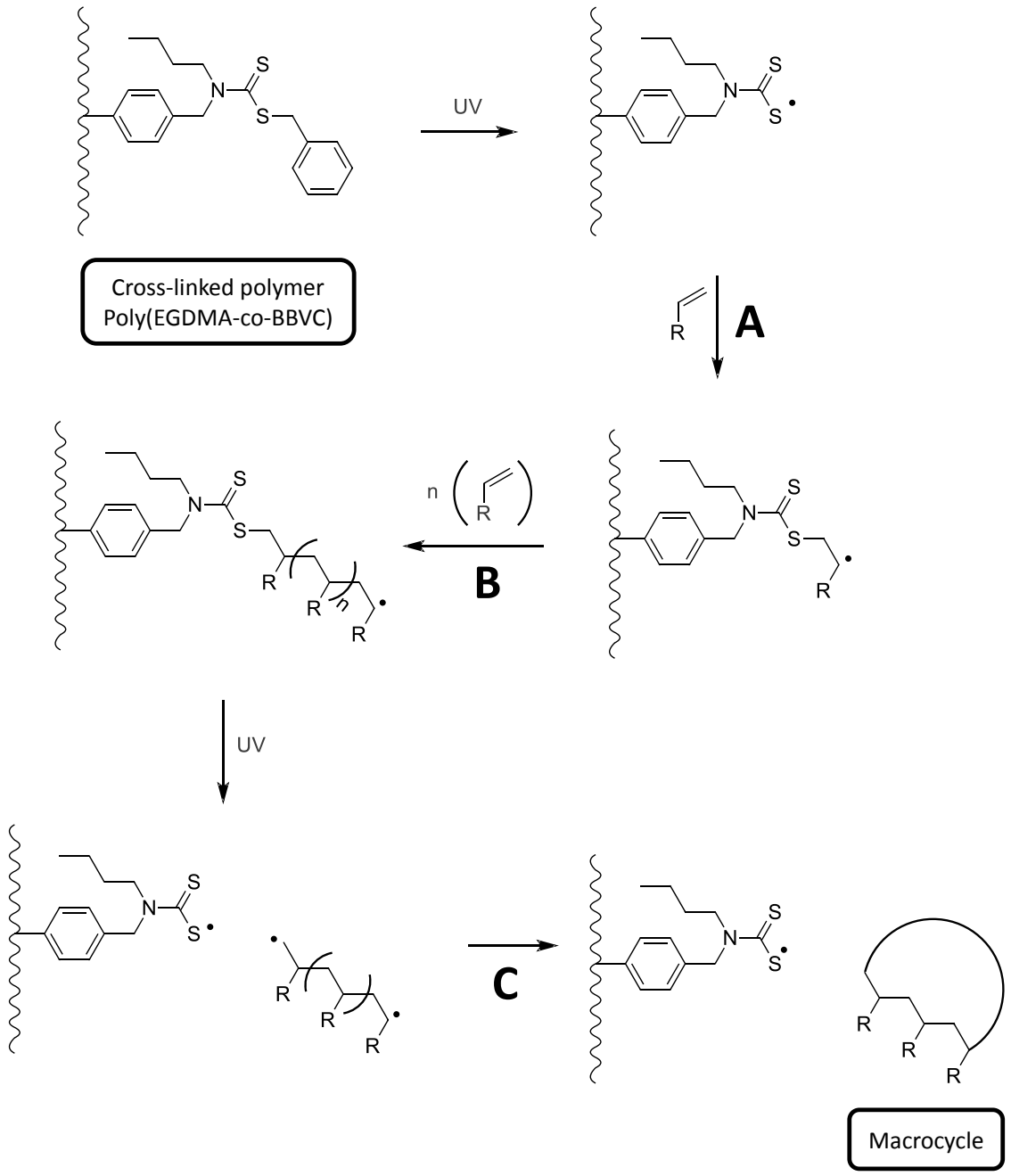
3.1 Introduction

Several cross-linked polymers were tested for their ability to house reactions in "cavities" in their structure. The "cavities" contain dithiocarbamate radicals, created under controlled conditions (i.e. using UV light). The aim was to investigate whether dithiocarbamate radicals in these cavities would be capable of initiating the polymerisation of monomers (**A** in **Scheme 3-2** and **Scheme 3-3**), allow elongation of the linear chain (**B** in **Scheme 3-2** and **Scheme 3-3**), and finally allow the recombination of a diradical to form a macrocyclic addition polymer (**C** in **Scheme 3-2** and **Scheme 3-3**). The process could be repeated indefinitely as the polymer active centres should remain intact. Therefore it could be proposed a catalytic synthetic process.

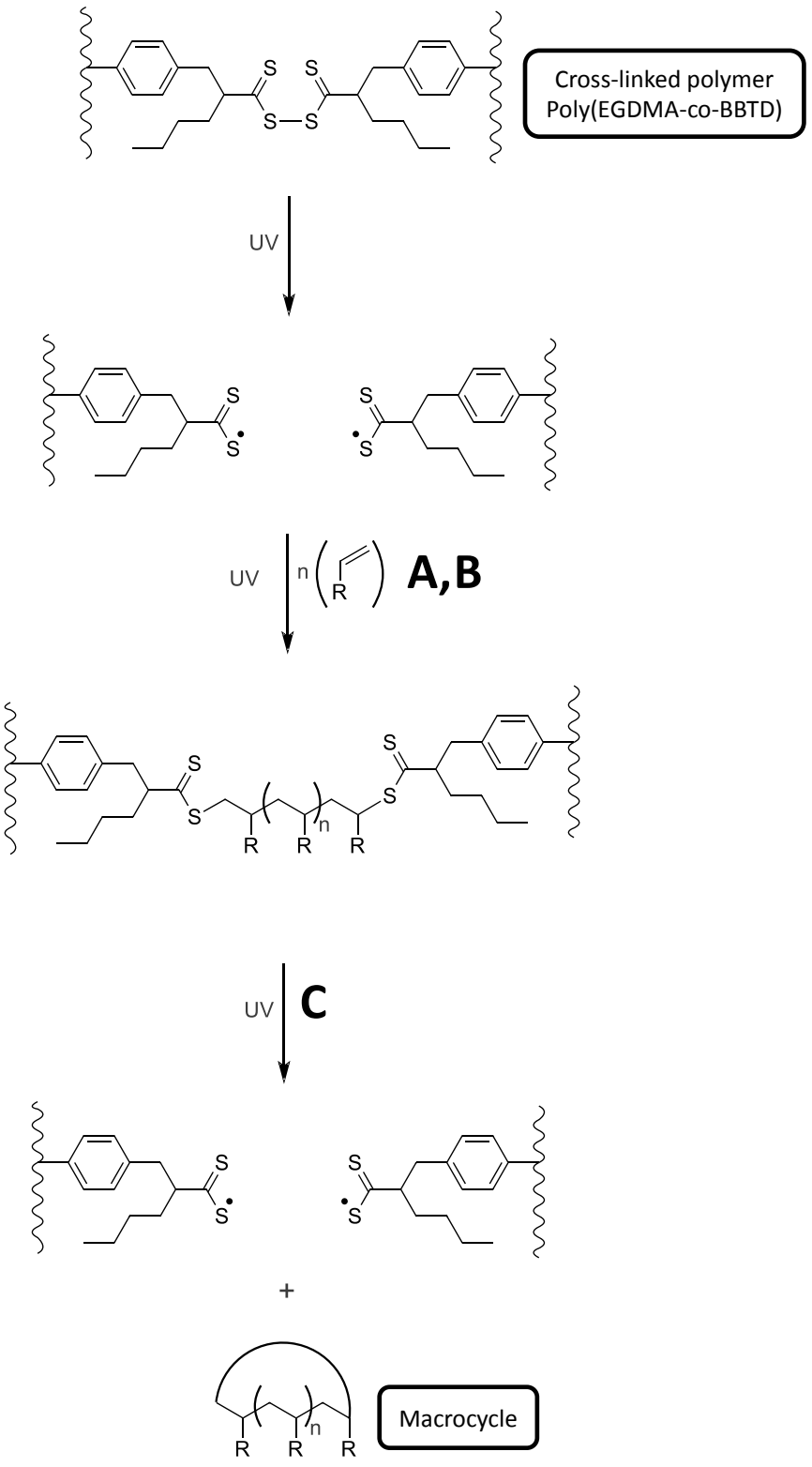
Since the polymers are cross-linked they will not be soluble they will be suspended in a certain solvent and then a monomer will be added. Then the solution will be irradiated with UV light generating active and dormant radicals. A "living" radical polymerisation will be carried out. The chain attached to the sulphur atom/s will increase in length until a diradical would have been formed. The diradicals would be very reactive species and they would generate cycles (**Scheme 3-1**). The formation of the cycle will be more favourable in the case of the more stable cyclic structures (5 and 6 atoms) but in the case of the bigger cycles it would maybe lead to a very interesting synthetic process because that will create a macrocycle in the cavities of the net.



Scheme 3-1: The pentane diradical is stabilised forming the cyclopentane ring



Scheme 3-2: Synthesis of a macrocycle using dithiocarbamate groups in the matrix of the cross-linked polymer Poly(EGDMA-*co*-BBVC) irradiated with UV light



Scheme 3-3: Synthesis of a macrocycle using dithiocarbamate groups in the matrix of the cross-linked polymer Poly(EGDMA-*co*-BBTD) irradiated with UV light

Two different polymers were tested: one polymer having dithiocarbamate functionalities (**Figure 3-1**) and the other polymer containing thiuram functionalities (**Figure 3-2**). Both of the functionalities are able to generate sulphur-centred radicals upon irradiation of UV light but two sulphur-centred radicals are created within the thiuram. That would allow a different mechanism for both approaches.

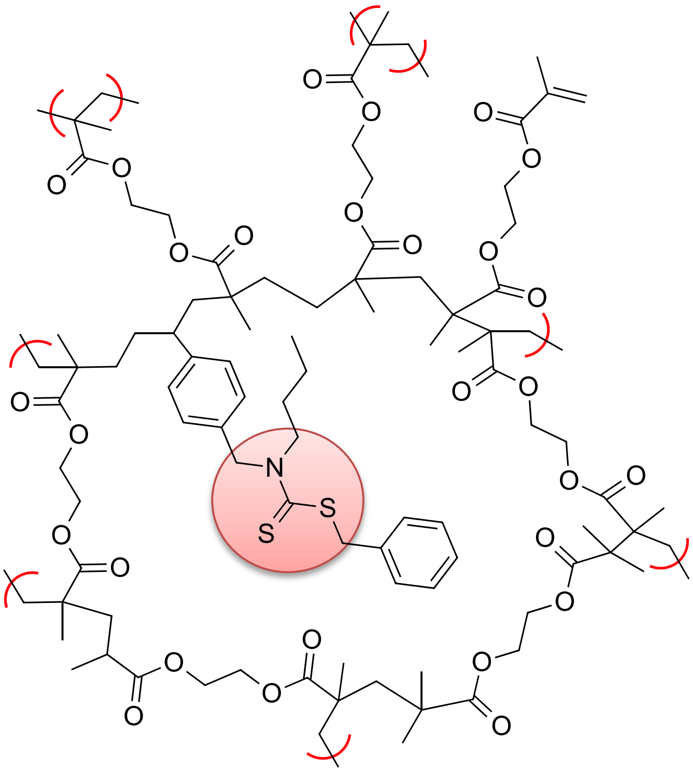


Figure 3-1: Cross-linked polymer with dithiocarbamate functionalities (red circle) in its cavities: Poly(EGDMA-*co*-BBVC); the red brackets represent links to other molecules

The cross-linked polymer with dithiocarbamates in its cavities would be made with the inimer BBVC (**Figure 3-4**), synthesised in the **Section 2.3**, and a cross-linker of choice, ethylene glycol dimethacrylate (EGDMA) (**Figure 3-3**). The method of efficiently synthesising polymers with that combination of inimer / cross-linker was investigated.

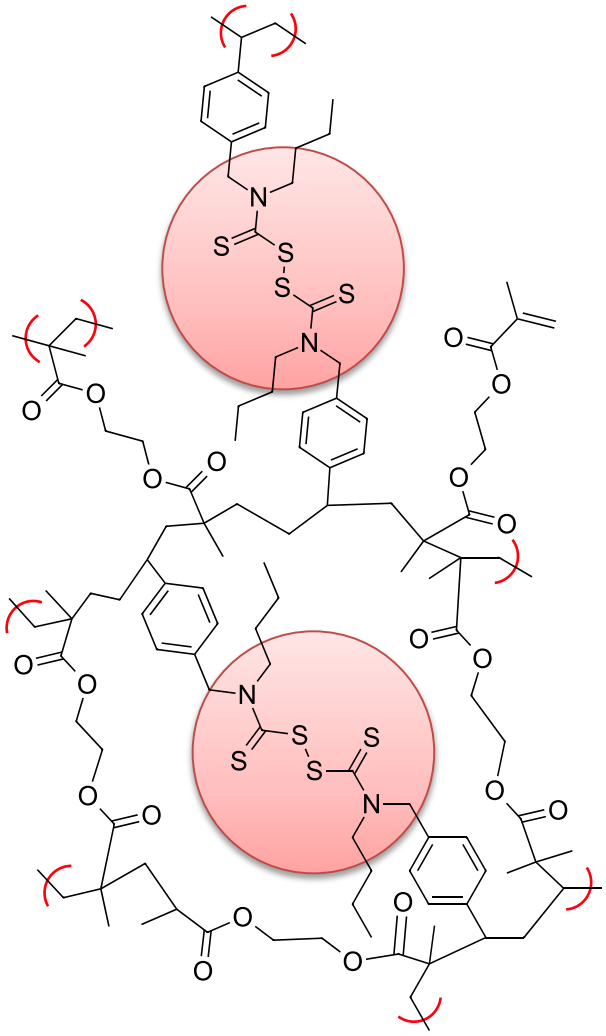


Figure 3-2: Cross-linked polymer with dithiocarbamate functionalities (red circles) in its cavities: Poly(EGDMA-*co*-BBTD); the red brackets represent links to other molecules

To generate the cross-linked polymer with thiurams in its cavities it was necessary to synthesise another inimer. The new inimer should have a thiuram functionality. To generate that inimer the secondary amine NBVA (**Figure 3-5**), created to synthesise the inimer BBVC, would be used. This lead to an inimer that also had a symmetric structure with two double bonds (**Figure 3-6**). Therefore it could act as a cross-linker. It was investigated whether the cross-linked polymer could be generated just with the new symmetrical inimer or an

extra cross-linker would be necessary. The way to efficiently synthesise that symmetrical inimer was also investigated.

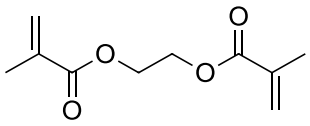


Figure 3-3: A cross-linker: the ethylene glycol dimethacrylate (EGDMA)

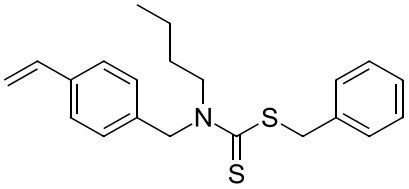


Figure 3-4: The Inimer BBVC, a dithiocarbamate with a double bond

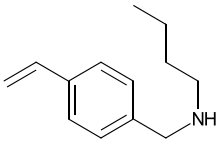


Figure 3-5: The secondary amine N-(4-vinylbenzyl)butan-1-amine [NVBA]

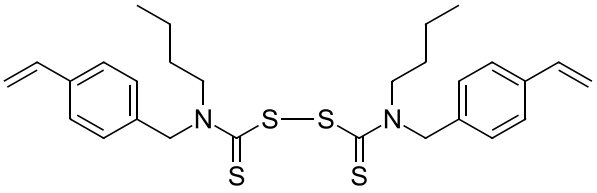
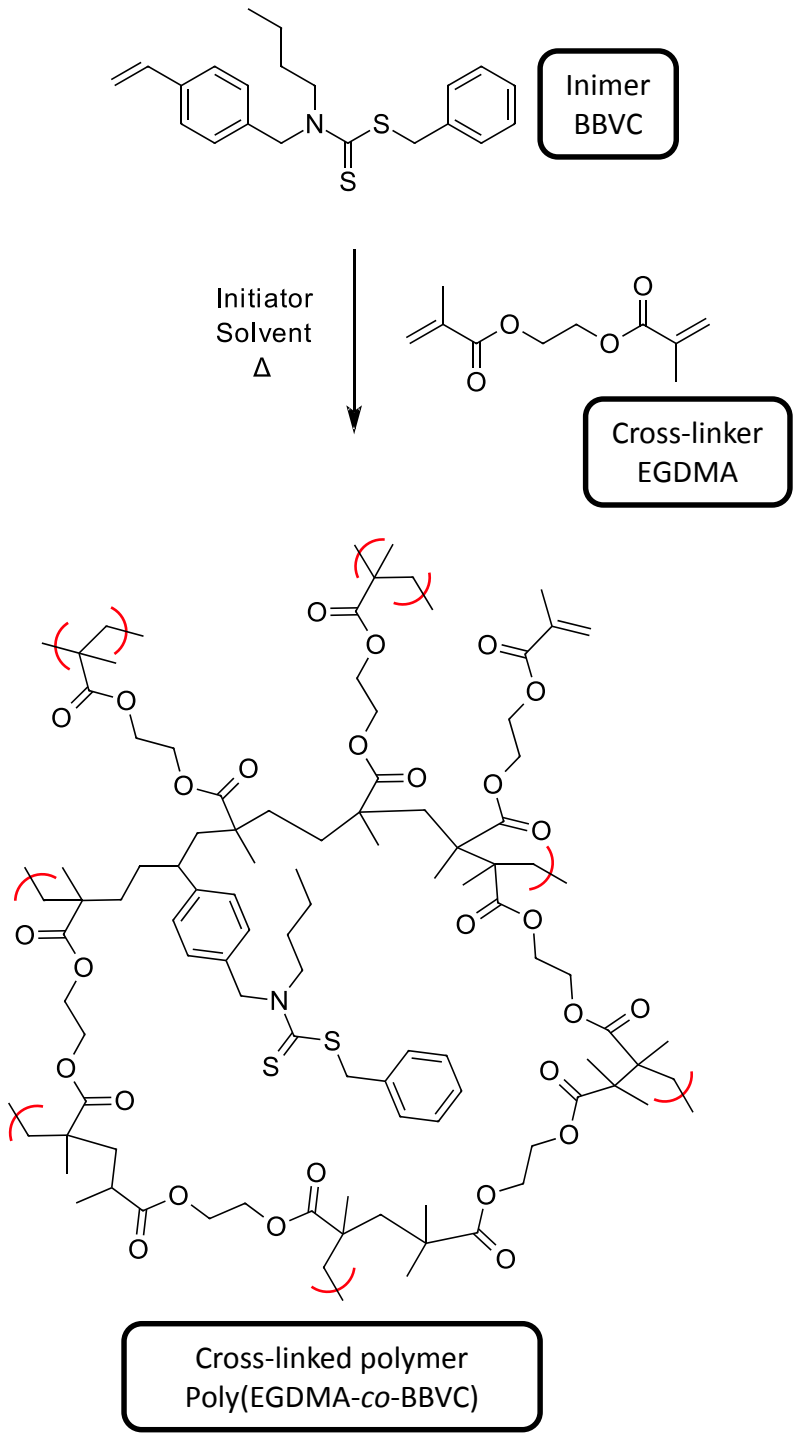


Figure 3-6: The inimer BBTD, a symmetrical molecule with two double bonds and a thiuram functionality

3.2 Synthesis of the cross-linked copolymer with dithiocarbamate functionality: Poly(Ethylene glycol dimethacrylate-*co*-Benzyl N-butyl-N-(4-vinylbenzyl)dithiocarbamate) [Poly(EGDMA-*co*-BBVC)]

The molecules used to synthesise the cross-linked polymer Poly(EGDMA-*co*-BBVC) were the inimer BBVC and the cross-linker ethylene glycol dimethacrylate (EGDMA) (**Scheme 3-4**). The commercially available cross-linker EGDMA is supplied as a mixture with an inhibitor to avoid its polymerisation in the bottle, so it was removed before the cross-linker was added to the reaction vessel. This polymerisation was done in the absence of light to keep the dithiocarbamate functionality intact. Once the polymer was generated it was ground and washed by continuous extraction in a Soxhlet apparatus to remove unreacted monomer and initiator fragments and other low molar mass impurities. The solvent initially used in the Soxhlet apparatus was methanol, followed by ethyl acetate. The latter would be the solvent of choice in any subsequent polymer synthesis since all the starting materials are soluble in it, its toxicity is low, it is cheap, its boiling point is relatively low and it is not very reactive.

Looking at the elemental analysis of the Poly(EGDMA-*co*-BBVC) (**Table 3-1**) it was noticed a decrease in the amount of the sulphur, and a decrease in the amount of carbon. These facts suggest the loss of a part of the inimer molecule via decomposition as it was explained in the **Section 1.9.3**. The calculations showed the proportions 1:2:15 for the BBVC, secondary amine and EGDMA respectively inside the thermally cross-linked polymer (**Appendix D**), so 1 of every 3 molecules of inimer from the polymer has probably lost its sulphur. Some conclusions about the stability of the dithiocarbamate under the effect of the temperature and the time can be considered from the elemental analysis. The DTC groups are stable until 100°C for a period of 24 hours. On the other hand, the DTCs in the thermally cross-linked polymer were showing signs of decomposition after 9 months of storage in the dark at room temperature.



Scheme 3-4: Synthesis of a cross-linked copolymer with dithiocarbamate functionality; red brackets shows connexions to other molecule / s

The important fact is the existence of sulphur in the sample which is coming from the dithiocarbamate functionality. If that functionality decomposes it

liberates CS_2 which would not be possible to detect in the elemental analysis since is highly volatile.

Table 3-1: Elemental analysis of the cross-linked polymer Poly(EGDMA-*co*-BBVC)

Thermally cross-linked polymer	C	H	N	S	O
Theory	62.55	7.07	0.74	3.37	26.28
Experimental	61.73	7.16	1.32	1.84	27.91

The thermally cross linked-polymer was completely insoluble, rendering it impossible to record solution ^{1}H NMR spectra. However ^{1}H NMR tests of unreacted material showed that the amount of unreacted inimer was negligible (**Figure 3-8**).

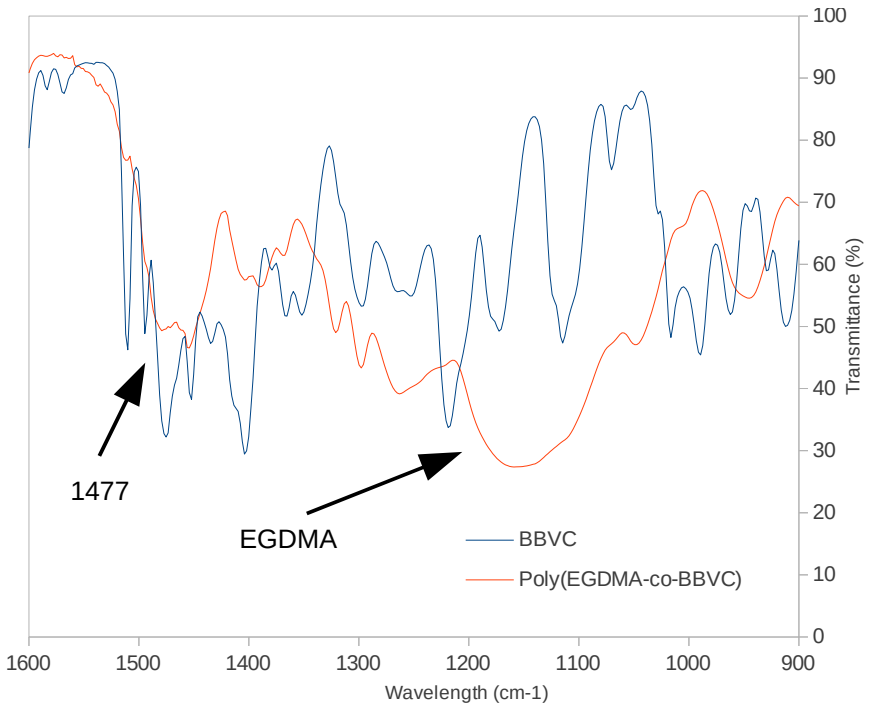


Figure 3-7: Comparison of FTIR spectra of the inimer BBVC and the polymer Poly(EGDMA-*co*-BBVC)

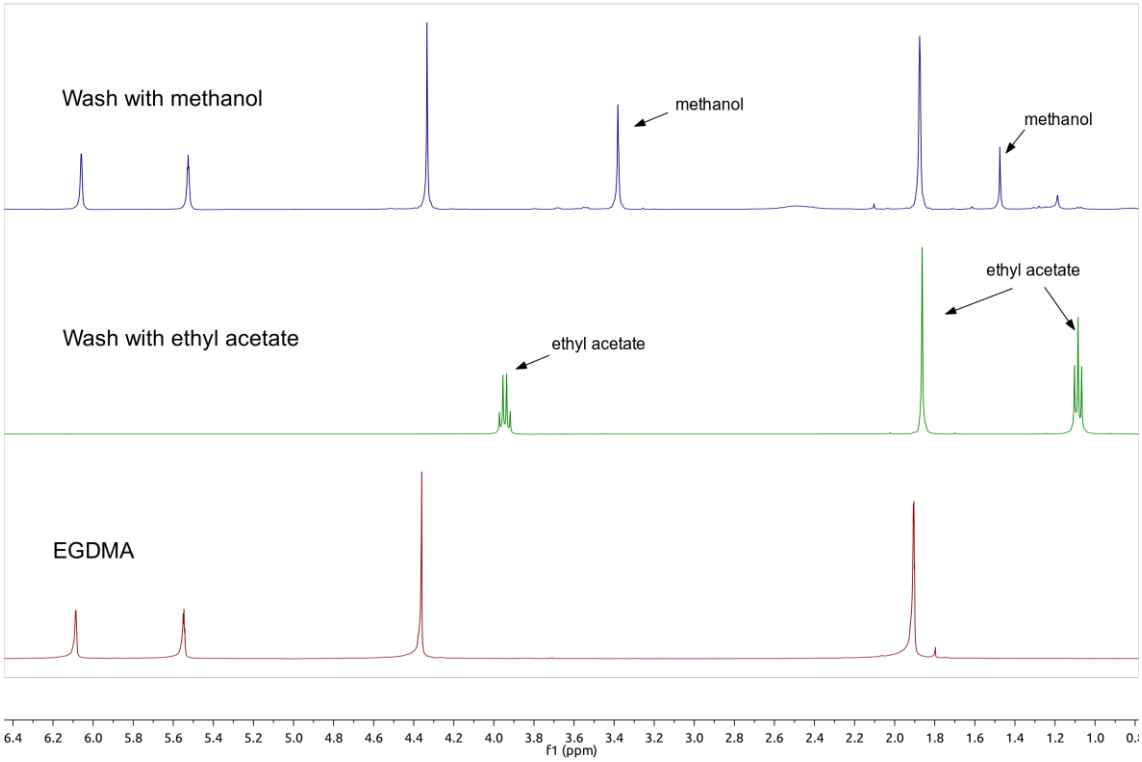


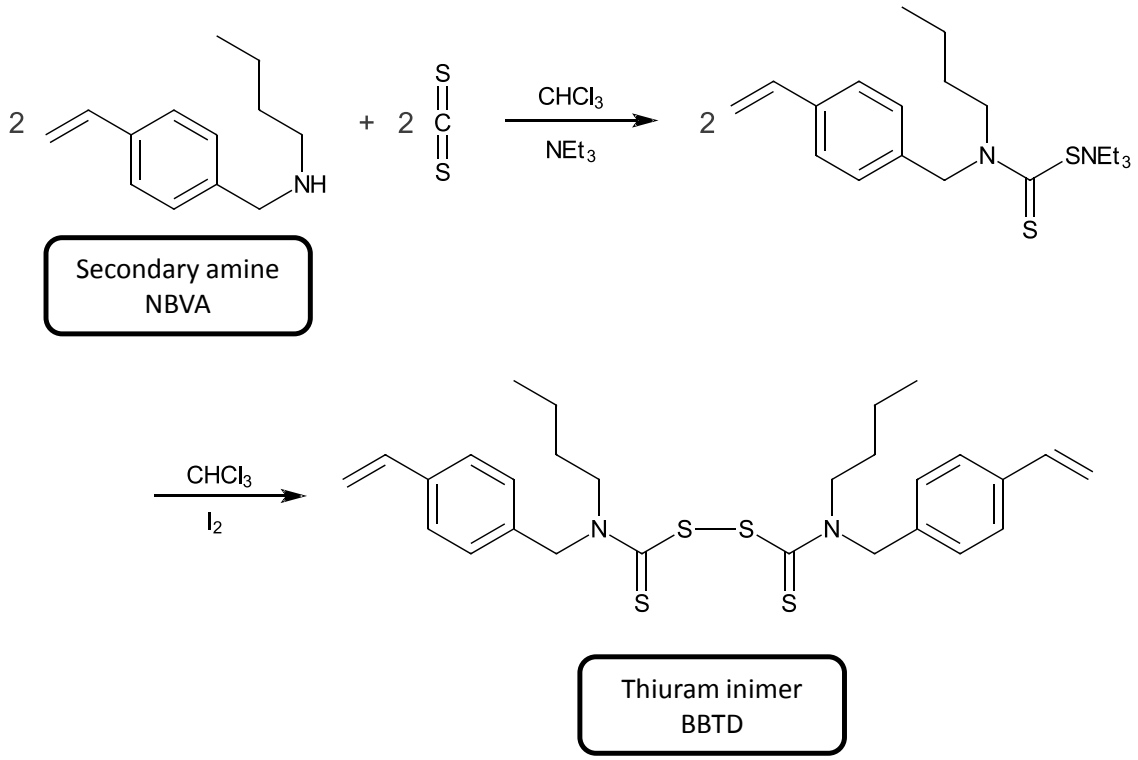
Figure 3-8: ^{1}H NMR of Soxhlet wash impurities of Poly(EGDMA-*co*-BBVC)

In the thermally cross-linked polymer it was only found the peak at 1477 cm^{-1}, of low intensity due the low concentration of dithiocarbamate in the polymer. The peak at 1174 cm^{-1} was overlapped by the intense peak of the C-O bond of the ester group in the EGDMA (**Figure 3-7**). The value of the normalized peak area of C=C stretching was 0.445 for the thermally cross-linked polymer and 0.653 for the cross-linker (EGDMA), changes observed earlier in photopolymerisation reactions (S A Piletsky *et al.*, 2005). The degree of cross-linking derived from that data was 32% (**Appendix C**).

3.3 Synthesis of the thiuram inimer: N,N'-bis(4-bibenzyl)-N,N'-dibutyldithiuram disulphide (BBTD)

In the synthesis of the inimer containing the thiuram functionality, the protocol designed by Patel and Mequanint (A. Patel & Mequanint, 2008) was followed (**Scheme 3-5**). It is a very convenient and easy one-pot procedure. First the triethylamine salt of the dithiocarbamic acid is formed using the amine NVBA synthesised in the **Section 2.2**, carbon disulphide and triethylamine, (the same reagents used in the synthesis of the inimer BBVC in the **Section 2.3**), although this time chloroform (or dichloromethane) is used as the solvent. The dithiocarbamate salt created was warmed from 0°C to room temperature, and then an oxidant was added to create the disulphide bonds between the sulphur atoms of different molecules. The intermediate dithiocarbamate salt is not isolated. The oxidant of choice in this protocol is iodine (I_2) in chloroform; the solvent was chosen because the reaction works better in non-polar solvents (Caughley & Robertson, 1933). The choice is quite convenient because the strong colour of the I_2 / chloroform solution turns the solution violet / brownish once the reaction is complete. The sequence of colours starts from light yellow, then orange and finally light brown. One downside of this method is that the colour is a quite a subjective factor and the moment when to stop the reaction is very difficult to judge, although the reaction can be monitored by Thin Layer Chromatography (TLC). In the different syntheses of this monomer using this oxidant more I_2 / chloroform had to be added compared to that suggested by the stoichiometry of the reaction. The reason could be the addition of the iodine to some of the double bonds. Also the violet / brown colour was difficult to achieve since once that colour appears the addition of oxidant solution is stopped but after a while that colour disappears and the addition must be restarted. Another downside of this oxidant is that an addition of the iodine molecule to the double bond could happen, although it is not very favourable as it is for chlorine and bromine (Vollhardt & Schore, 2002). It would be possible that some iodine could be added to the double bond if the reaction is left to react for too long (Zanger & Rabinowitz, 1975), the temperature is high enough

or it is helped with light (Caughley & Robertson, 1933) although the yield of the whole reaction does not change much.



Scheme 3-5: Synthesis of the thiuram inimer (BBTD) from a secondary amine (NBVA)

Once synthesised the crude product was analysed and showed good purity. Since the polymerisation can be affected by relatively small quantities of impurities the product was purified even further using preparative column chromatography. The separation was relatively easy and in some of the columns some iodine was observed at the top of the silica column. It was found that when the main reaction was carried out at room temperature less iodine was found in the column compared to the reactions in which a cold ice / water bath was used. It could be that at low temperatures the reaction does not take place in great extent.

Table 3-2: Elemental analysis of the inimer BBTD

Thermally cross-linked polymer	C	H	N	S
Theory	63.59	6.86	5.29	24.26
Experimental	63.72	6.70	5.48	24.21

The elemental analysis showed the correct amount of sulphur in the molecule (**Table 3-2**). That is a proof itself of the existence of the disulphide bonds since the only possible content of sulphur in the molecule is because of the thiuram functionality. If the disulphide bond is broken two dithiocarbamate radicals would be created, which would became dithiocarbamic acid as it was explained before in the **Section 1.9.3** and they would decompose into the parent amines and carbon disulphide. The carbon disulphide would evaporate very fast showing then no sulphur content.

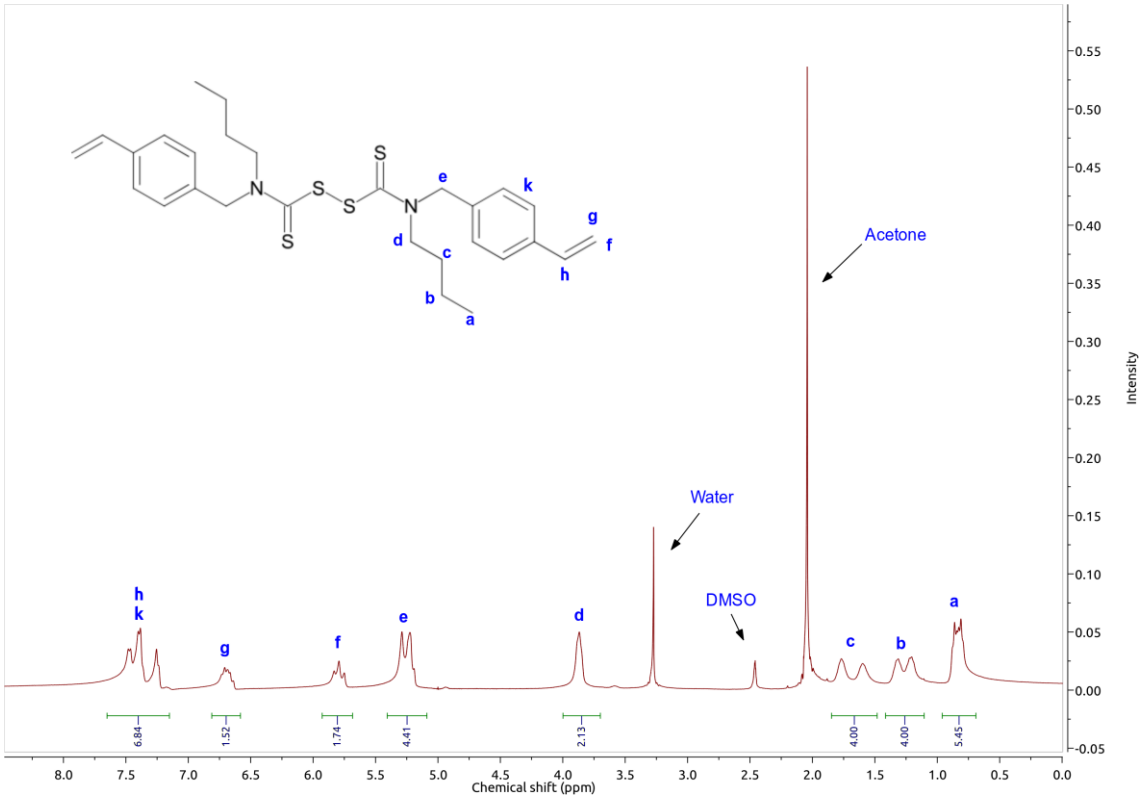


Figure 3-9: ^{1}H NMR spectrum of the inimer BBTD at 30°C in DMSO-d_6

The ^{1}H NMR of the inimer BBTD (**Figure 3-9**), as that of the inimer BBVC (**Figure 2-4**, **Section 2.3**), does not show sharp peaks at 30°C. The dithiocarbamate functionality in this case is subject to the same effects giving rise to significant double bond character in the C-N bond. Apart from that the molecule is symmetrical but it can rotate through the disulphide bond (**Scheme 3-6**) generating several configurations and causing splitting of the peaks. That can be overcome heating up the solution (**Figure 3-10**).

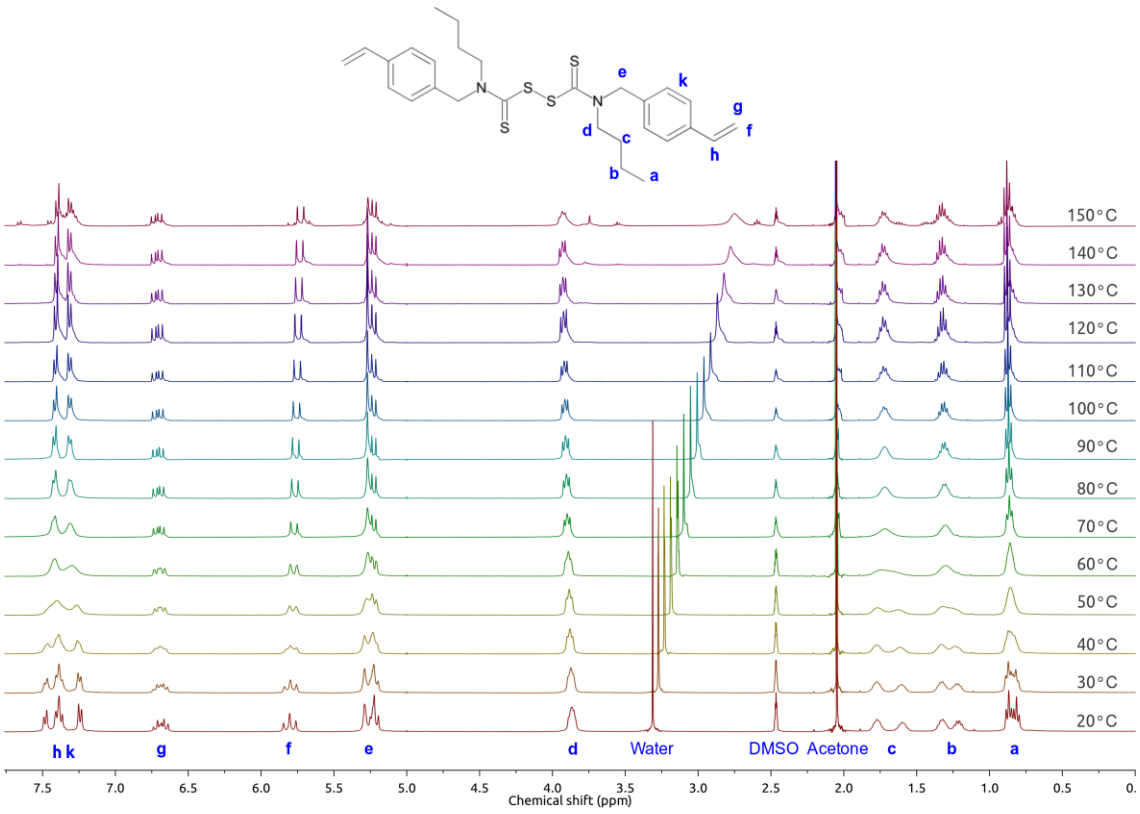
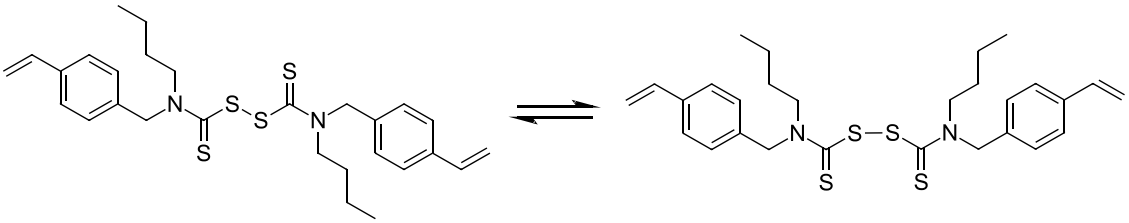


Figure 3-10: ^{1}H NMR gradient of the inimer BBTD in DMSO-d_6

In the FTIR spectra of the inimer BBTD (**Figure 3-11**) they were only found peaks at 712-760 cm^{-1} (A. Patel & Mequanint, 2008) that correspond to the disulphide bond. It was also found a peak at 1167 cm^{-1} assigned to C=S stretching vibrations (A. Patel & Mequanint, 2008) and a strong absorption band

at 1478 cm^{-1} confirming the C-N bond (Cervantes *et al*., 1997; Desai *et al*., 2008; A. Patel & Mequanint, 2008).



Scheme 3-6: Different configurations of the thiuram BBTD flipping around the disulphide bond

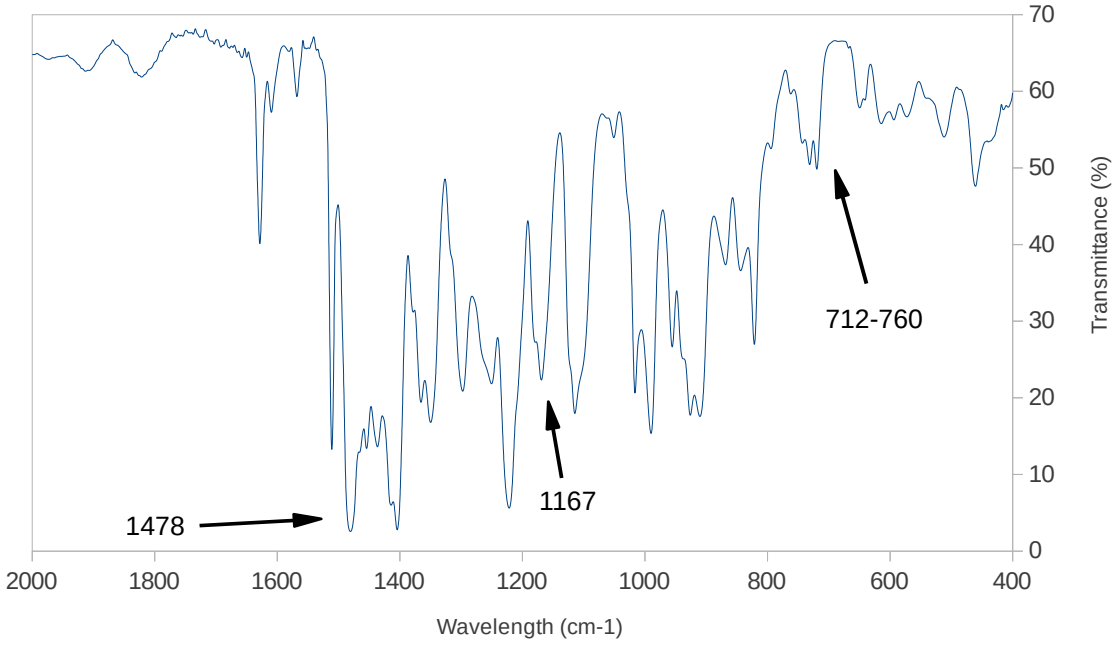
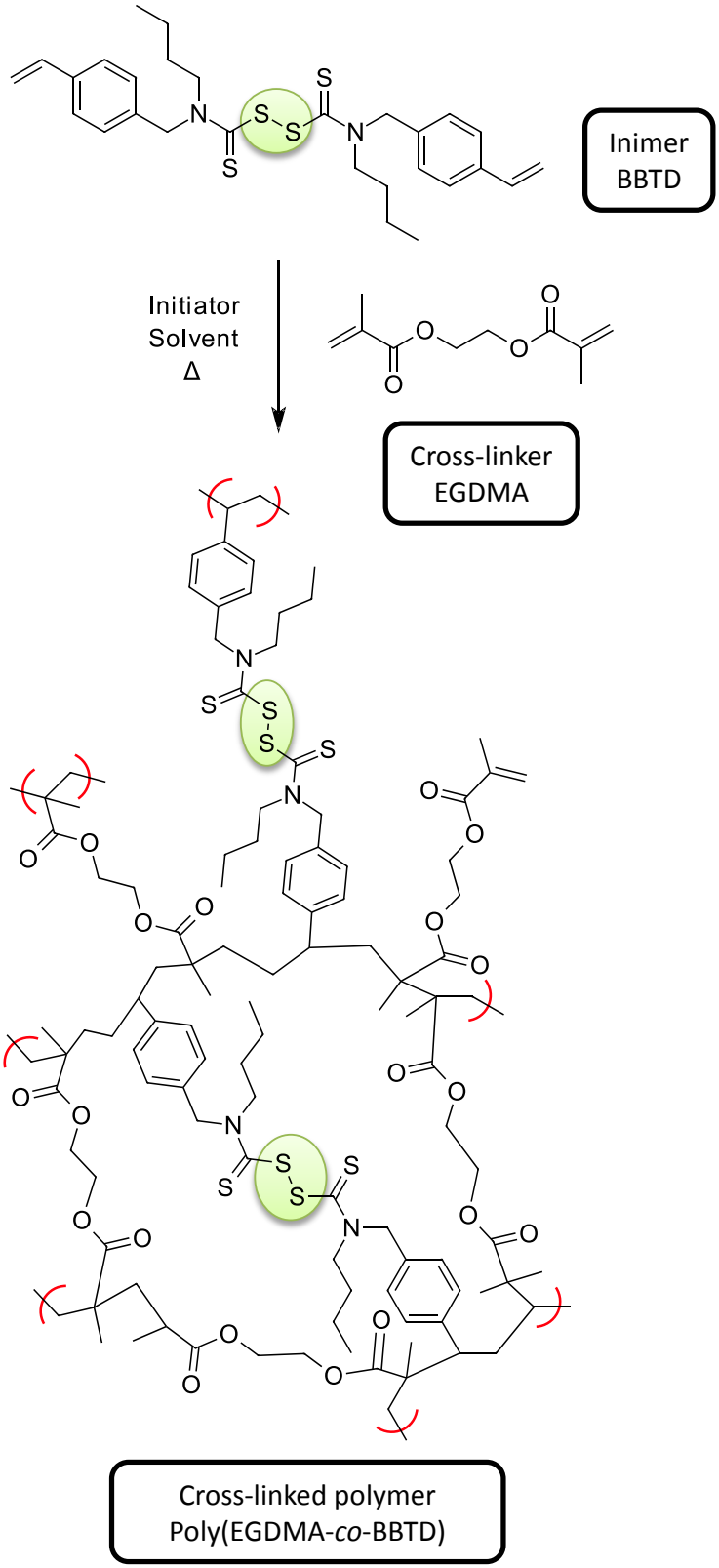


Figure 3-11 : FTIR spectrum of the inimer BBTD with the most representative peaks highlited

3.4 Synthesis of the cross-linked copolymer with thiuram functionality: Poly(ethylene glycol dimethacrylate-*co*-N,N'-bis(4-bibenzyl)-N,N'-dibutyldithiuram disulphide) [Poly(EGDMA-*co*-BBTD)]

The synthesis of the cross-linked polymer with thiuram functionality was not as straightforward as was first thought. Since the polymer has two double bonds, thermally-initiated polymerisation using AIBN and 80°C should lead to a cross-linked polymer but that was not what was found to happen in the experimental results. This kind of monomers required aggressive conditions since the synthesis of the linear polymer poly[BBVC] required 100°C to synthesise it in a satisfactory yield, as it was showed in the **Section 2.4**. Therefore the temperature of the polymerisation was increased but it was not until it reached the temperature of 105°C degrees that a polymer was found in the reaction vessel. Due to the conditions being more aggressive there were doubts about the quality of the synthesised polymer so a cross-linker was introduced to create a co-polymer. The introduced cross-linker was again ethylene glycol dimethacrylate (EGDMA) and its use allowed the temperature used in the reaction to be much lower, around 65°C (**Scheme 3-7**). The procedure to synthesise the polymer was similar to the synthesis of the polymer Poly(EGDMA-*co*-BBVC) synthesised in the **Section 2.4**, except the temperature used was lower and the solvent used to wash the ground polymer was chloroform in this case.

In the elemental analysis (**Table 3-3**) the higher amount of oxygen with respect to the theoretical data means that the reactivity of the EGDMA was higher than the inimer BBTD. Therefore the ratio of BBTD / EGDMA is lower than expected but it is not much different so the difference in the final structure would be difficult to notice respect to its performance.



Scheme 3-7: Synthesis of a cross-linked copolymer with thiuram functionality, the disulphide bonds are kept in the matrix of the cross-linked polymer (in green); the red brackets represent links to other molecules

Table 3-3: Elemental analysis of the cross-linked polymer Poly(EGDMA-*co*-BBTD)

Cross-linked polymer Poly(EGDMA-*co*-BBTD)	C	H	N	S	O
Theory	62.00	7.00	2.49	11.42	17.09
Experimental	61.26	6.92	3.11	12.16	19.72

The most important aspect is the existence of sulphur in the polymer, since sulphur can only come from intact thiuram functionalities. When the thiuram groups decompose they will liberate sulphur as CS_2 and no sulphur would be detectable in the polymer.

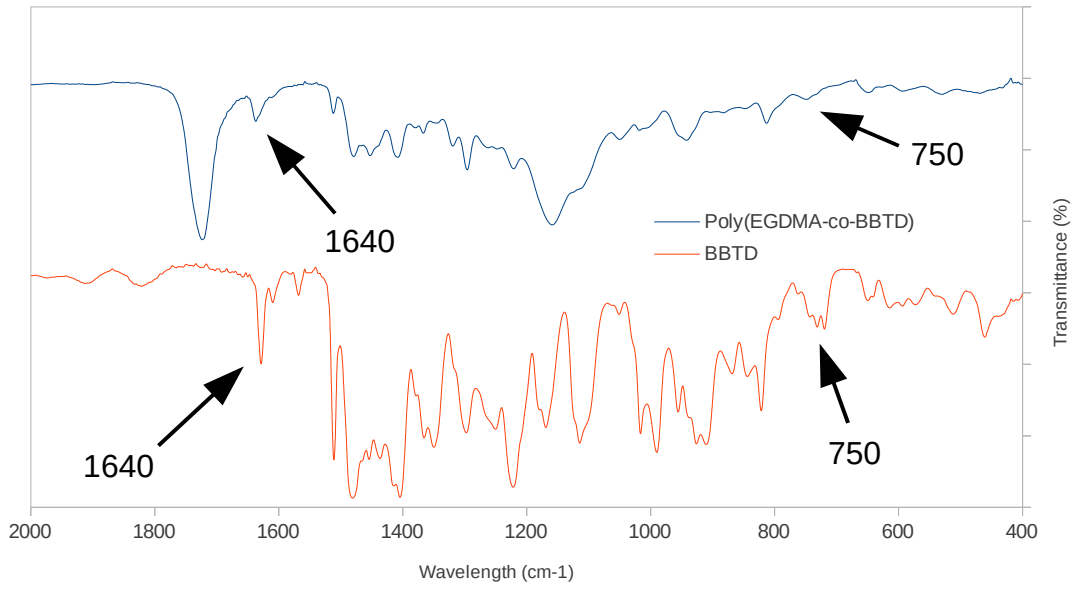


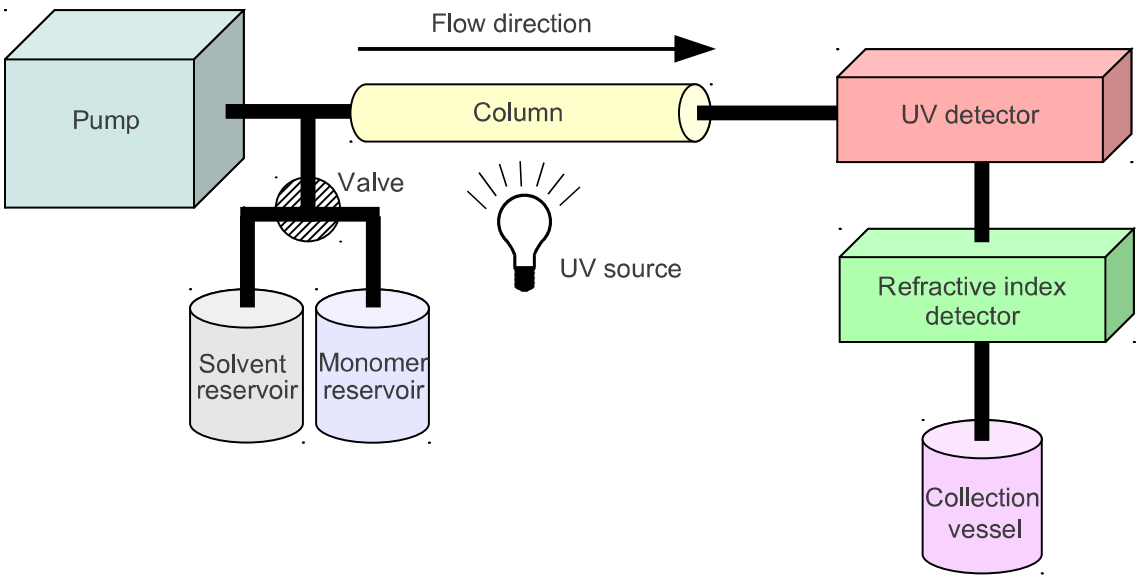
Figure 3-12: FTIR spectrum of the comparison of the inimer BBTD and the cross-linked polymer poly(EGDMA-*co*-BBTD)

In the FTIR analysis (**Figure 3-12**) of the cross-linked polymer poly(EGDMA-*co*-BBTD) can be seen the peak corresponding to the disulphide bond, at around 750 cm^{-1}. Its intensity is significantly lower compared to the inimer BBTD due the proportions of BBTD and EGDMA within the polymer. It happens with all the peaks associated to the inimer fragment are difficult to see in the polymer since

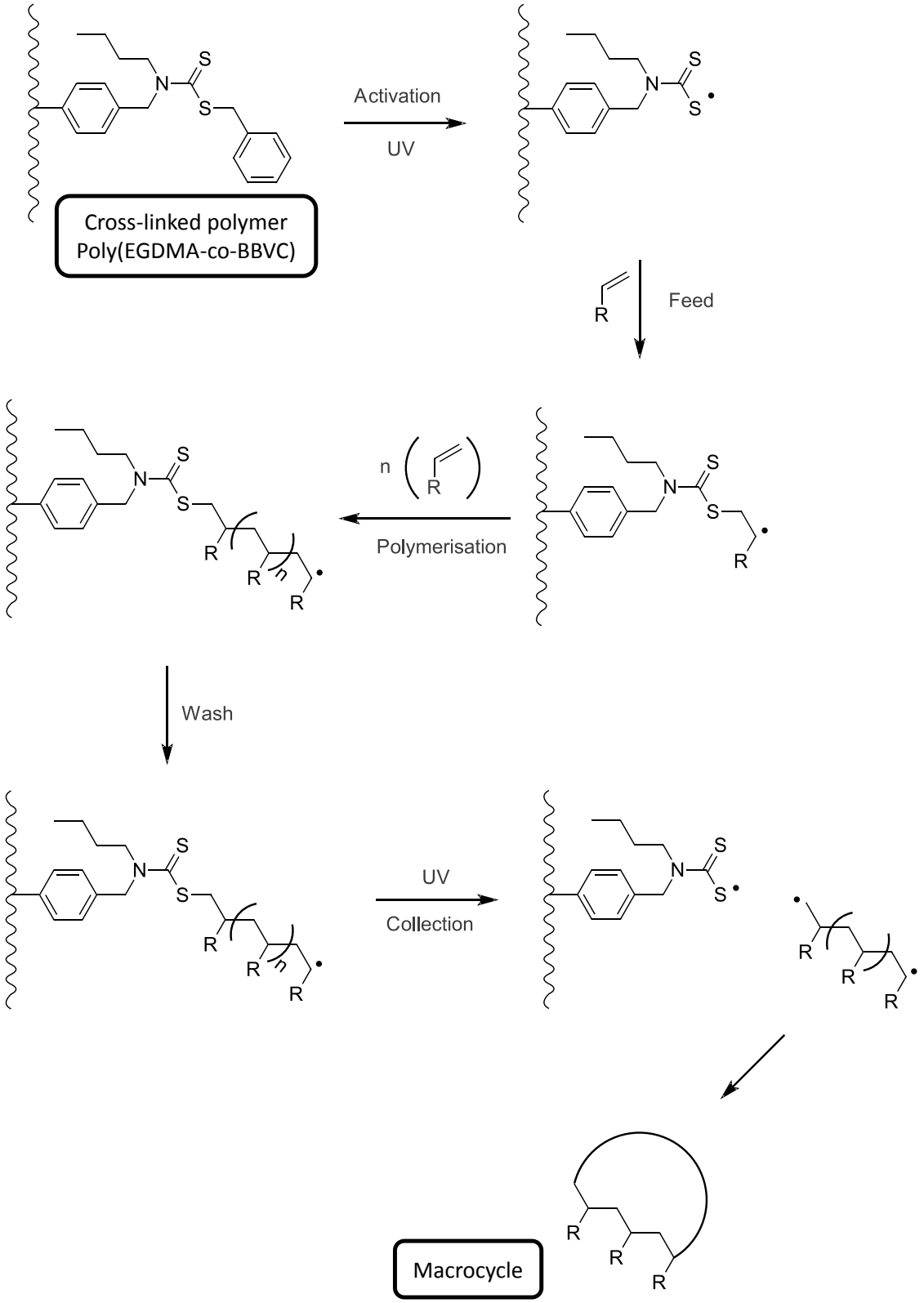
they are covered by the highly intense peaks of the EGDMA. The peak corresponding to the C=C bond around 1640 cm^{-1} appears especially intense. It therefore appears that there are many double bonds remaining which were not consumed during the polymerisation process.

3.5 HPLC photo-polymerisation system

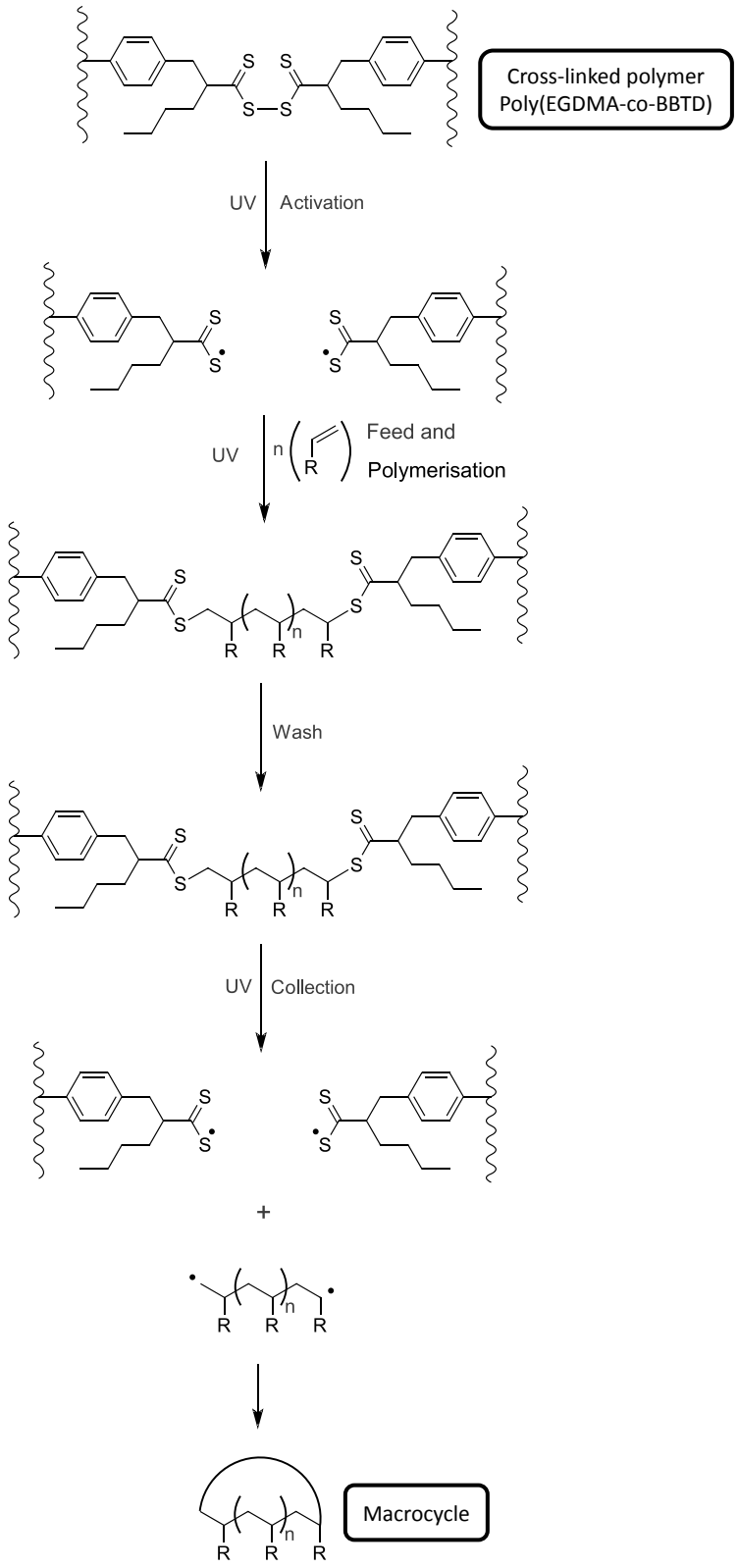
The best way to monitor and analyse the synthesis of macrocycles would be packing the polymers in a column and connect the column to a High-Performance Liquid Chromatography (HPLC) system (**Scheme 3-8**). The polymers were first packed in glass columns since the polymer had to be irradiated with a UV source. The packing of the polymers was done while applying pressure in order to produce a homogeneous filling. Once the column was packed it was connected to an HPLC system. The connection to the HPLC system had to be optimised since the high pressures could break parts of the system such as joints or the glass column. The system consisted of a pump, reservoirs of solvent and monomer, column, detectors and the collection vessel (**Scheme 3-8**). The column was inside a photochemical safety cabinet since it had to be irradiated during the process.



Scheme 3-8: HPLC photo-polymerisation system to synthesise macrocycles



Scheme 3-9: Steps in the synthesis of the macrocycles when the polymer used is the Poly(BBVC-*co*-EGDMA)



Scheme 3-10: Steps in the synthesis of the macrocycles when the polymer used is the Poly(BBTD-*co*-EGDMA)

3.6 Steps in the synthesis of the macrocycles using a HPLC photo-polymerisation system

The process had several steps:

1) Activation: Radicals are generated in the matrix of the polymer in order to create reactive sites.
2) Feed: Monomer is introduced to react with the reactive sites in the polymer.
3) Polymerisation: The solution of monomer is left inside the column in order to allow the formation of oligomers.
4) Wash: Unreacted material is washed away.
5) Collection: The oligomers created in the polymer are removed from the reactive sites. They are allowed to recombine in order to create the create macrocycles.

Depending on the polymer used to pack the column, the feeding and polymerisation step had different conditions. If the polymer used to pack the column was the Poly(BBVC-*co*-EGDMA) then the feed and polymerisation step was done with a UV source (**Scheme 3-9**). If the polymer used to pack the column was the Poly(EGDMA-*co*-BBTD) then the feed and polymerisation step was done with in the dark (**Scheme 3-10**). The activation step it is not really required when the polymer Poly(EGDMA-*co*-BBTD) is used but it is carried out as a precautionary measure.

3.7 Results

The first experiments were merely qualitative, in order to observe the appearance of peaks in the chromatogram. Different monomers were tried (methyl methacrylate, methacrylic acid and styrene), different solvents (THF, Toluene and Acetonitrile), different UV sources (4W, 15W and 300W), different concentrations, different times and different flow rates at each step. One interesting aspect was the instantaneous peak that appeared in the chromatogram when the UV source was turned on. The peak was especially intense when the polymer Poly(BBVC-*co*-EGDMA) was used. To confirm that

the effect was caused by the UV the column was heated but no peak appearance was observed.

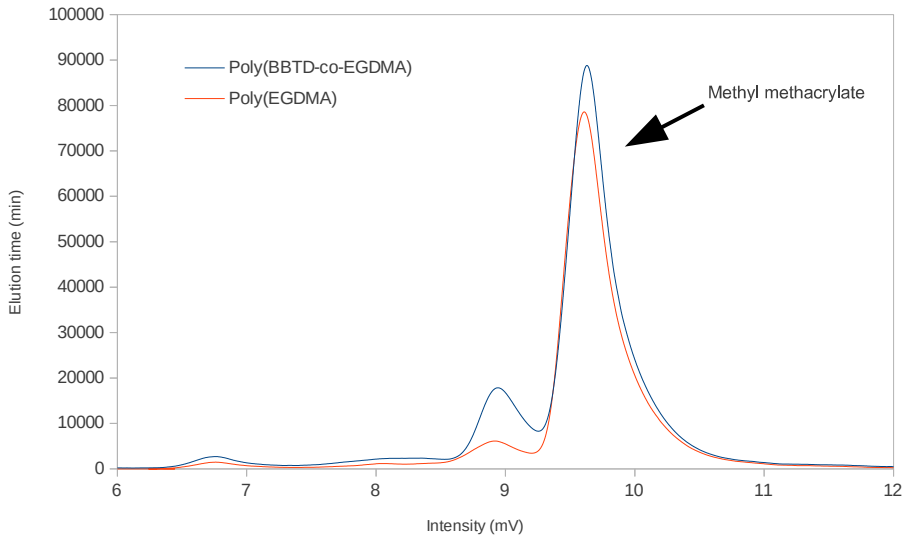


Figure 3-13: Synthesis of macrocycles using Poly(BBTD-*co*-EGDMA) as a column packing polymer, the results compared with the blank (Poly(EGDMA)) were too similar

Promising results appeared when the polymer Poly(BBVC-*co*-EGDMA) was used with THF as a solvent and methyl methacrylate as a monomer. Following the steps some peaks appeared during the collection step. The following procedures were directed to reproduce the experiment and to collect different fractions to analyse with GPC. Not enough high molecular weight material was found in any of the samples analysed. In the analysis low molecular weight material was found. When the results were compared with the blanks it was found that the material obtained from the irradiations was not coming from the inimer parts, it was coming from the EGDMA fragments. The material was analysed also with Mass Spectrometry (MS) but no positive results were obtained either. Similar results were also found when the polymer Poly(BBTD-*co*-EGDMA) was used (**Figure 3-13**).

3.8 Conclusions

- An inimer with thiuram functionality was designed and synthesised with good yields using an easy protocol.
- A protocol to synthesise a cross-linked polymers with dithiocarbamate functionalities in its cavities was developed. Ethylene glycol dimethacrylate was used as cross-linker. A protocol to synthesise a cross-linked polymer with a similar structure but with thiuram functionalities in its cavities instead of dithiocarbamate groups was also developed.
- A protocol to fill glass columns with the synthesised polymers was developed.
- An HPLC system to test the ability of the cross-linkers polymers to generate macrocyclic addition polymers was designed.
- The generation of macrocycles in the system suggested could not be proved

3.9 Future work

There was an evident problem in the detection of the macrocycles, even with the mass spectrometry analysis, because maybe some macrocycles were obtained but the amount was not enough to be detected. Therefore in future work the nature of the cross-linkers should be done carefully.

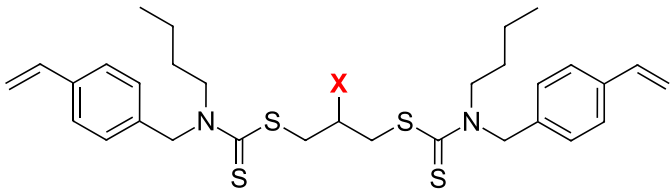
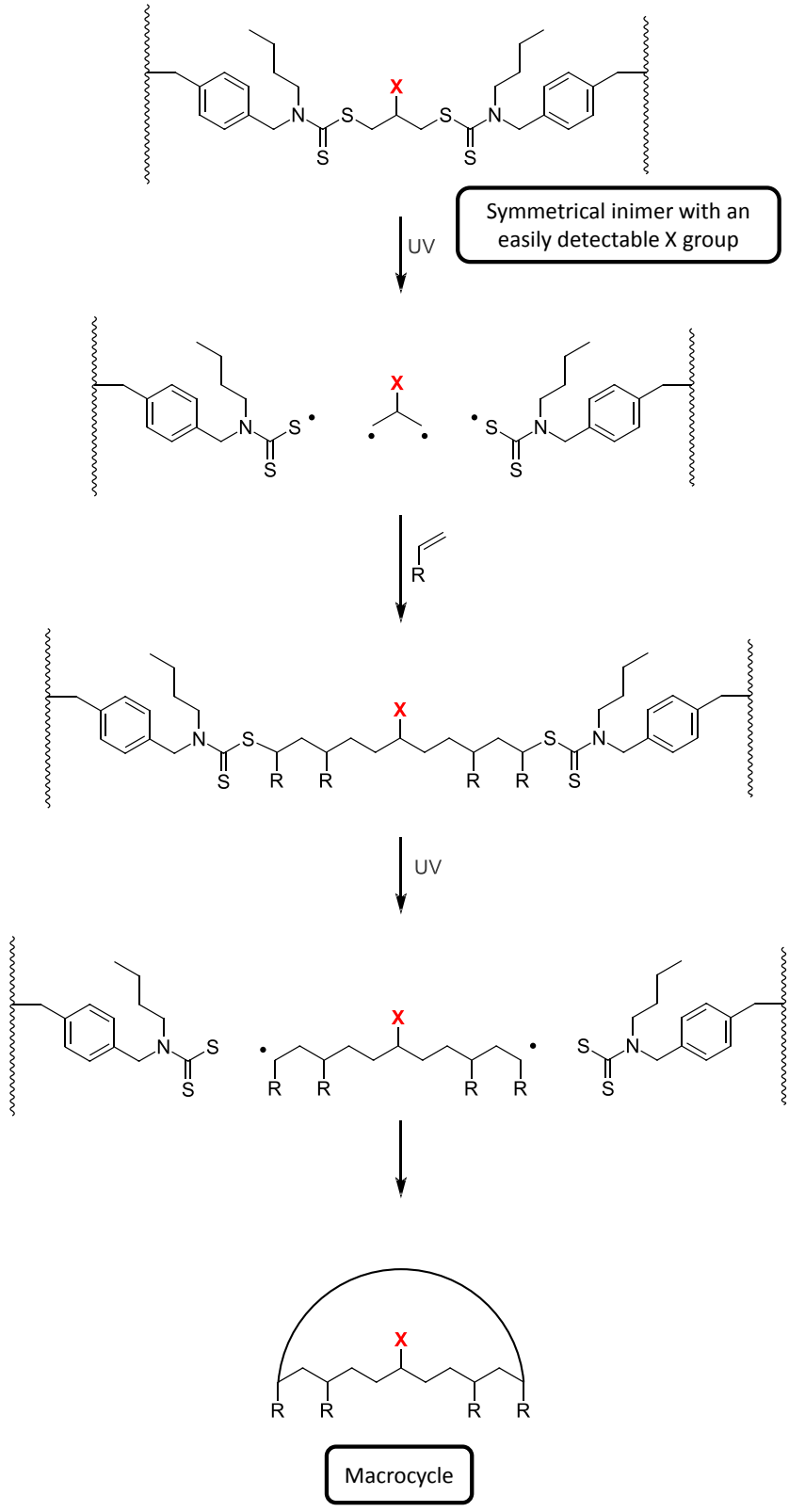


Figure 3-14: A symmetric inimer with two dithiocarbamate functionalities, two styryl groups and a X group (in red) easily detected with any analytical technique



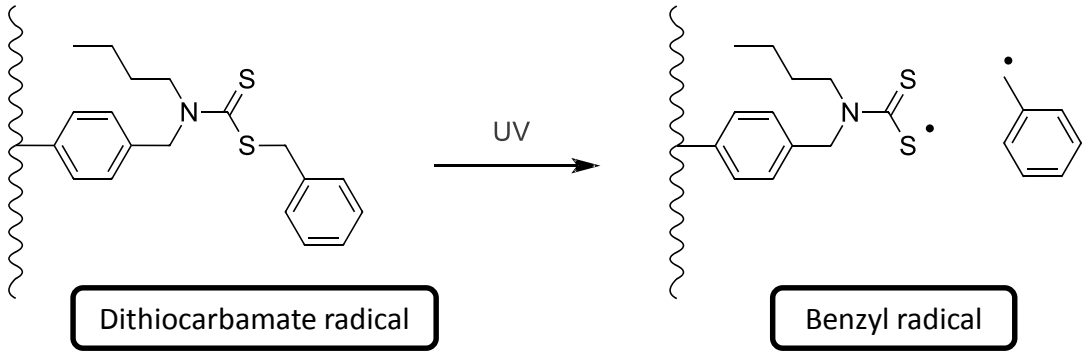
Scheme 3-11: Synthesis of macrocycles using a cross-linked polymer with dithiocarbamate groups in the cavities; the X group (in red) is an easily detectable functionality with any analytical technique

A symmetric molecule with two dithiocarbamate functionalities and two styryl groups (**Figure 3-14**) could be synthesised and used in the synthesis of macro-cycles in the way it was done in this chapter, synthesising a cross-linking polymer and testing it in a HPLC photo-polymerisation system. Between the two sulphur atoms there would be a group that could be easily detected with any analytical technique (X group in red in **Scheme 3-11**). That group could therefore facilitate the detection of the cyclic polymers.

4 Chromatography columns containing dormant radicals

4.1 Introduction

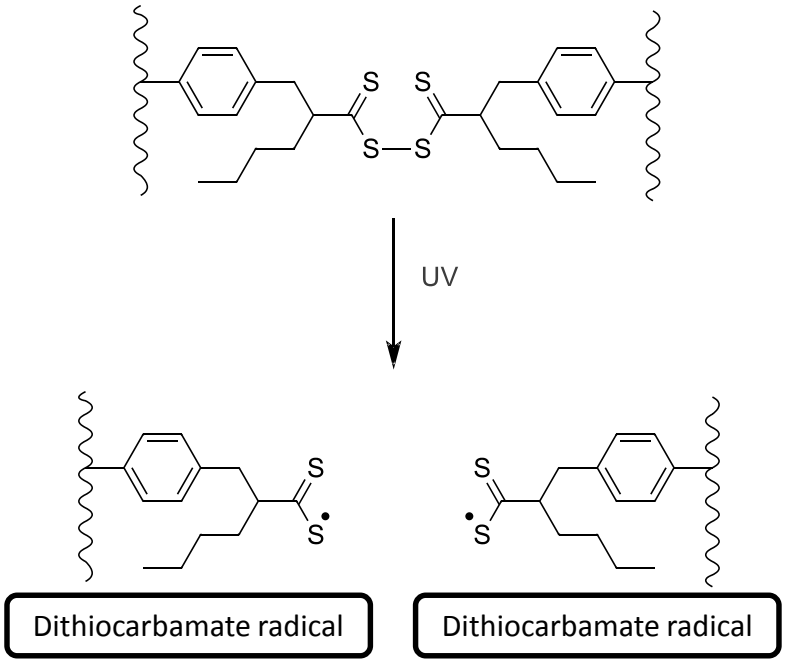
The aim in this section is the separation of mixtures of molecules using chromatography techniques. The columns of the HPLC system used for the separations were packed with cross-linked polymers that contained dithiocarbamate and thiuram groups in their cavities. Upon UV irradiation dithiocarbamate radicals could be generated in the matrix of the polymers (**Scheme 4-1** and **Scheme 4-2**).



Scheme 4-1: Photo-generation of dithiocarbamate and benzyl radicals in the matrix of the cross-linked polymer Poly(EGDMA-*co*-BBVD)

Since the polymers were cross-linked, the live of the dormant radicals could be long due the restricted movement of the polymer chains. Some traditional chromatographic techniques are based in the interaction of the mobile phase with the static phase, for instance based on polarity in columns packed with silica gel. It was expected that the dormant radicals could interact with the different chemical functional groups located in the molecules, generating different retention times for different functional groups and allowing effective separations of mixtures of compounds. The polymers used were the ones

synthesised in the **Chapter 3**: Poly(EGDMA-*co*-BBVC) and Poly(EGDMA-*co*-BBTD).



Scheme 4-2: Photo-generation of dithiocarbamate radicals from thiuram groups in the matrix of the cross-linked polymer Poly(EGDMA-*co*-BBTD)

4.2 Reactivity of dormant radicals with different functional groups

It was important to know the reactivity of the sulphur dormant radicals with other functionalities in order to know possible incompatibilities with certain groups. That is crucial to know since the sulphur dormant radical could react with atoms creating covalent bonds and spoiling the separation; the compounds from the mobile phase, analytes and solvent, could be attached to the static phase and the molecules could be indefinitely retained capping the column.

Due the large amount of functionalities to investigate, the best way to perform an easy, fast and reliable screening test based was the thin TLC, an inexpensive, sensitive, safe and consistent technique.

Two classical iniferters were tested: one with a dithiocarbamate group, the Benzyl-N,N-diethyldithiocarbamate (BDD)(**Figure 4-1**) and another one with a thiuram structure, the tetraethylthiuram disulphide (TETD)(**Figure 4-1**). Both molecules were dissolved in suitable solvents in different conditions and mixed with different molecules representing different groups (analytes). The solvents used were chosen to regard the low absorbance of UV light.

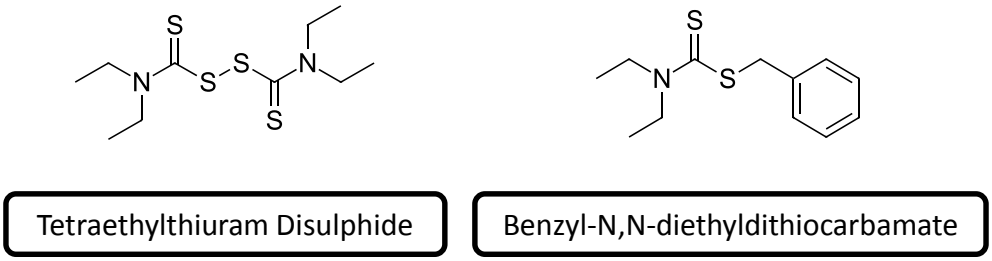


Figure 4-1: Two inimers: one with a thiuram structure, the tetraethylthiuram disulphide (TETD)(left), and another one with a dithiocarbamate functionality, Benzyl-N,N-diethyldithiocarbamate (BDD)(right)

Although the pyrex glassware used in the procedure absorbed UV irradiation (the pyrex-filtered UV light have wavelengths > 320 nm (Costantini *et al.*, 1994)), the absorbance by the solvent was reduced to a minimum, so several solvents were tested to be used with the iniferters. The solvents absorb too strongly at wavelengths shorter than their cut-off, therefore it cannot be used for spectroscopy, because of that solvents with the lowest cut-off were preferred. The results are summarised in the **Table 4-1** (Lorentz, 1991; Poole, 2003; Meyer, 2004; Robinson *et al.*, 2005); the solvents in blue were able to dissolve the iniferters / analytes, and the solvents in yellow could not dissolve the iniferters / analytes.

All the experiments were carried out using acetonitrile as a solvent, except in the case of the target n-decane which was insoluble in that specific solvent, so diethyl ether was used instead.

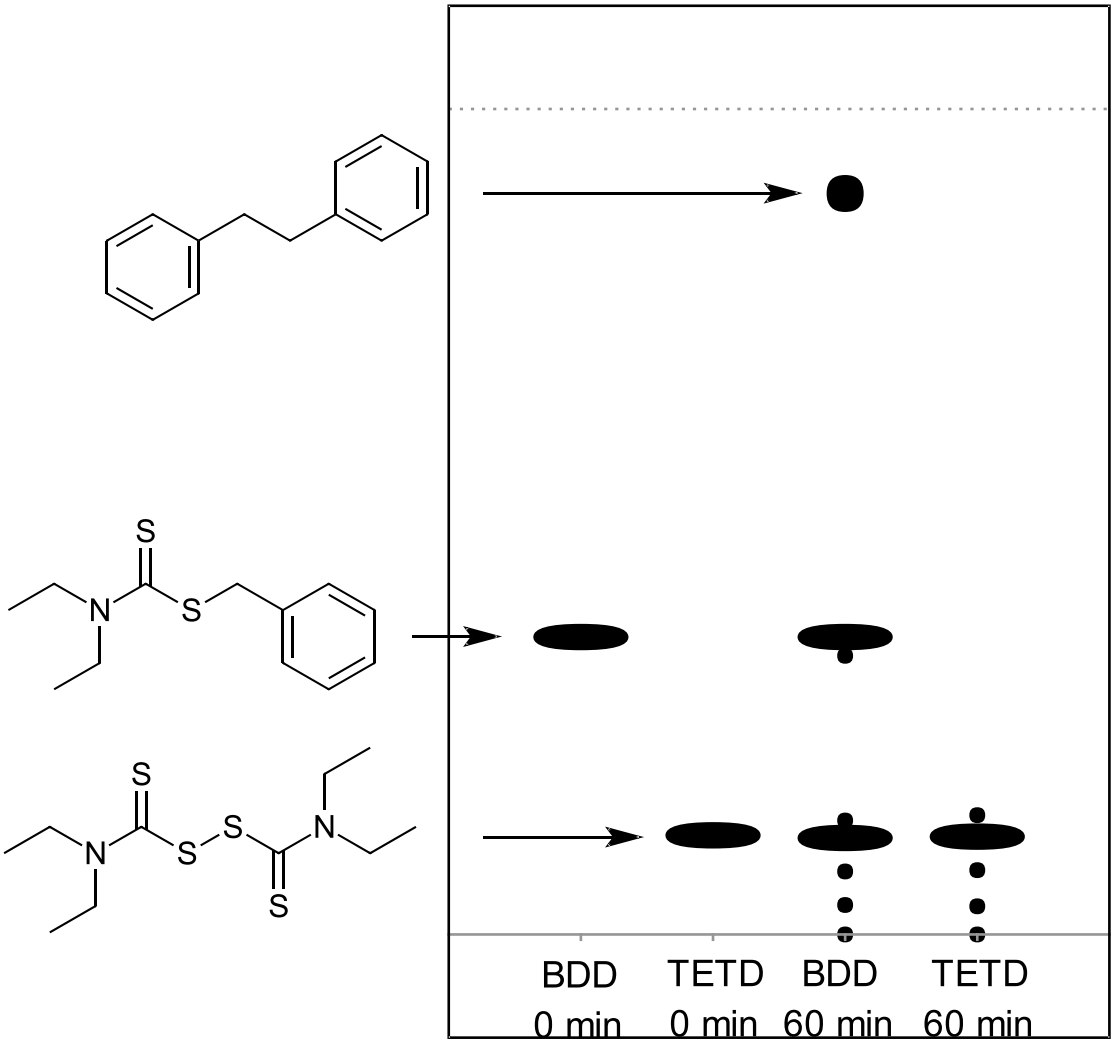


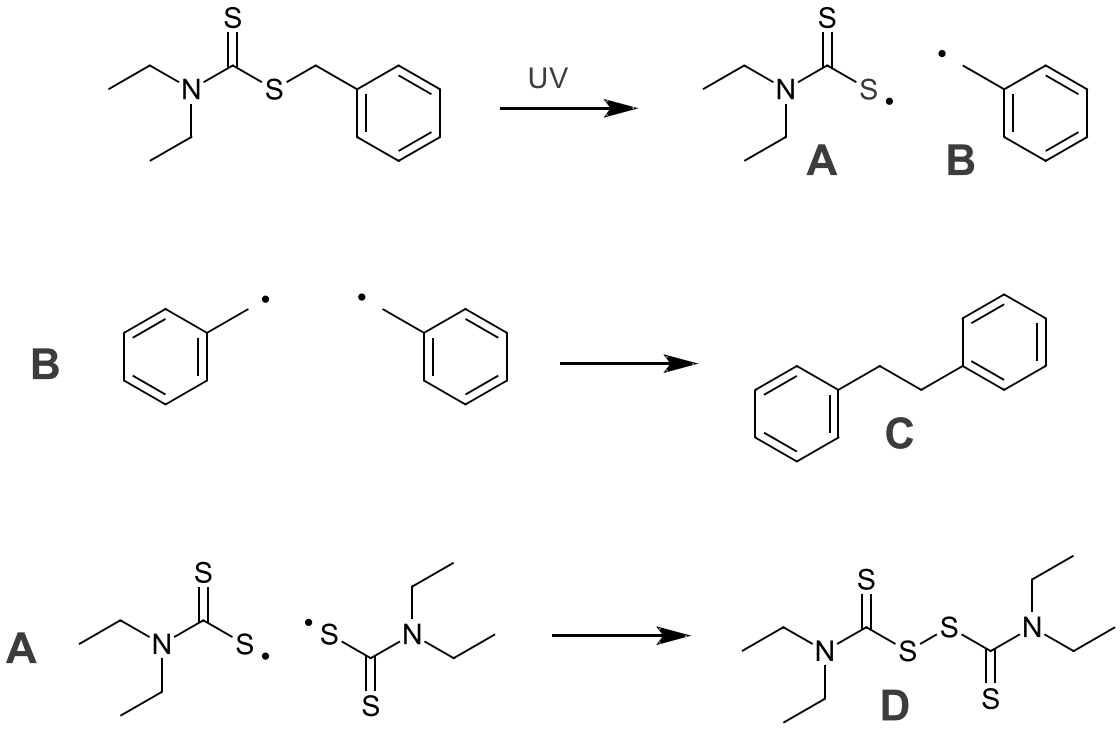
Figure 4-2: TLC analysis of the blank solutions in the screening test of the reactivity of dormant radicals; the lanes of the TLC plate are named after the iniferter analysed in solution and the time the solution was irradiated; in the left side are the structures

The iniferter / analyte solutions were degassed bubbling argon; distilled acetonitrile and non-degassed solutions were also used for the tests but no difference was observed. The solutions were irradiated with a 300W UV light source for a certain amount of time in a system with a water jacket to keep the temperature of the solutions constant (~22°C) (**Scheme 4-4**). When the irradiation time was finished the solutions were analysed by TLC.

Table 4-1: Elemental analysis of the inimer BBTD

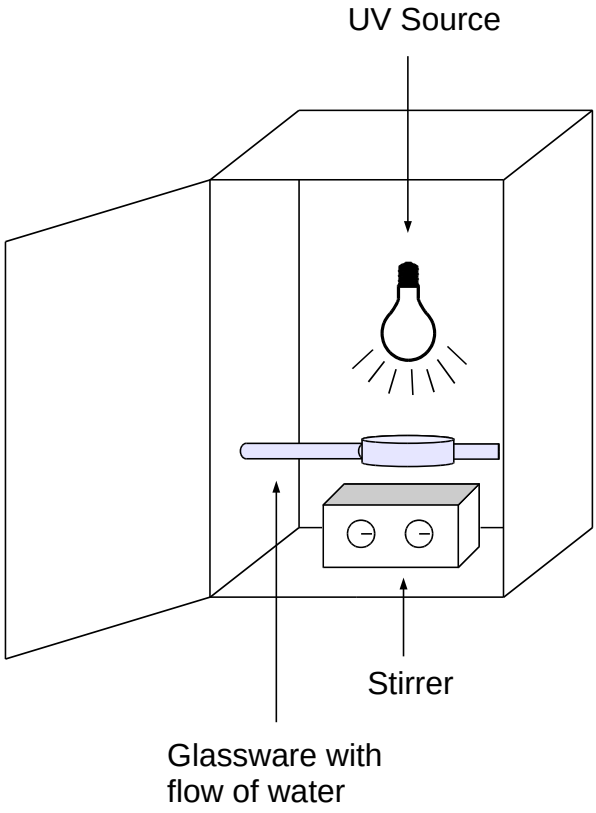
Solvent	UV cutoff (nm)
Acetonitrile	190
n-Hexane	190
n-Pentane	195
Cycloheptane	200
Cyclohexane	200
Isooctane	200
Diethyl Ether	205
Methanol	205
Amyl Alcohol	210
Ethanol	210
Fluoroalkane FC-78	210
Isopropanol	210
Methyl t-butyl ether	210
n-Decane	210

Solutions just made from the iniferters were analysed as blanks by TLC after 0 and 60 minutes of irradiation (**Figure 4-2**). In the lane of the TETD the main spots corresponded to the starting material. In the lane of the BDD appeared spots that were expected to see (Zverev *et al.*, 1980): Bibenzyl and TETD. Those products were generated because, upon UV irradiation, BDD generated benzyl and dithiocarbamate radicals (A and B respectively in **Scheme 4-3**); following a cross-coupling pathway, first the benzyl radicals could react to produce bibenzyl (C in **Scheme 4-3**). With the benzyl radicals out of the game the dithiocarbamate radicals could generate thiuram groups (D in **Scheme 4-3**).



Scheme 4-3: Generation of dithiocarbamate (A) and benzyl (B) radicals upon irradiation of a benzyl dithiocarbamate; bibenzyl (C) and thiuram (D) molecules are created after a cross-coupling process

Apart from those main spots, less intense spots were found. The concentration of the injection in the TLC plate had to be very concentrated prior elution to see those secondary spots under UV. In order to elucidate the nature of the products in the irradiation of BDD and TETD certain amount of BDD was synthesised and a solution in acetonitrile was made in the same way as the solutions made for screening. The solution was irradiated with a for certain period with UV irradiation and the products were tried to be isolated with preparative chromatographic procedures. Apart from TETD and bibenzyl only three compounds were found to be separable but in small quantity and with structures not easy to elucidate.



Scheme 4-4: Irradiation system, it is a photochemical safety cabinet with glassware that supports the reaction vessel and maintains the temperature with a flow of water (S. I. Patel *et al.*, 2004)

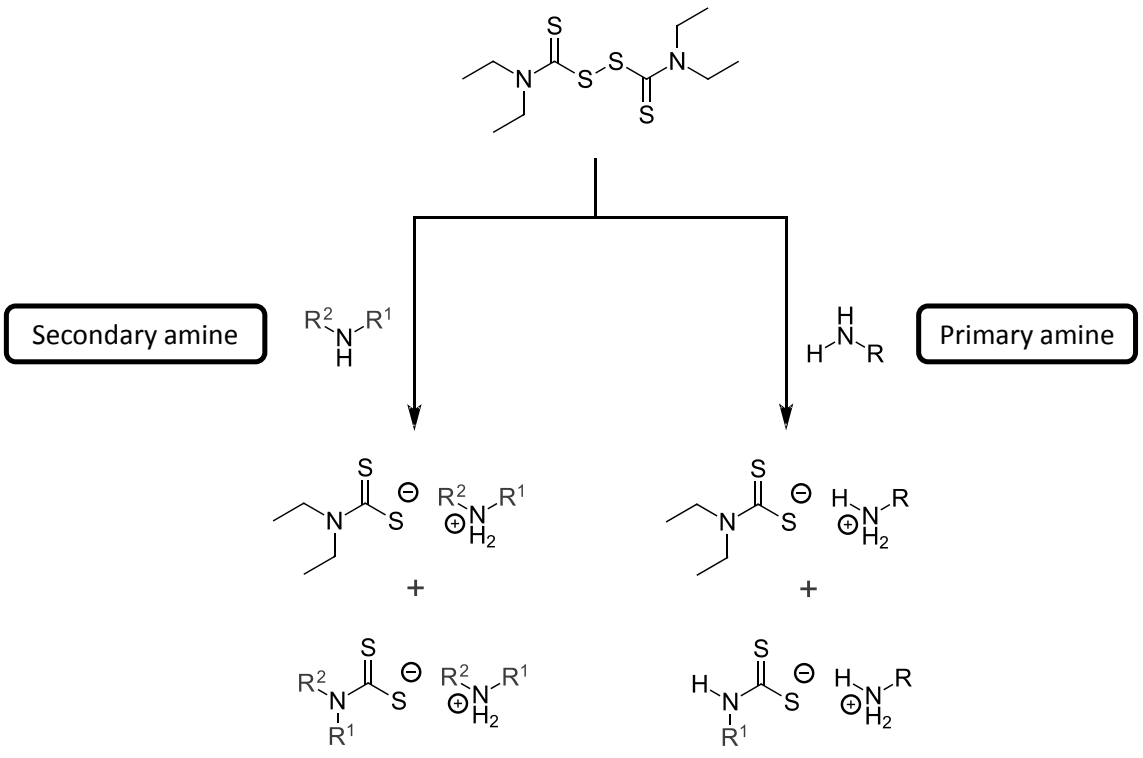
Although this experiment was complementary and it could throw some light to some of the reactivity of the dormant radicals it was especially important so it was not optimised / finished.

In the irradiation and analysis of the solutions of iniferter / analytes in the majority of cases no extra spots were observed compared with the blanks. The **Table 4-2** summarise the results:

Table 4-2: Summary of the screening test of the dormant radicals reactivity towards different chemical functional groups

Target Functionality (Molecule)	Extra Spots
Acrylate (Methyl Methacrylate)	
Alcohol (1-Pentanol)	
Alcohol (Cyclohexanol)	
Alcohol (Phenol)	
Aldehyde (Glutaraldehyde)	
Alkane (n-Decane)	
Alkene (Styrene)	
Amide (Dimethylformamide)	
Carboxylic Acid (Acetic Acid)	
Ester (Ethyl Acetate)	
Ether (Isopropylether)	
Halogenated (1-Bromoheptane)	
Halogenated (Chloroform)	
Ketone (Benzophenone)	
Primary Amine (Butylamine)	
Primary Amine (Ethylendiamine)	
Secondary Amine (Diethylamine)	
Tertiary Amine (Triethylamine)	
Thiol (1-Hexanethiol)	
Thiol (Ethenethiol)	

- **Thiols:** Extra spots were found in the irradiated solutions of BDD and TETD with thiols. It was also noticed a strong yellow colour in the solution containing BDD and ethenethiol. The appearance of extra spots could be because of the ability of the thiols to generate radicals and react with them (Koo *et al*., 2010).
- **Alkanes and Acrylates (monomers):** Evidences were found for polymerisation in the vessel containing methyl methacrylate with BDD although no sings were found in the vessel with TETD. The reactivity could be due the benzyl radicals instead of the dormant radicals. No evident polymerisation of those monomers initiate by dormant radicals was found in the screening test. However it is known that the dormant radicals are able to initiate reactions of polymerisation of the styrene (Otsu & Nayatani, 1958; Otsu *et al*., 1958).



Scheme 4-5: Generation of salts mixing secondary and primary amines with dithiocarbamates

- **Amines:** Although it was known that primary and secondary alkyl amines ordinarily possess poor UV absorption (Blau & King, 1993), a precipitate was found when both iniferters were mixed with primary and secondary amines and then irradiated. The case was exceptionally fast when ethylendiamine was used, coloured solution and precipitate appeared just mixing the reagents with no irradiation required. No precipitate was found though when a tertiary amine was used instead. The precipitate was analysed and it was definitive that the use of amines with dormant radicals generated with dithiocarbamates it is not recommended since it is known that some reactions will occur (**Scheme 4-5**) (Van Boi, 2000).

4.3 HPLC Irradiation system

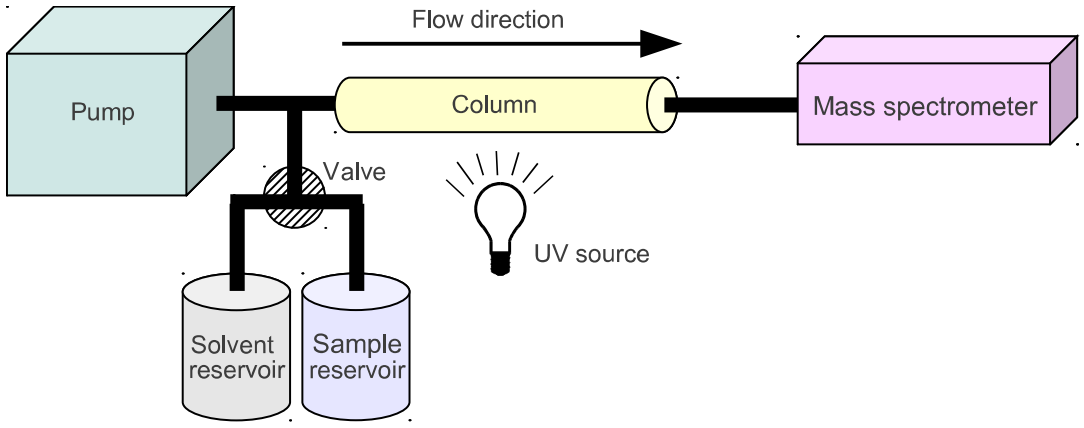
The polymers were first packed in columns applying pressure in order to produce a homogeneous filling.

4.4 Steps and results in the separation of mixtures using a HPLC irradiation system

4.4.1 Poly(BBVD-*co*-EGDMA)

1. The column filled with polymer was firstly connected to a HPLC system (**Scheme 4-6**) that consisted of a pump, reservoirs of solvent and sample, column and a detector (mass spectrometer). The column was inside a photochemical safety cabinet since it had to be irradiated during the process.
2. The column was prepared for the experiment washing it through with eluent in the dark to remove possible impurities.
3. The column was irradiated to remove the benzyl radicals (**Scheme 4-1**) washing the column through with eluent.
4. The column filled with polymer was then connected to another HPLC system (**Scheme 4-7**) that consisted of a pump, reservoirs of solvent and sample, column and a detector (UV detector). The column was inside a photochemical safety cabinet since it had to be irradiated during the process.

5. The analytes were investigated one by one, passing them through the columns in the dark to know their retention times.
6. The dormant radicals were created in the polymer cavities irradiating the columns with UV light (**Scheme 4-1**).
7. The analytes were passed again through the irradiated columns to know their new retention times, this time under UV light.



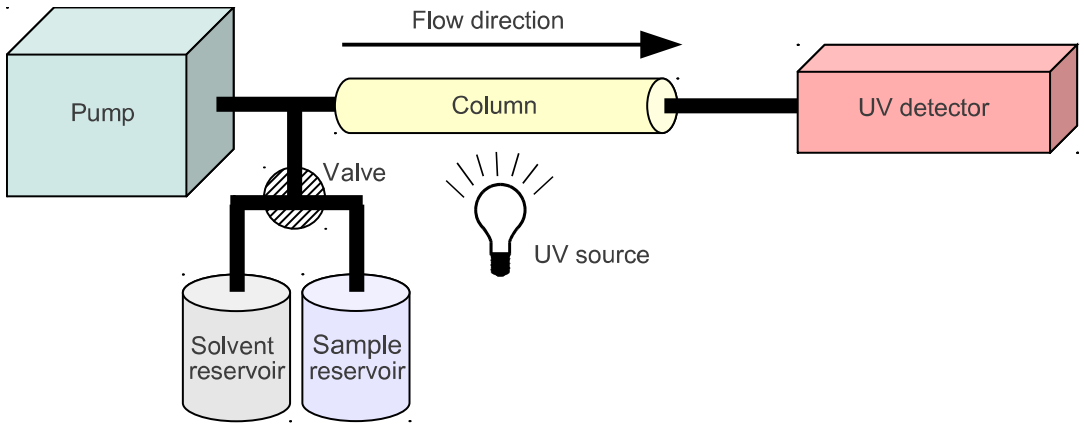
Scheme 4-6: HPLC system (equipped with a mass spectrometer) used to perform chromatography separations of mixtures using columns packed with dithiocarbamate and thiuram based polymers that generate radicals upon UV irradiation

With the help of the mass spectrometer it was possible to detect the benzyl coming out from the column. When no more benzyl was detected the next part of the experiment was performed. The analytes analysed were:

- Benzene
- Acetic acid
- Phenol
- Aniline
- Acetone
- Benzoic acid
- (2,2,6,6-Tetramethylpiperidin-1-yl)oxyl (TEMPO)

- Methyl methacrylate
- Styrene

Some changes in the retention times of the analytes with and without irradiation were noticed but they were not especially significant.



Scheme 4-7: HPLC system (equipped with a UV detector) used to perform chromatography separations of mixtures using columns packed with dithiocarbamate and thiuram based polymers that generate radicals upon UV irradiation

4.4.2 Poly(BBTD-*co*-EGDMA)

1. The column filled with polymer was firstly connected to a HPLC system (**Scheme 4-7**) that consisted of a pump, reservoirs of solvent and sample, column and a detector (UV detector). The column was inside a photochemical safety cabinet since it had to be irradiated during the process.
2. The column was prepared for the experiment washing it through with eluent in the dark to remove possible impurities.
3. The analytes were investigated one by one, passing them through the columns in the dark to know their retention times.
4. The dormant radicals were created in the polymer cavities irradiating the columns with UV light (**Scheme 4-2**).

5. The analytes were passed again through the irradiated columns to know their new retention times, this time under UV light.

The analytes analysed were:

- Benzene
- Acetic acid
- Phenol
- Aniline
- Acetone
- Benzoic acid
- (2,2,6,6-Tetramethylpiperidin-1-yl)oxyl (TEMPO)
- Methyl methacrylate
- Styrene

Like in the previous experiment, some changes in the retention times of the analytes with and without irradiation were noticed but there were not especially significant.

4.5 Conclusions

A screening test of the dormant radical reactivity towards different chemical functional groups was done throwing interesting results for alkanes, thiols and amines.

A HPLC system perform chromatography separations of mixtures, using columns packed with dithiocarbamate and thiuram based polymers that generate radicals upon UV irradiation, was set.

A series of molecules with different functional groups were studied to determine the effectiveness of the separation process.

Although it was found some effect of the dormant radicals interacting with different functional groups, the use this feature for the chromatographic separation of mixtures was not transcendental.

5 Chiral separations

5.1 Introduction

The aim of the work described in this section was the chiral resolution of racemic mixtures. The separation of enantiomers could be done by chiral chromatography using a polymer with a high density of chiral centres (**Figure 5-1**) as a column packing. To synthesise that, a hyper-branched polymer, a monomer-initiator (inimer) with a chiral centre in its structure must be designed and synthesised. The inimers can generate hyper-branched polymers (highly branched structures) under specific reaction conditions; therefore the resulting polymer will have a large number of chiral centres. It is expected that the high density of chiral centres will allow the efficient separation of mixtures of enantiomers. The chiral centres should interact more strongly with one stereoisomer than the other, allowing different retention times for different enantiomers, and therefore efficient chromatographic separations. Since the hyper-branched polymers are soluble in some solvents they could be dissolved by the eluents used in the chromatographic protocols. The hyper-branched polymer therefore had to be attached to a solid support before the polymeric material could be used as a packing for the chromatographic column. The objectives in this section are:

1. The design and synthesis of a secondary amine. The inimer will be synthesised from a secondary amine. This secondary amine will be the molecule that will introduce the polymerisable part and the chiral centre in the subsequent inimer.
2. The synthesis of an inimer. The inimer will have a dithiocarbamate structure with a polymerisable part and also an enantiomerically pure chiral centre.
3. The polymerisation of the monomer to generate a hyper-branched polymer. The polymerisation of the inimer will be performed under specific conditions to generate a hyper-branched polymer. Since the polymer will be attached to a solid support, a co-monomer will be added.

The co-polymer will provide the polymer with suitable functionality to allow it to become attached to the solid support

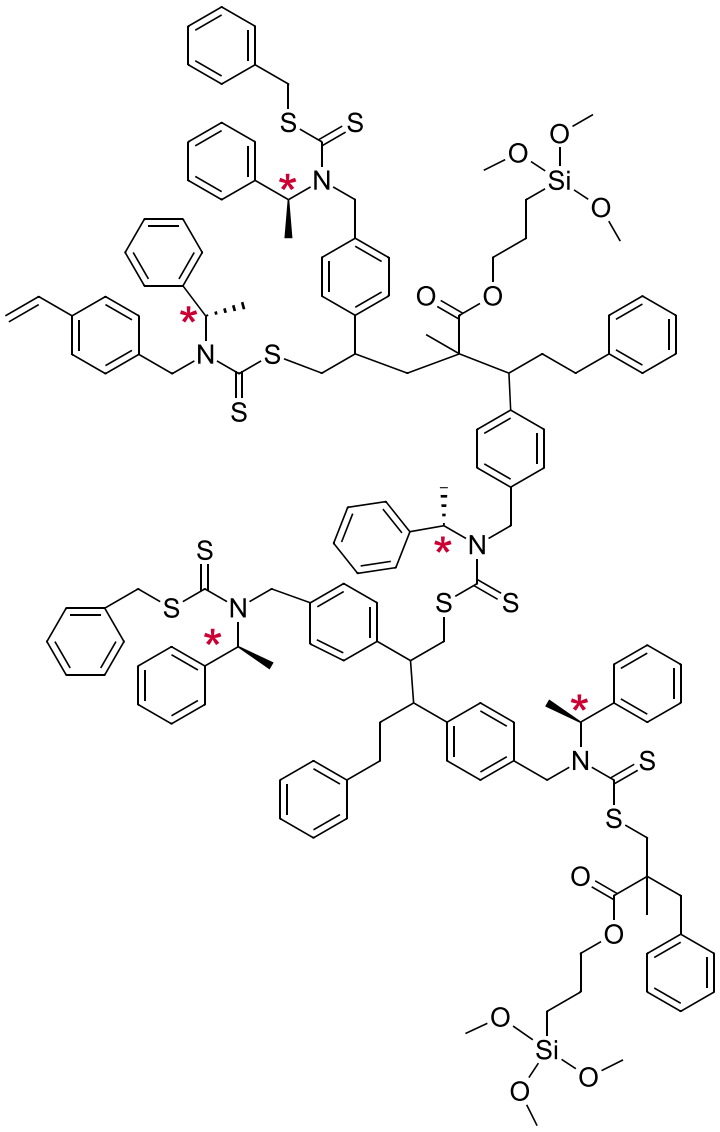


Figure 5-1: First generations of a hyper-branched polymer generated from inimers with styryl groups, dithiocarbamate functionalities and chiral-centres (red asterisks) in their structures

4. <u>The development a protocol to attach the hyper-branched polymer to a solid support.</u> A specific solid support will be chosen. A protocol to attach the hyper-branched polymer to the solid support will be developed.

5. The test of the chiral resolution. The chromatographic column packed with the hyper-branched polymer attached to the solid support will be connected to a HPLC system to test its ability to separate enantiomers.

5.2 Synthesis of the secondary amine with chiral centre: (S)-N-(4-vinylbenzyl)1-phenyl-ethanamine [S-VBPE]

In order to synthesise the secondary amine it is crucial to know the structure that the monomer that would generate the hyper-branched polymer has to have:

- It has to be a molecule with a polymerisable centre (double bond, highlighted with a blue circle in **Figure 5-2**).
- It has to have a chiral centre (highlighted with a green circle in **Figure 5-2**)
- It has to have a functional group that will allow the creation of radicals upon irradiation (dithiocarbamate group, highlighted with a red circle in **Figure 5-2**).

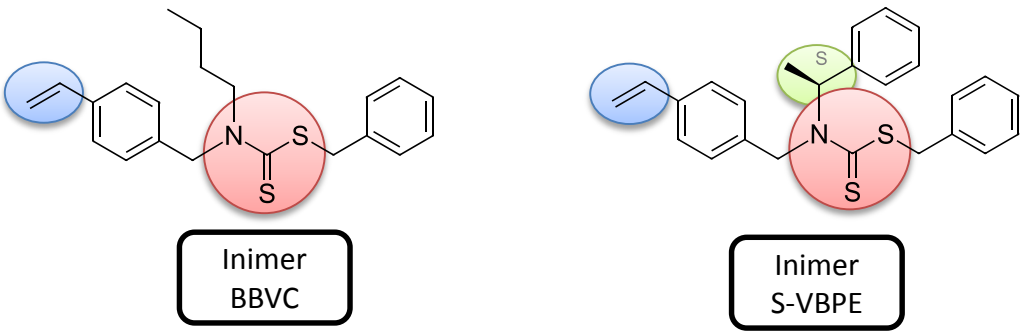
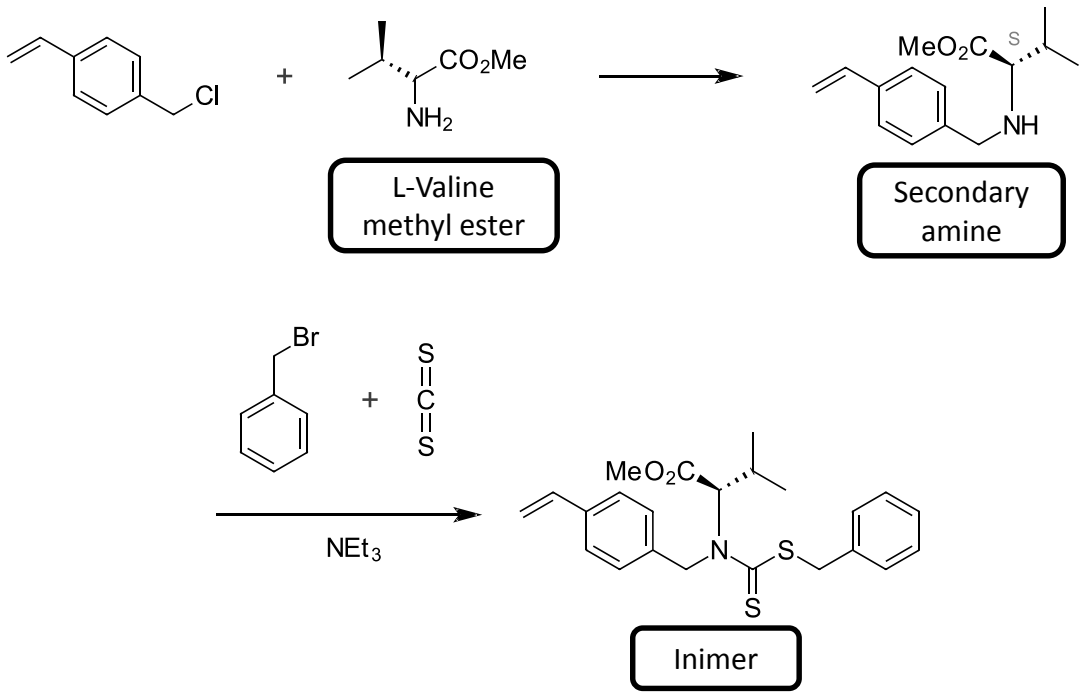


Figure 5-2: On the left the inimer BBVC with a styryl part (blue circle) and a dithiocarbamate functionality (red circle); and on the right the inimer (S)-N-(4-vinylbenzyl)1-phenyl-ethanamine [S-VBPE] with a styryl part (blue circle), a dithiocarbamate functionality (red circle) and also a chiral centre (green circle)

Two of those three requirements can be found in the already synthesised inimer BBVC in the **Section 2.3** (**Figure 5-2**), as it is a molecule with a double bond and a dithiocarbamate functionality, so it can be polymerised to generate a

hyper-branched polymer. However the inimer BBVC lacks of a chiral centre and therefore the subsequent hyper-branched polymer will not have an asymmetric structure. That could be solved including a chiral centre in the secondary amine used to synthesise the inimer. If the butyl group in the inimer BBVC could be replaced with a group with a chiral centre, the structure will match the prototype of the required monomer (**Figure 5-2**).



Scheme 5-1: Schematic view of the synthesis of the L-Valine-secondary amine and L-Valine-inimer

After the easy and straightforward synthesis of the secondary amine NVBA and the inimer BBVC (see **Section 2.2** and **Section 2.3**) it was expected the same behaviour for secondary amines made from enantiomerically pure amino acid ester derivatives; those secondary amines could produce inimers with chiral centres in an enantiomerically pure form (**Scheme 5-1**). Since the carboxylic functionality could interfere with the stability of the dithiocarbamates (as it could be seen in the **Section 1.9.3**) the ester derivative could be used instead the free

carboxylic acid. However the truth was revealed to be quite different and the process was full of difficulties. The synthesis of the secondary amines with a chiral centre derived from amino acid ester derivatives needed a lot of work because the available reagents were expensive and they could not be used in the Hoffman procedure. Different routes were designed and the secondary amines were finally produced. However the correspondent inimer was impossible to synthesise.

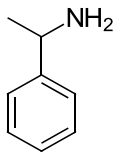
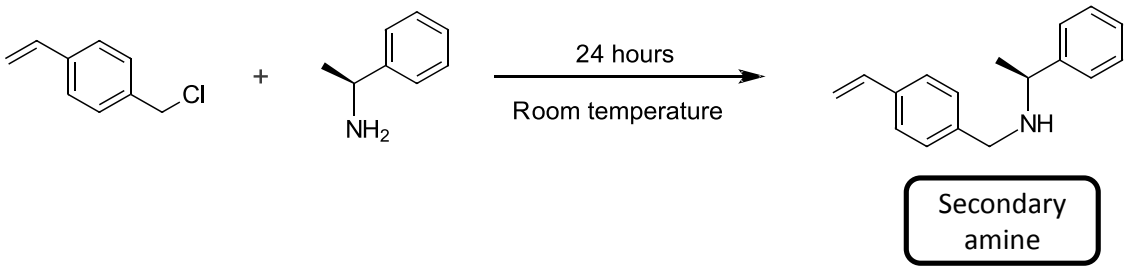


Figure 5-3: 1-Phenylethylamine

Although the idea of using a range of enantiomerically pure amino acid ester derivatives to generate a series of secondary amines was a good idea it was not possible to synthesise the inimers from those secondary amines so another approach was taken. A study of the commercially available chiral amines was done and the best choice regarding availability, price per gram and suitable structure was the 1-phenylethylamine (**Figure 5-3**).

The protocol to synthesise the secondary amine with a chiral centre using the 1-phenylethylamine as starting material (**Scheme 5-2**) was very similar to the protocol used to synthesise the secondary amine NVBA in **Section 2.2**. It is an easy protocol but this time it is not as inexpensive since the primary amine is not cheap, although it is affordable. For that reason the unreacted primary amine was recovered by extracting it from the aqueous phase. Since the reaction is simple not many byproducts were created and the recovered primary amine could be reused in following reactions without much further purifications. When the reaction was finished a standard aqueous work-up was carried out to obtain the crude product. To generate a secondary amine of high enough purity the crude material was purified by preparative column chromatography.



Scheme 5-2: Synthesis of the secondary amine with a styryl part and a chiral centre, (S-VBPE)

All the protons of the secondary amine could be assigned in the analysis of the ^{1}H NMR spectrum (**Figure 5-4**). An interesting effect was found in the area where the benzyl protons appeared (between 3.5 and 4 ppm). Instead of finding a quartet and a double doublet, two quartets were found. The explanation could be found in the diasterotopic nature of the CH_2 of the styryl part (proton **c** in **Figure 5-4**) due the existence of a chiral centre in the molecule. Those protons generate two different signals because they are in different chemical environments (Silverstein *et al.*, 2005), but instead of two singlets, in the spectrum an “apparent” quartet was found. They were “apparent” because it was not really a quartet; it was a pair of doublets. Firstly they were doublets due the exchange of the proton of the nitrogen atom is slow. The peaks of the doublets should have the same intensity but sometimes, when the separation between the peaks (coupling constant or *J*) within a doublet is close to the distance between the doublets, the intensity of the outer peaks decrease and the system have the appearance of a quartet.

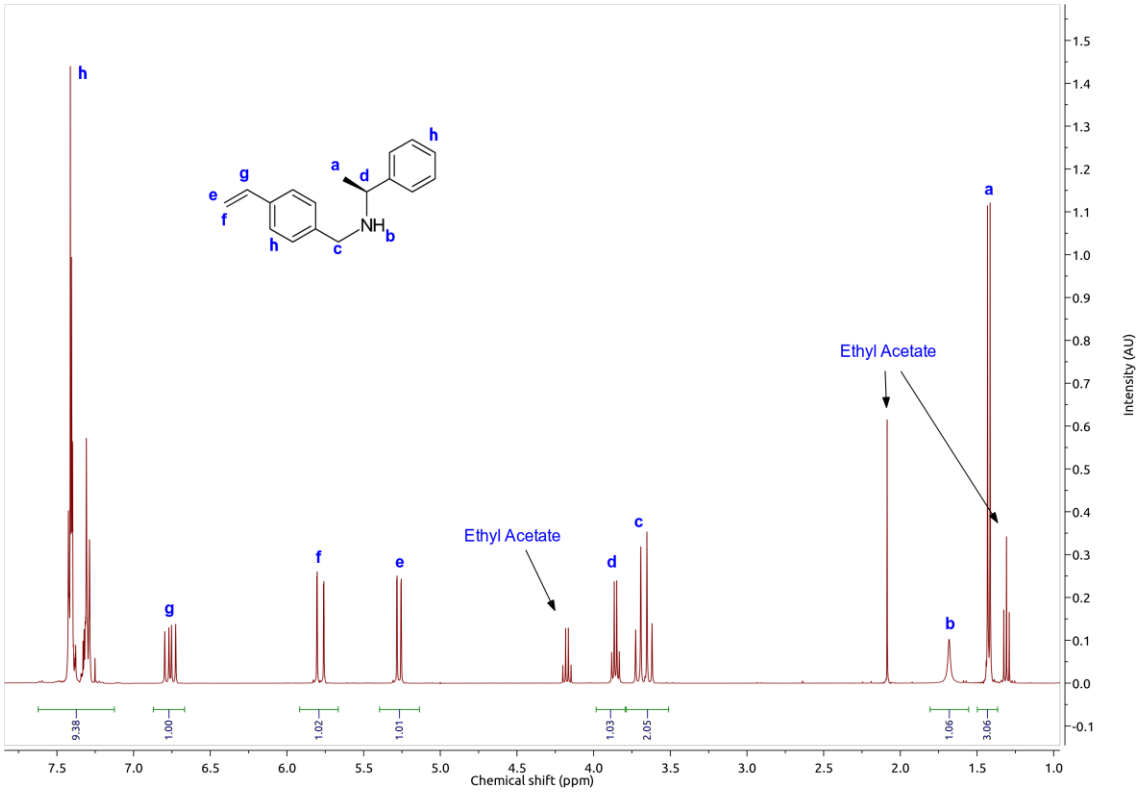


Figure 5-4: ^{1}H NMR of the secondary amine with a chiral centre

5.3 Synthesis of the inimer with chiral centre: (S)-Benzyl 1-phenylethyl(4-vinylbenzyl)dithiocarbamate [S-BPVD]

The synthesis of the dithiocarbamate inimer with a chiral centre from the secondary amine S-VBPE (**Scheme 5-3**) was very easy and also similar to the synthesis of the inimer BBVC (see **Section 2.3**). The inimer was synthesised from a secondary amine with a chiral centre and, since that centre was not affected during the reaction, that fragment should have the chirality unaffected in the inimer.

In order to purify the inimer a preparative chromatographic column was required. The process was not difficult except for loading the sample onto the column because it was a very dense black oil. If the oil was loaded onto the sand the sample got stuck and irregularities of the sand did not make an even elution front with the consequent failure of the separation.

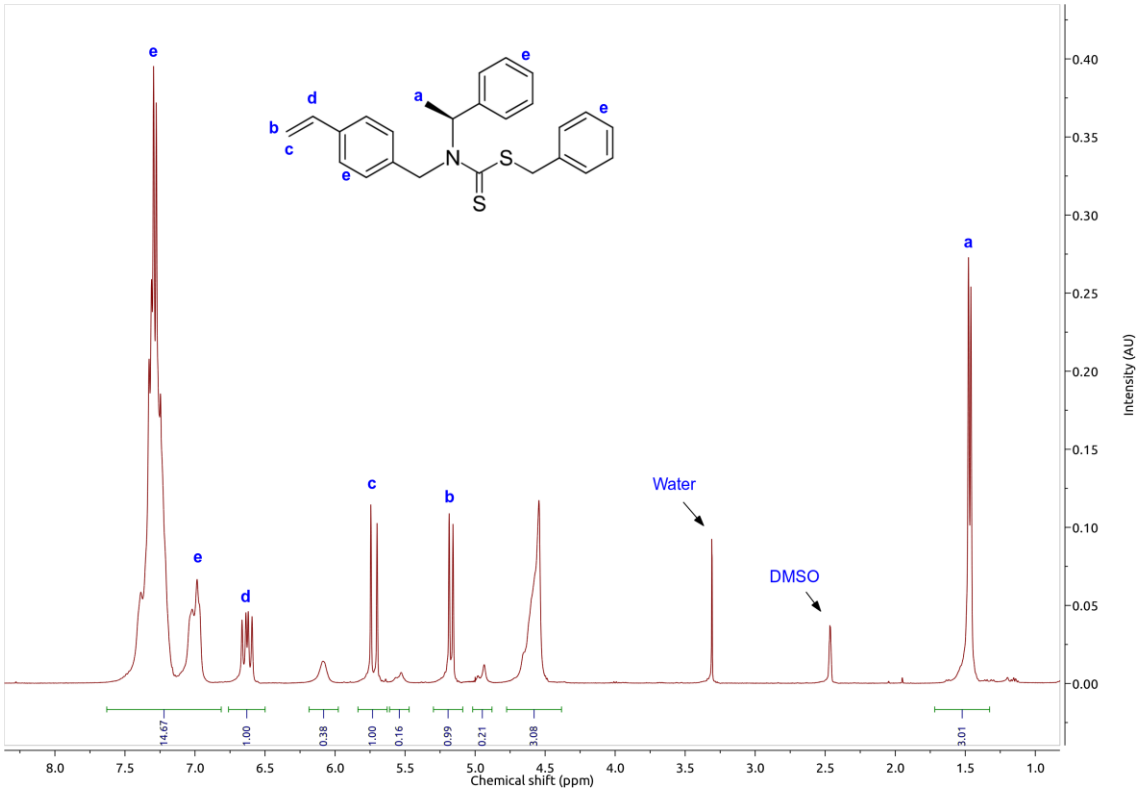
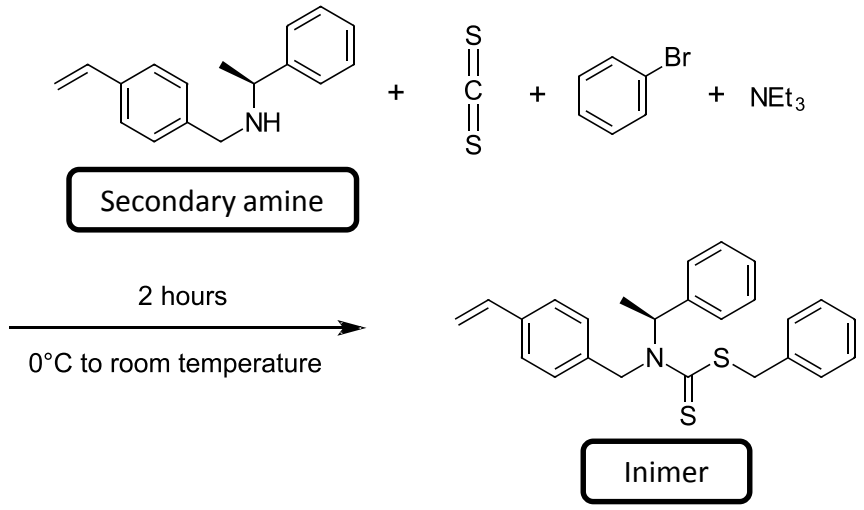


Figure 5-5: ^{1}H NMR of the inimer with chiral centre in DMSO-d_6 at 30°C

Therefore the sample was loaded directly onto the silica gel. Once the product was purified, a yellow oil was obtained. The oil crystallised after standing overnight in the fridge, producing a pale yellow solid which was analysed to confirm that the monomer did not polymerise.

In the ^{1}H NMR spectra of the inimer in DMSO-d_6 at 30°C (**Figure 5-5**). It was not possible to assign some peaks. It was necessary to heat the molecule to avoid the same effect that was found in the other two inimers BBVC and BBTD (see **Sections 2.3** and **3.3**). A gradient ^{1}H NMR was also performed to confirm that effect (**Figure 5-6**). In the ^{1}H NMR of the compound in DMSO-d_6 at 150°C all the signals were visible and easy to assign (**Figure 5-7**). It can be seen also that the false quartet that appeared from the benzylic protons of the styryl part in the secondary amine (peaks **c** in the **Figure 5-4**) are now the double doublets (peaks **c** in the **Figure 5-7**) explained before in **Section 5.2**.



Scheme 5-3: Synthesis of the inimer with chiral centre

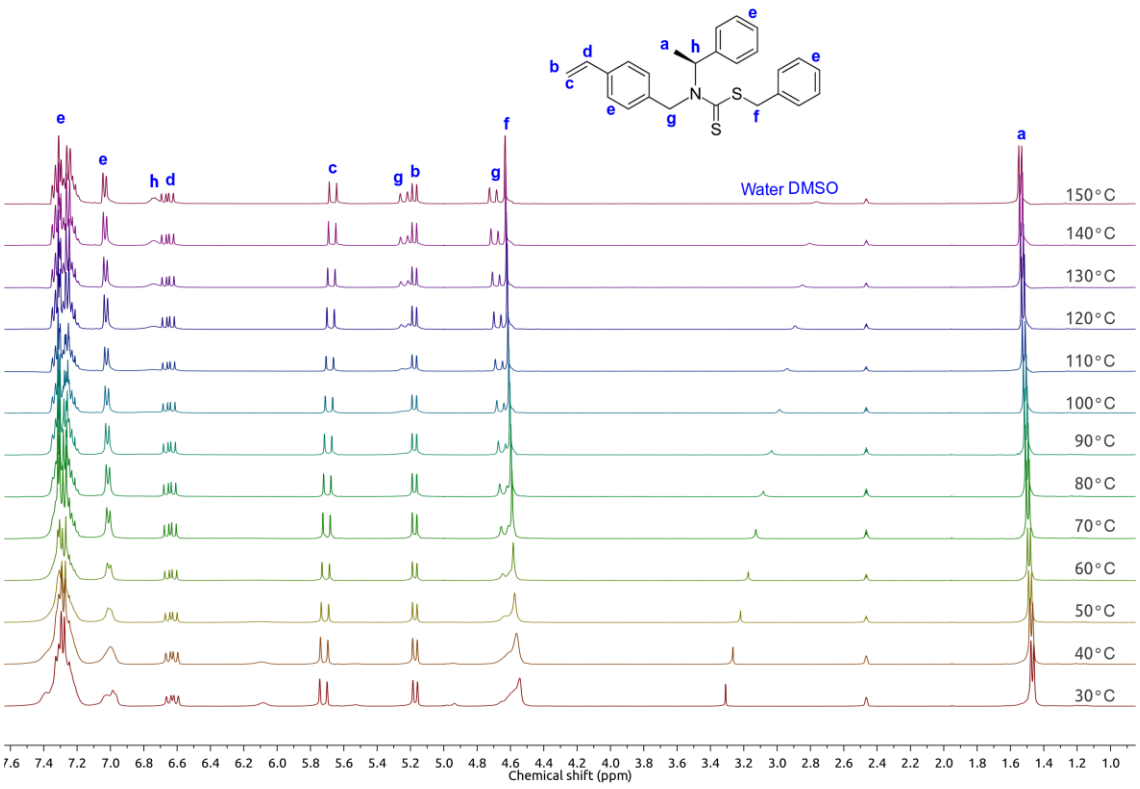


Figure 5-6: ^{1}H NMR gradient of the inimer with chiral centre in DMSO-d_6

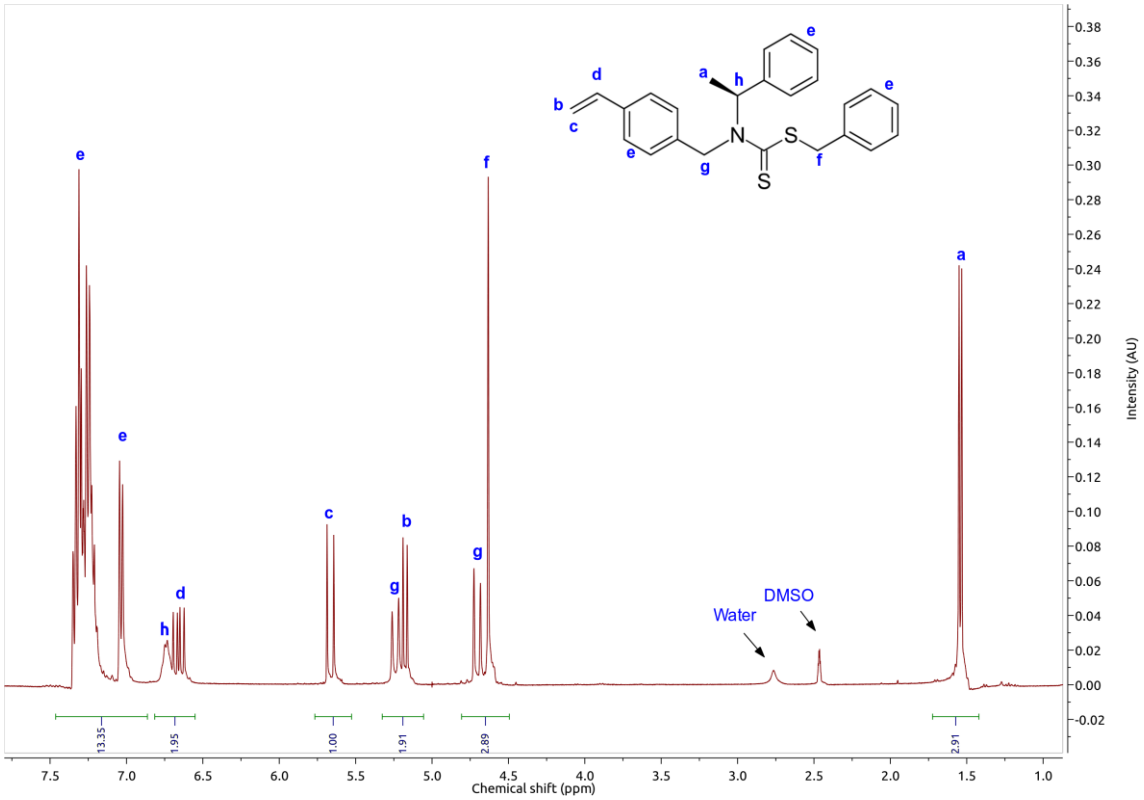
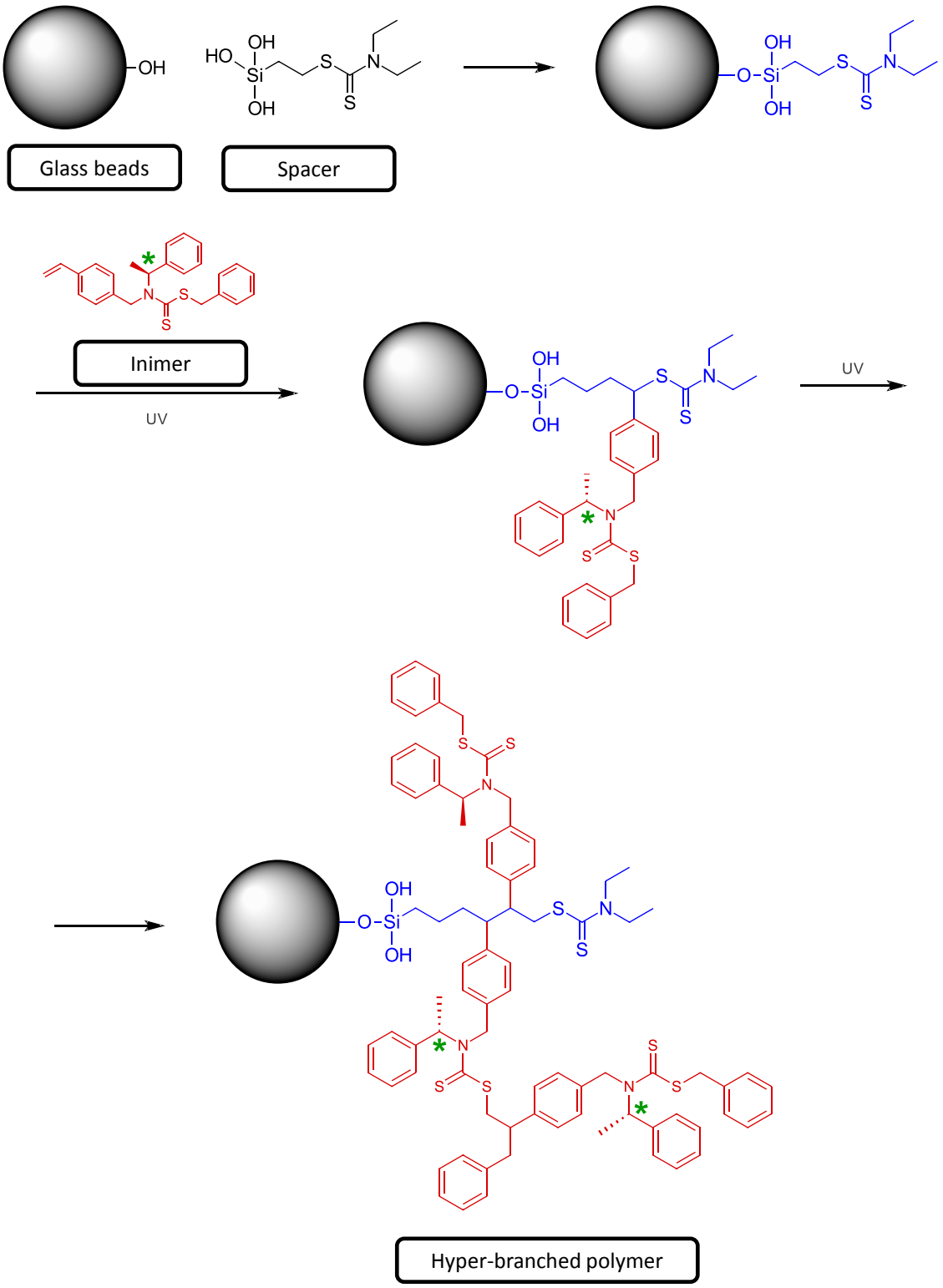


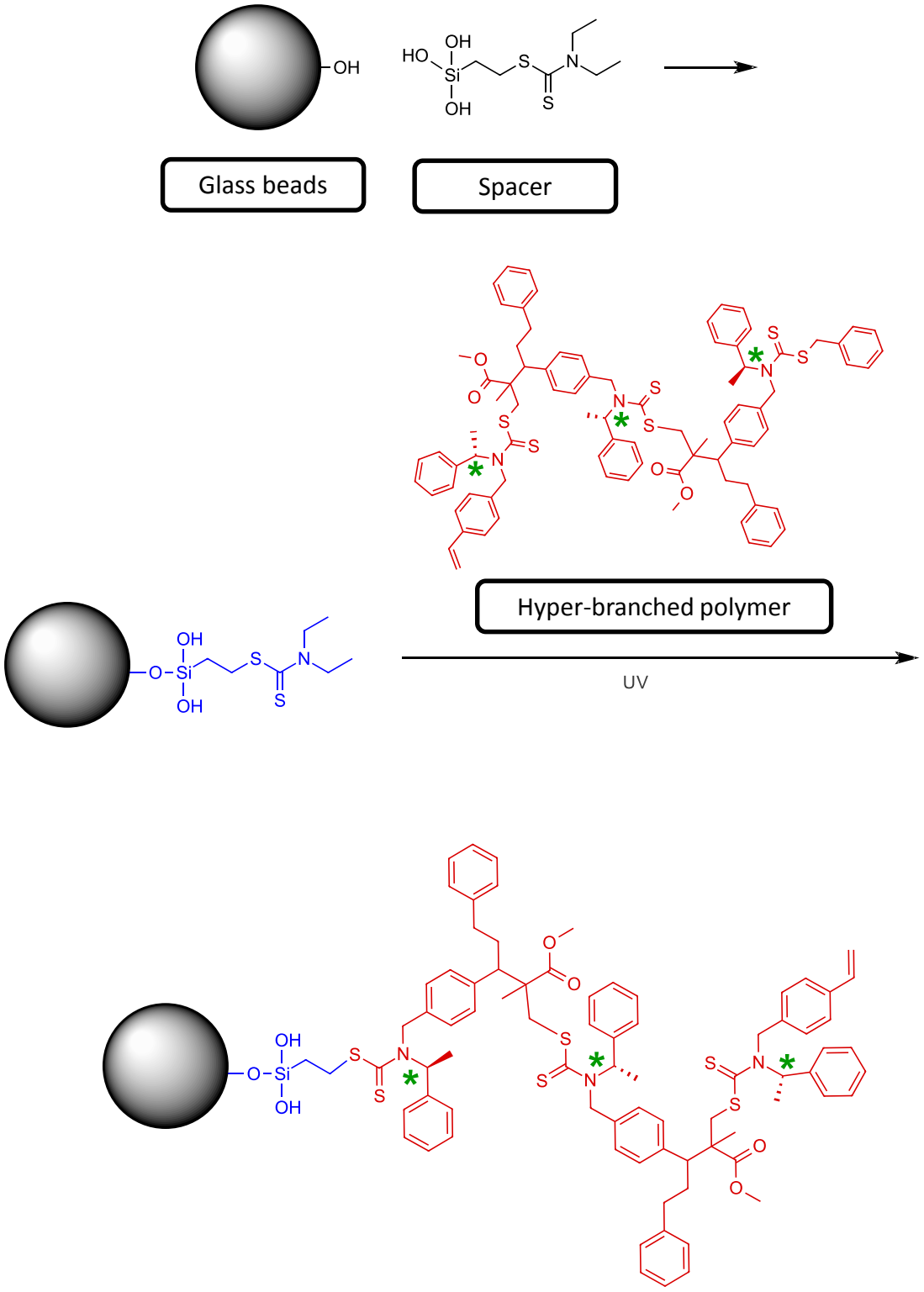
Figure 5-7: ^{1}H NMR of the inimer with chiral centre in DMSO-d_6 at 150°C

5.4 Synthesis of the hyper-branched polymer

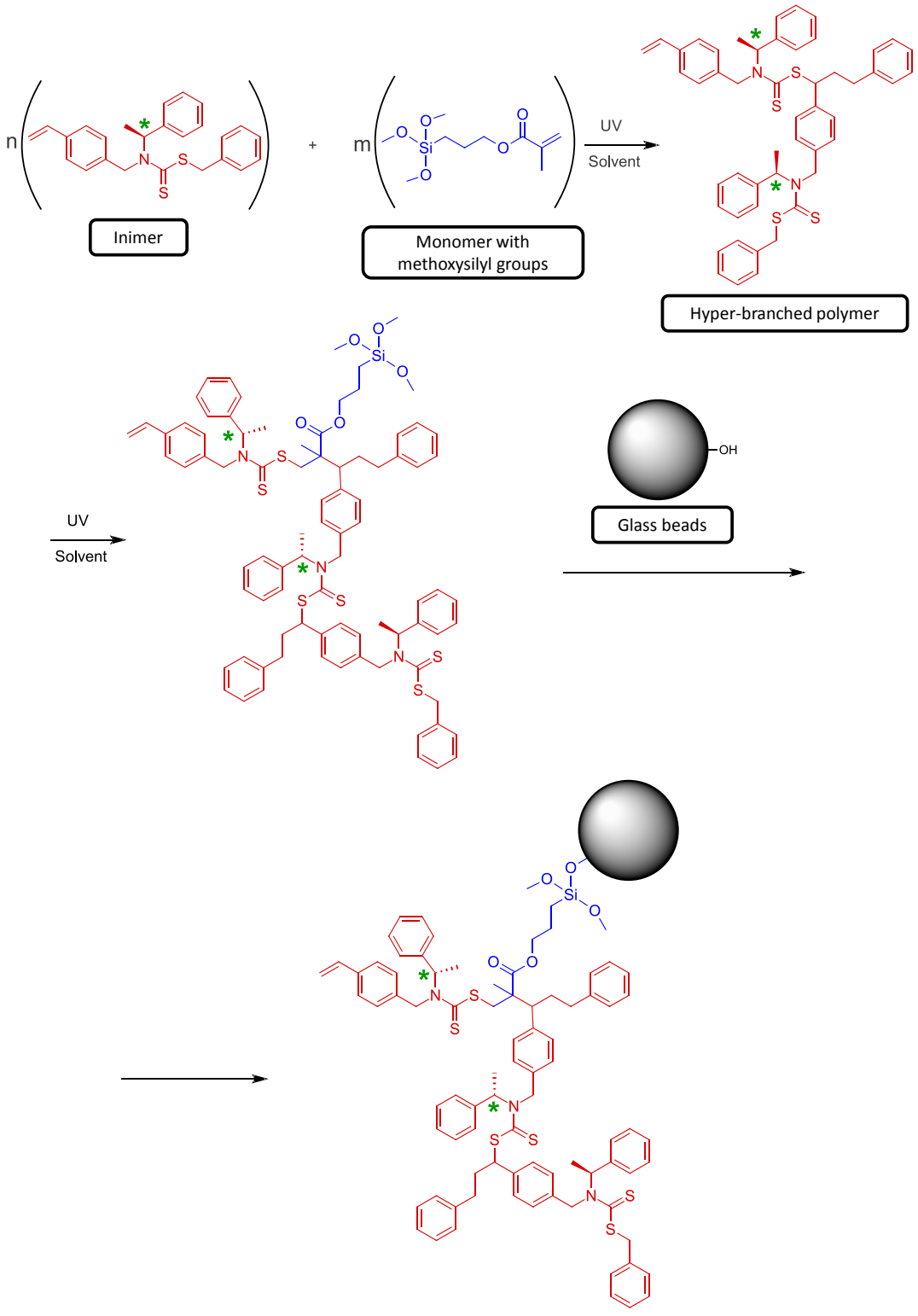
The next step was the creation of a hyper-branched polymer from the inimer with a chiral centre. In this experiment the initiator properties of the inimer could be used for the photopolymerisation process, either in the presence or absence of additional monomers. The resulting hyper-branched polymer will be chiral since the inimer used had a chiral centre and that centre should not be affected during polymerisation. The way to synthesise the hyper-branched polymer will depend on the way that the polymer is attached to the surface of the solid support; by this stage the support was chosen to be glass beads since they were convenient to handle, cheap, available in the laboratory, and also several protocols to modify the surface of those beads were have been done in the past. Three ways to graft the surface of glass beads with a hyper-branched polymer were proposed:



Scheme 5-4: First approach, grafting of glass beads using a spacer with dithiocarbamate functionality (in blue) and subsequently an inimer (in red) with chiral centres (green asterisks)



Scheme 5-5: Second approach, grafting of glass beads using a spacer with dithiocarbamate functionality (in blue) and subsequently a hyper-branched polymer (in red) with chiral centres (green asterisks)



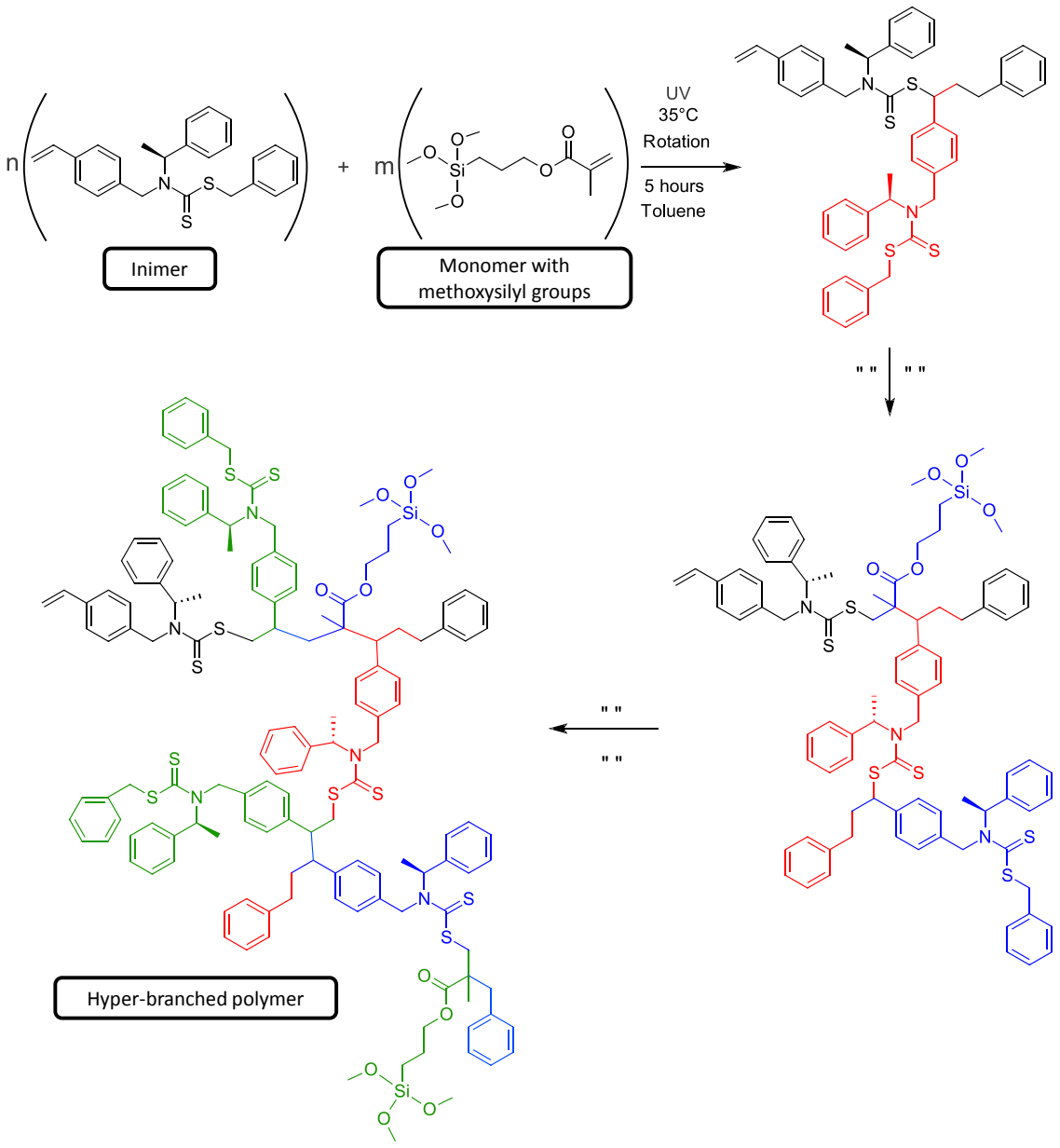
Scheme 5-6: Third approach, grafting of glass beads using a hyper-branched polymer made from an inimer (in red) with chiral centre (green asterisks) and a monomer with methoxysilyl groups (in blue)

1. In the first approach (**Scheme 5-4**) the glass beads could be modified by the attachment of a functional spacer that had siloxane groups in its structure. The spacer should have also another functionality that could allow us to graft the hyper-branched polymer to the surface of the system "bead-spacer". That could be accomplished if the spacer had a dithiocarbamate functionality. Irradiating with a UV source a suspension of the beads in a solution of the inimer S-BPVD polymer in certain solvent would generate radicals. The radicals generated on the surface of the beads will react with the double bond of the inimer and a hyper-branched polymer could be generated at the surface of the beads.
2. In the second approach (**Scheme 5-5**) the hyper-branched polymer could be generated first and then it could be attached in the same way the inimer is attached in the first approach.
3. In the second approach (**Scheme 5-6**) the hyper-branched polymer could be generated from a mixture of two monomers, one of the monomers could be the inimer BVPD and the another one could be a siloxane monomer. The hyper-branched polymer formed from that mixture will have reactive siloxane groups in its structure and those groups could allow the attachment of the polymer to the surface of the glass beads.

The three approaches were tried but only the third one proved to be effective. Therefore only the details and results of the third procedure, which by the date was a novel solution to the problem, will be discussed in this section.

5.4.1 Synthesis of the hyper-branched polymer: branched poly(3-(trimethoxysilyl)propyl methacrylate-*co*-(S)-Benzyl 1-phenylethyl(4-vinylbenzyl)dithiocarbamate) [branched poly(TMSPMA-BVPD)]

The inimer S-BPVD and the monomer poly(3-(trimethoxysilyl)propyl methacrylate (TMSPMA) were mixed in toluene, the solution was degassed and irradiated for several hours meanwhile the reaction vessel was slowly rotated (**Scheme 5-7**). The polymeric material was precipitated / centrifuged using a mixture of THF / EtOH and the solid was finally dried in the oven. The yellow solid was hard but easy to grind.



Scheme 5-7: Self-addition photopolymerisation, synthesis of a hyper-branched polymer with the inimer S-BPVD and the monomer with methoxysilyl groups TMSPMA

The ^{1}H NMR analysis showed that the polymer contained both monomers in its structure (**Figure 5-8**). The analysis had to be performed in $CDCl_3$, since the material was not soluble in DMSO-d_6, and therefore the peaks were broad. Toluene-d_8 could have been used instead, but the toluene signal would appear in the same region of the spectrum as the reference signal for the BVPD inimer.

Therefore the solution could not be heated above 60°C and the peaks that appeared in the ^{1}H NMR analysis were broad. This means that the ratio of BVPD / TMSPMA = 1 / 3.85 is at best a rough approximation (**Appendix E**).

In the comparison of FTIR spectra (**Figure 5-9**), peaks for the C=O (1722 cm^{-1}), C-N (1475 cm^{-1}) and O-CH_3 (1200 cm^{-1}, 1162 cm^{-1}, 1085 cm^{-1}) groups where found in the hyper-branched polymer (Paunikallio *et al*., 2008). The peak for the double bond at 1625-1638 cm^{-1} disappeared in the spectrum of the polymer.

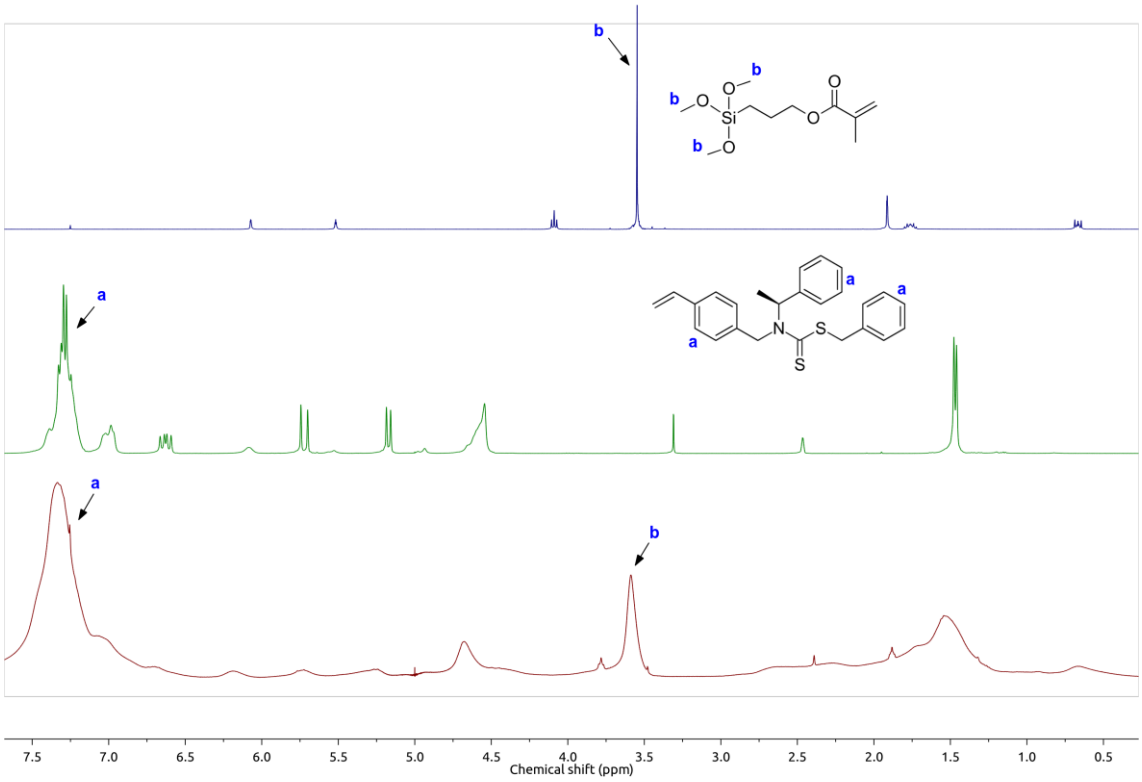


Figure 5-8: ^{1}H NMR of the hyper-branched polymer branched-poly(TMSPMA-*co*-BVPD)

In the comparison of the chromatograms obtained from the GPC analysis (**Figure 5-12**) it can be seen how upon irradiation the monomer is polymerised. The distribution of the polymer is quite broad but the result was expected since the hyper-branched obtained following this mechanism show bimodal patterns.

The size of the polymer is rather small but that was also expected since those polymers have globular conformations in solution and therefore these GPC analysis cannot give accurate values.

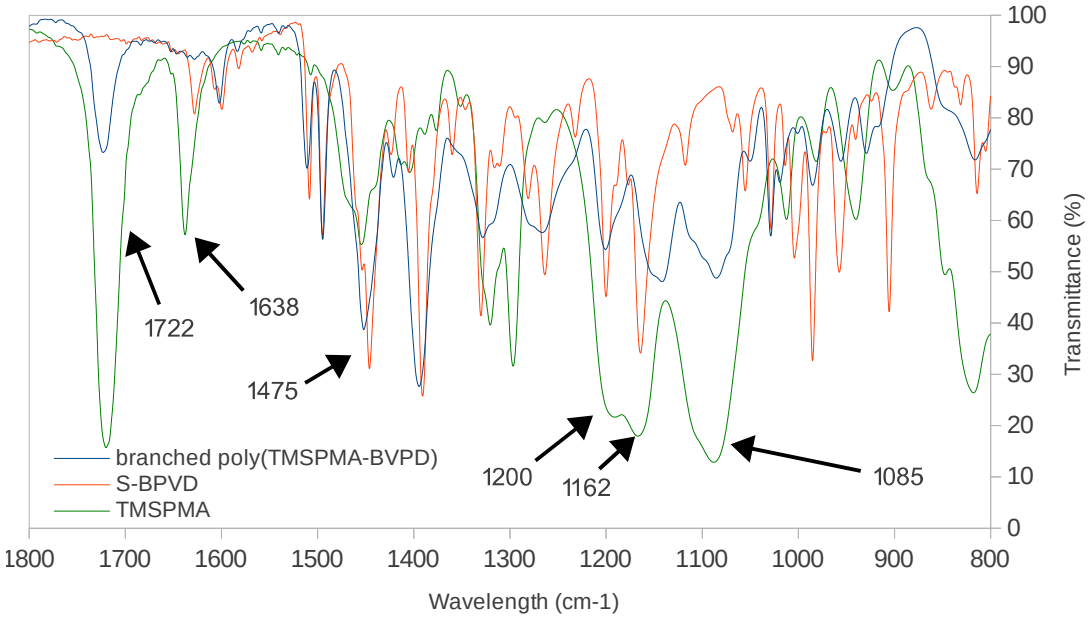


Figure 5-9: FTIR analysis of the hyper-branched polymer compared with the two monomers used in its polymerisation

5.5 Modification of the glass beads with the hyper-branched polymer

Glass beads were chosen as a solid support for the hyper-branched polymers since they are cheap and easy to modify with molecules containing alkoxysilyl groups.

5.5.1 Activation of the glass beads

In order to have the highest number of silanol groups (-Si-OH) available in the surface of the glass beads the commercially obtained glass beads must go through an activation process. The silanol groups will react with the hyper-branched polymer and will allow modification of the surface (**Scheme 5-7**). To

activate them, the beads, 9-13 or 75 μm, were suspended in $NaOH_{aq}$ and refluxed for some minutes. Then the beads were washed with deionised water, followed by acetone, and then dried in the oven. The 75 μm glass beads were easier to activate, since the 9-13 μm ones had high polydispersity and they blocked the filters very easily.

5.5.2 Derivatisation of the 9-13 and 75 μm glass beads with the hyper-branched polymer branched poly(TMSPMA-BVPD)

Since the hyper-branched polymer contained methoxysilyl groups it can be grafted onto the surface of activated glass beads via reaction with the silanol groups of the freshly-activated glass surface.

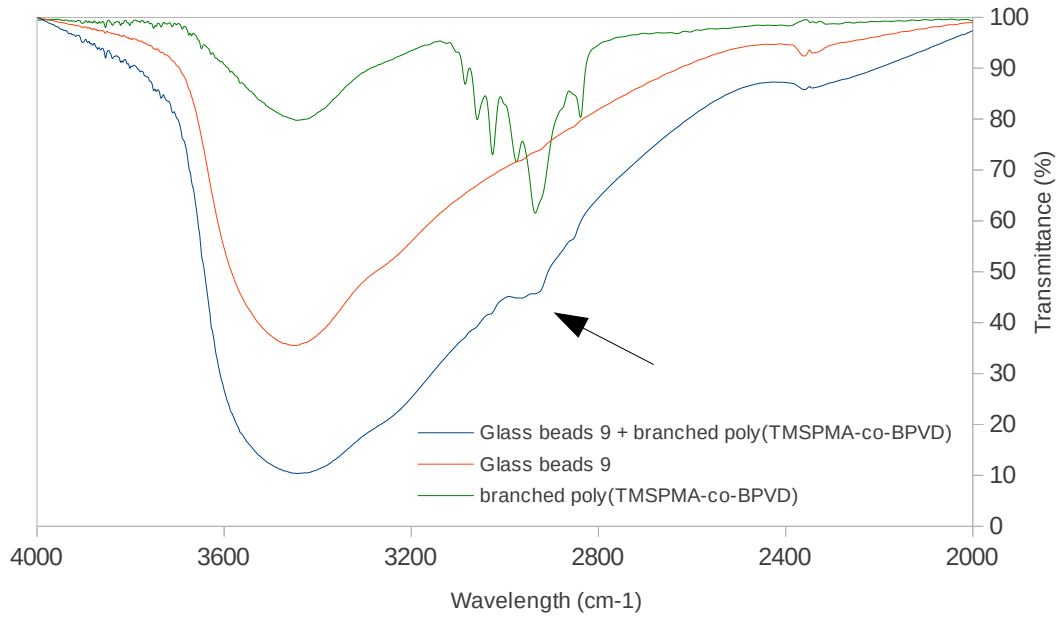


Figure 5-10: Comparison of the FTIR spectra of the reactive hyper-branched polymer with that of the unmodified and modified 9-13 μm glass beads (I)

The activated glass beads were suspended in a solution of the hyper-branched polymer, the suspension was degassed and it was left to react overnight at room temperature in the dark. The vessels were also rotated to promote even coverage of the beads during the reaction. After the reaction time the beads were washed thoroughly and dried.

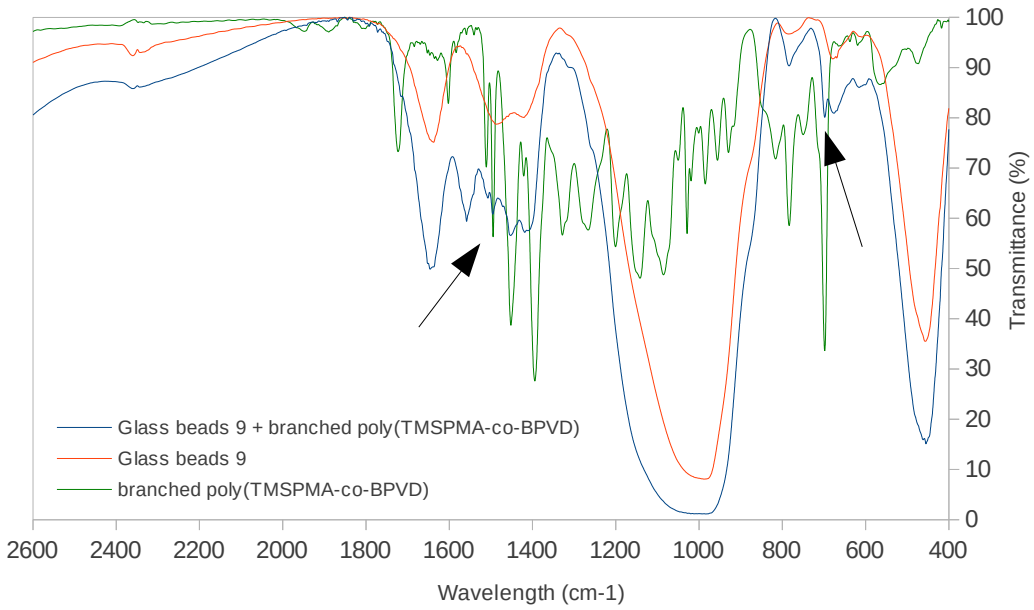


Figure 5-11: Comparison FTIR of the modified 9-13 µm glass beads (II)

In the analysis of the FTIR spectrum of the 9-13 µm modified glass beads (**Figure 5-10** and **Figure 5-11**) some peaks corresponding to the hyper-branched polymer could be observed. The intensity of those peaks was very low, the sensitivity for the measurements of the grafting could be compromised due to the low concentration of grafted polymer in comparison to the higher concentration of glass beads.

The elemental analysis of these beads (**Table 5-1**) showed that the content of C, H, N and S was especially high in the modified glass beads. This was sufficiently encouraging to try the beads in the chiral separations. However the small size of the beads caused very high pressures in the HPLC system and made it impossible to use of such small beads for the separation.

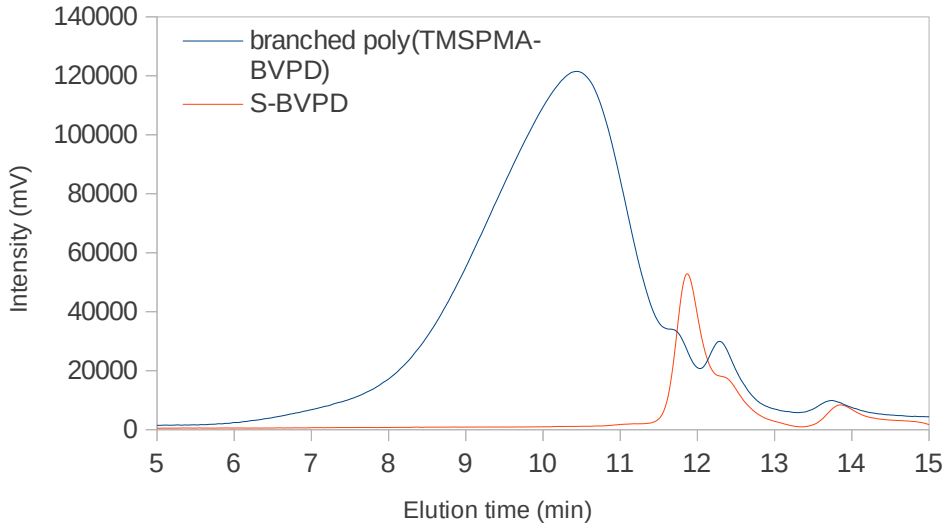


Figure 5-12: GPC of the hyper-branched polymer branched poly(TMSPMA-*co*-BPVD)

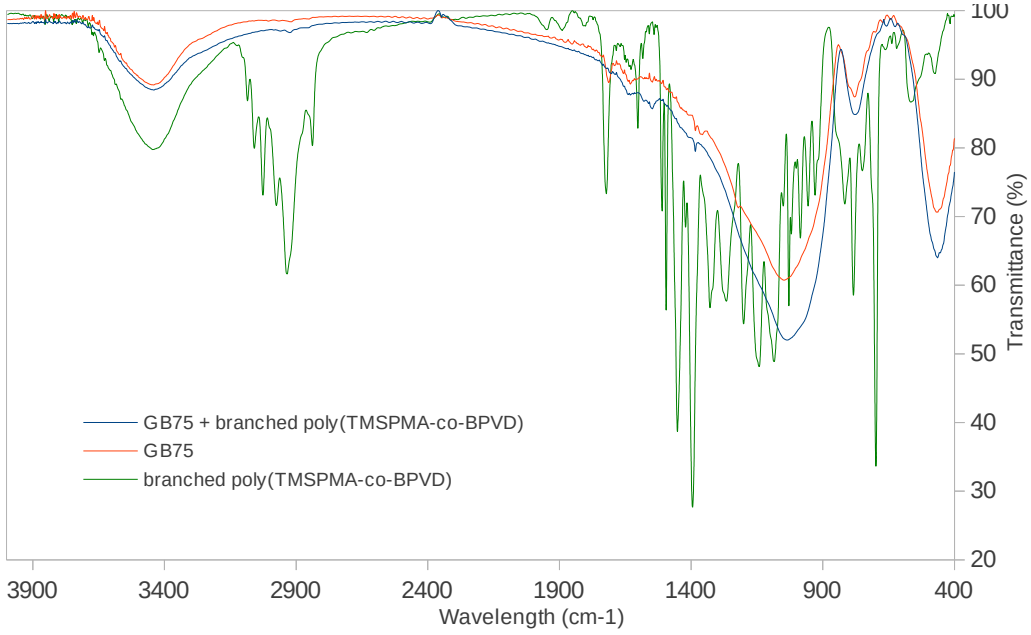


Figure 5-13: Comparison FTIR of the modified 75 µm glass beads

The next step was the analysis of the 75 µm modified beads. The FTIR analysis of these beads (**Figure 5-13**) did not show significant changes compared to the un-modified glass beads. There were some minor peaks but close to the detection limit of the technique. The elemental analysis of these beads (**Table**

5-2) did not show better results, the amount of C, H, N and S did not change comparing with the un-modified glass beads. The size of the beads was analysed with a particle size analyser and the values indicated an increase in the size of about one micron.

Table 5-1: Elemental analysis of 9-13 µm modified and un-modified glass beads

	C	H	N	S
9-13 µm modified glass beads	9.40	1.72	0.29	1.19
9-13 µm un-modified glass beads	0.80	<0.10	<0.10	<0.10

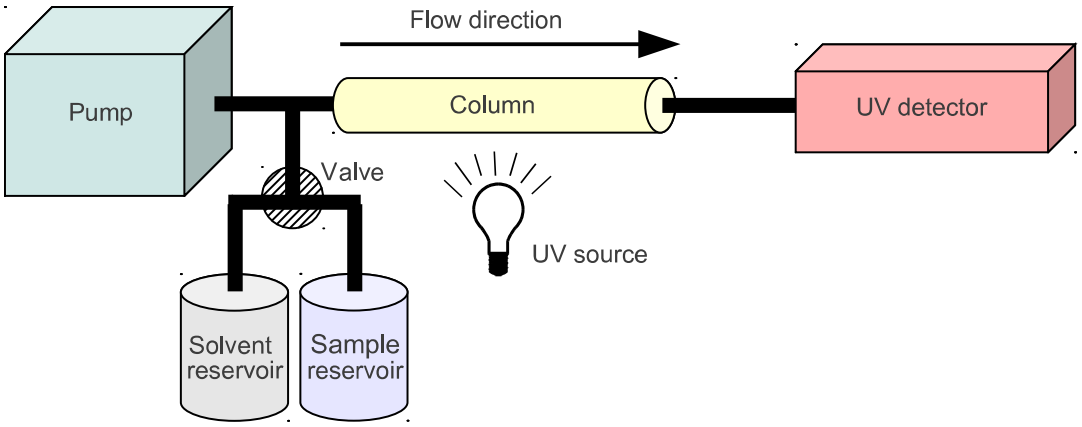
The analysis of the surface area, using nitrogen as the adsorbate, gave a change from 27.43 m^2 / g to 6.53 m^2 / g from the un-modified beads to the modified ones. The results of those analyses were not encouraging but it was decided to carry on with the separations using those beads since they looked physically different.

Table 5-2: Elemental analysis of 75 µm modified and un-modified glass beads

	C	H	N	S
75 µm modified glass beads	0.11	<0.10	<0.10	<0.10
75 µm un-modified glass beads	0.95	<0.10	<0.10	<0.10

5.6 HPLC separation system

The stainless steel column equipped with frits was packed with the 75 µm modified glass beads applying pressure in order to produce a homogeneous filling. The column was connected to a HPLC system (**Scheme 5-8**) that consisted of a pump, reservoirs of solvent and sample, column and detectors. The column was inside a photochemical safety cabinet since it had to be irradiated during the process.



Scheme 5-8: HPLC system to perform chromatography separations of mixtures using columns packed with dithiocarbamate and thiuram based polymers that generate radicals upon UV irradiation

5.7 Separation

Volumes of solutions of different concentrations of the (+) and (–) forms of ephedrine were injected separately and their retention times were recorded. The results, including the retention factors, can be seen in **Table 5-3**. The retention factors ($\kappa = (t_a - t_e) / t_e$, being t_a and t_e the retention times of the acetone and the ephedrine respectively) are very low but the chiral resolution has been achieved in some extent, with separation factors ($\alpha = \kappa_{-e} / \kappa_{+e}$, being κ_{+e} and κ_{-e} the retention factors for (+) and (-) ephedrine respectively) around 1.4 for both concentrations.

Table 5-3: Results from the chiral resolution of (+) and (-)-ephedrine

Analyte : Concentration	Retention time (t_i)	Retention factors (κ_e)	Separation factors (α)
(+)-Ephedrine : 1 mg / mL	6.85	0.038	1.38
(-)-Ephedrine : 1 mg / mL	6.95	0.053	
Acetone	6.6	-	
(+)-Ephedrine : 0.1 mg / mL	7.7	0.069	1.41
(-)-Ephedrine : 0.1 mg / mL	7.9	0.097	
Acetone	7.2	-	

5.8 Conclusions

1. A secondary amine and an inimer with a specific structure and chiral centre were designed and synthesised.
2. The inimer was polymerised under controlled conditions to generate a hyperbranched polymer with chiral centres.
3. The hyperbranched polymer was attached to a solid support: glass beads.
4. The modified glass beads were used as column packing for columns connected to HPLC systems. Those systems were used to test the ability of the polymer to resolve chiral mixtures.
5. The hyperbranched polymer attached to glass beads showed some potential to use it in the separation of enantiomers.

5.9 Future work

It was impossible to synthesise inimers using the secondary amines generated from the methyl ester derivatives of several amino acids. It could be possible that the ester functionality affected severely the reactivity of the secondary amine. The reasons behind that behaviour were not further investigated. It is suggested to continue the investigation because it could be beneficial to have more functional groups in the inimer and therefore in the polymer. More functional groups could help in the separations because the analytes could be retained by the interaction of their polar functional groups with the stationary phase. That last point could be solved adding a monomer with specific functionalities to the synthesised hyper-branched polymer; the polymer is a macromer-iniferter so the addition of new monomers should be easily photo-induced.

The modified 9-13 micron beads were too small for the HPLC system, or maybe their high polydispersity affected the columns seriously having continuous blockages. It is suggested to buy a better quality beads or buy a beads with bigger size. But not as big as the beads of 75 microns, since these beads did not compromise the HPLC system but they did not perform very well, they were probably too big and with a very small surface area. Alternatively to the glass

beads, it could be a good solution trying another solid support, like for instance monodisperse porous silica particles.

The inimer, hyper-branched polymer and beads should be analysed to check that the chirality remained unaffected during the process.

6 MATERIALS AND METHODS

6.1 General materials

4-Vinylbenzylchoride (VBC), n-butylamine (NBA), carbon disulphide (CS), benzyl bromide (BB), triethylamine (TEA), ethylene glycol dimethacrylate (EGDMA), styrene (St), methyl methacrylate (MMA), methacrylic acid (MA), toluene, acetone, diethyl ether, acetonitrile (ACN), ethyl acetate (EtOAc), hexane, tetrahydrofuran (THF), ethanol (EtOH), methanol (MeOH), chloroform, dichloromethane, magnesium sulphate, hydrochloric acid, iodine, sodium hydroxide were used as received from Fisher (Loughborough, UK) / Sigma–Aldrich (Gillingham, UK) / Acros (Loughborough, UK) / BDH (Poole, UK).

The initiator Azobisisobutyronitrile (AIBN) was bought from BDH (Poole, UK) and recrystallized from ethanol before use.

The distilled water was obtained from a Millipore Direct-Q 3 Ultrapure Water Systems (Watford, UK) fitted with a Millipak-20 Express, 0.22 µm non-sterile filter.

The 60Å 200µm thickness silica gel Macherey-Nagel TLC plates with F254 fluorescent indicator were bought from Fisher (Loughborough, UK). The support of the plates was flexible aluminium or glass; it did not affect the performance of the plates.

The solutions were concentrated in a Buchi rotavapor R-114 (Oldham, UK) using a Buchi B-480 waterbath and a Neuberger KNF Laboport diaphragm pump (Oxon, UK) with a 10 l / min flow rate and 8 mbar ultimate vacuum.

The reactions were stirred and or heated with a magnetic stirrer / hot plate IKA-Werke RCT Basic (Staufen, Germany) with a ETS-D4 fuzzy &Temperature Controller attached.

The Pyrex glassware used to synthesise the different polymers with UV irradiation was purchased from Fisher, Sigma-Aldrich and Radleys (Essex, UK). The pyrex-filtered UV light have wavelengths > 320 nm (Costantini *et al*., 1994).

The different UV sources used in the experiments were:

- CERMAX 300W Xenon Arc Lamp (ILC Technology Inc., USA)
- Philips original home solaria UV lamp, HB 171-A, 4x Philips CLEO 14W, UV Type 3 (Surrey, UK)
- UVP UVGL-25 Compact UV lamp 254 / 365 nm UV, 4W (Cambridge, UK)

6.2 Elemental analysis

All the elemental analyses were carried out by MEDAC LTD (Surrey, UK). The accuracy of the analyses was ±0.30% absolute and the detection limit was <0.1%

6.3 FTIR analysis

FTIR spectra were recorded using an AVATAR 370 ThermoNicolet spectrometer (Madison, USA). To record the FTIR spectra just a few milligrams of sample were mixed with 200 mg of potassium bromide (Sigma-Aldrich, Gillingham, UK) and the mixture was pressed into a tablet which was then used in the analysis. Before mixing, the solids (including the KBr) were ground into a fine powder and then dried in the oven for 30 minutes at 50ºC to avoid the signals due to the water imbibed from atmospheric moisture.

6.4 NMR analysis

NMR spectra were recorded using a JEOL ECX-400 NMR spectrometer (Welwyn Garden City, UK). The deuterated solvents used for the NMR analysis were purchased from Goss Scientific Instruments Ltd. (Cheshire, UK). The signal of the DMSO-d_6 was chosen as the reference (R. E. Hoffman, 2006) in the temperature gradient ^{1}H NMR analysis of the three synthesised inimers.

6.5 EPR analysis

In the EPR studies an ELEXSYS E 500 CW EPR Spectrometer (Bruker, Germany) fitted with an SHQ resonator at X-Band frequency was used. For

irradiation during EPR measurement, an ER203 UV System with a 100W Hg arc lamp was used as UV source.

6.6 GPC analysis for all the experiments in Chapter 2

The Gel Permeation Chromatography (GPC) system used to determine the molecular weights was a WATERS 717 plus autosampler GPC system (Waters, Hertfordshire, UK) equipped with Gilson 305 pump (Anachem, UK), WATERS millipore lambda-max 481 LC spectrophotometer detector, and Phenomenex 300 × 7.8 mm 5 µ GPC column (Phenonenex, Macclesfield, UK) at 25ºC under dark conditions, using THF as the eluent at a flow rate of 1 mL / min. Monodisperse polystyrene molecular weight standards (Phenomenex, Macclesfield, UK) were used for GPC calibration.

6.7 GPC analysis for all the experiments in Chapters 3 and 5

The GPC system used was a Shimadzu system (Milton Keynes, UK) with a degasser DGA-20A5, a LC-20AD Pump, an autosampler SIL-20A, a column oven CTO-10ASVP, a UV-Vis Detector SPD-20A and a refractive index detector RID-10A. The columns used to determine the molecular weights were a Phenomenex Phenogel 5µ 50Å 300 × 7.8 mm and a Phenomenex Phenogel 5µ 104 Å 300 × 7.8 mm GPC column (Phenonenex, Macclesfield, UK). The columns were used in the analysis at 25ºC under dark conditions, using THF as eluent at a flow rate of 1 mL / min. Monodisperse polystyrene molecular weight standards (Phenomenex, Macclesfield, UK) were used for GPC calibration.

6.8 Measurement of the size of the modified and un-modified glass beads

The particle size distribution of the modified and un-modified glass beads was analysed with methods based on laser diffraction (Mastersize X, Worcestershire, UK) using a focal length of 100 mm and a beam length of 2.4 mm. The beads were suspended in ethanol for the analysis.

Measurement of the surface area of the modified and un-modified glass beads

The BET surface area results (Lowell, 2004) of the modified and un-modified glass beads were obtained with the NOVA 1000e surface area analyser (Hook, UK). The analyses were done at 77.4 K, using carbon as the adsorbent model and nitrogen as the adsorbate.

6.9 Preparative chromatography columns

The preparative chromatography columns were prepared using silica gel 0.035-0,070 mm 60Å from Acros (Loughborough, UK) as stationary phase. Sand of 50-70 mesh particle size (Sigma–Aldrich, Gillingham, UK) was used to protect the lower and upper extremes of the silica. The mobile phases were mixtures of hexane and ethyl acetate in a gradient of progressively increasing polarity. The different fractions were collected in test tubes and analysed with TLC plates developed with a 4W 254 nm UV lamp.

6.10 Synthesis of secondary amines

6.10.1 N-(4-vinylbenzyl)butan-1-amine [NVBA]

VBC (5.00 g, 32.8 mmol) and NBA (23.99 g, 328 mmol) were mixed and the mixture was stirred for 24 hours at room temperature. A sample of the mixture (0.75 g) was taken and the excess of NBA was removed in a rotary evaporator. The resulting solid was dissolved in diethyl ether to precipitate the salt formed in the reaction which was removed by filtration. The remaining salts were removed by extraction with brine / diethyl ether (× 3) since the product has good solubility in water. The organic phase was dried over magnesium sulphate and the solvent removed in rotavapor. The product was purified by distillation using a rotary pump and heating the solution up to 80ºC with a silicon oil bath at 130ºC to give a yellow oil (yield: 90%). ^{1}H NMR, 400MHz, CDCl3, 25ºC, δ: 0.92 (t, 3H, *CH*$_3$-), 1.37 (hex, 2H, CH$_3$-*CH*$_2$-), 1.52 (pen, 2H, CH$_3$-CH$_2$-*CH*$_2$-), 1.71 (s, 1H, -N*H*-), 2.64 (t, 2H, -CH$_2$-C*H*$_2$-NH-), 3.79 (s, 2H, -NH-C*H*$_2$-Ar), 5.23 (d, 1H, *H*-CH=CH-Ar, $^{3}J_{cis}$ = 10.48 Hz), 5.74 (d, 1H, *H*-CH=CH-Ar, $^{3}J_{trans}$ = 17.63 Hz), 6.72 (ddt, 1H, CH2=C*H*-Ar, $^{3}J_{cis}$ = 10.48 Hz, $^{3}J_{trans}$ = 17.63 Hz), 7.30 (d, 2H, -C$_6$*H*$_4$-), 7.38 (d, 2H, -C$_6$-). ^{13}C NMR, 100.5 MHz, CDCl$_3$, 25ºC δ: 13.85 (*C*H$_3$-), 19.98 (CH$_3$-*C*H$_2$-), 31.74 (CH$_3$-CH$_2$-*C*H$_2$-), 48.36 (-NH-*C*H$_2$-Ar), 52.81 (-CH$_2$-*C*H$_2$-NH-),

113.17 (CH_2=CH-Ar), 125.77, 127.94 (-C_6H_4-), 141.01 (CH_2=CH-Ar). FTIR (KBr) 3315 cm^{-1}, 1515 cm^{-1} (N-H), 1629 cm^{-1} (CH=CH2). Analysis $C_{13}H_{19}N$, calcd: C, 82.48; H, 10.12; N, 7.40, found: C, 81.52; H, 10.42; N, 7.15.

6.10.2 (S)-N-(4-vinylbenzyl)1-phenyl-ethanamine [S-VBPE]

4-VBC (5.00 mL, 32.8 mmol) and (*S*)-1-phenylethanamine (Sigma–Aldrich, Gillingham, UK) (25 mL, 193.93 mmol) were mixed and the mixture was stirred for 24 hours at room temperature. After that time diethyl ether (25 mL) was added and the organic phase was washed with water repeatedly to remove salts and the unreacted primary amine. The organic phase was dried over magnesium sulphate and the solvent was removed. The product was purified by column chromatography on silica (hexane / ethyl acetate, from 9.5:0.5 to pure ethyl acetate) giving a light-yellow oil (yield: >90%). Rf = 0.68 (ethyl acetate, silica gel). ^{1}H NMR, 400MHz, $CDCl_3$, 30 ºC, δ: 1.37 (d, 3H, CH_3-CH-C_6H_5, ^3J = 6.60 Hz), 1.66 (s, 1H, -N*H*-), 3.62 (dd, 2H, -NH-CH_2-Ar, ^3J = 13.22 Hz, ^3J = 16.31 Hz), 3.81 (q, 1H, -C*H*-C_6H_5, ^3J = 6.60 Hz), 5.22 (d, 1H, *H*-CH=CH-Ar, ^2J = 0.97 Hz, $^3J_{cis}$ = 10.77 Hz), 5.73 (d, 1H, *H*-CH=CH-Ar, ^2J = 0.97 Hz, $^3J_{trans}$ = 17.74 Hz), 6.71 (ddt, 1H, CH_2=C*H*-Ar, $^3J_{trans}$ = 17.74 Hz, $^3J_{cis}$ = 10.77 Hz), 7.32 (m, 9H, -C_6H_5, CH_2=CH-C_6H_4-). FTIR (KBr) 3322 cm^{-1}, 1505 cm^{-1} (N-H), 1626 cm^{-1} (CH=CH_2). Analysis $C_{17}H_{19}N$, calcd: C, 86.03; H, 8.07; N, 5.90, found: C, 81.13; H, 8.15; N, 5.03.

The aqueous phase obtained in the first extraction was saturated with sodium chloride and the unreacted primary amine was extracted several times with diethyl ether. The solvent was evaporated in the rotavapor, the yellow oil was analysed to check the purity and was used in the following synthesis.

6.11 Synthesis of the inimers

6.11.1 Benzyl N-butyl-N-(4-vinylbenzyl)dithiocarbamate [BBVC]

Because of the light-sensitive features of the molecule the synthesis and purification was done trying to keep exposure to light to a minimum in order to

keep the dithiocarbamate groups intact and to avoid undesirable photochemical polymerisations from occurring.

CS (0.402 g, 5.28 mmol) and BB (0.334 g, 2.64 mmol) were added to a 100ml round bottomed flask in an ice / water bath and the mixture was stirred with a magnetic stir bar for 5 minutes. The cooling bath is necessary to avoid the evaporation of the CS_2 and minimise the heating effect due to the exothermic nature of the reaction (Rudorf, 2007). NVBA (0.500 g, 2.64 mmol) and TEA (0.534 g, 5.28 mmol) were mixed separately and then added to the reaction flask drop wise. The reaction was stirred at 0ºC for 30 minutes and after that time the mixture was allowed to warm to room temperature and stirred until the reaction was complete (about 1 hour; as determined by TLC). The reaction mixture was diluted with water (50 mL) and the product extracted with diethyl ether (3 × 15 mL). The organic layers were dried over $MgSO_4$ and the solvent removed. The product was purified by column chromatography on silica with hexane / ethyl acetate (9.5:0.5) as eluent giving a dark-yellow oil (yield: 93%). Rf = 0.62 (hexane / ethyl acetate 9:1, silica gel). ^{1}H NMR, 400 MHz, DMSO-d_6, 100°C, δ: 0.87 (t, 3H, C*H*$_3$-), 1.31 (hex, 2H, CH_3-C*H*$_2$-), 1.66 (pen, 2H, CH_3-CH_2-C*H*$_2$-), 3.85 (t, 2H, -CH_2-C*H*$_2$-NH-), 4.61 (s, 2H, -C*H*$_2$-C_6H_5), 5.20 (s, 2H, -NH-C*H*$_2$-Ar), 5.24 (d, 1H, *H*-CH=CH-Ar, ^{2}J = 0.92 Hz, $^{3}J_{cis}$ = 10.89 Hz), 5.74 (d, 1H, *H*-CH=CH-Ar, ^{2}J = 0.92Hz, $^{3}J_{trans}$ = 17.77 Hz), 6.74 (dd, 1H, CH_2=C*H*-Ar, $^{3}J_{\text{trans}}$ = 17.77 Hz, $^{3}J_{\text{cis}}$ = 10.89 Hz), 7.32 (m, 9H, aryl). ^{13}C NMR, 100.5 MHz, DMSO-d_6, 100°C, δ: 12.32 (*C*H_3-), 18.60 (CH_3-*C*H_2-), 27.79 (CH_3-CH_2-*C*H_2-), 40.96 (-*C*H_2- C_6H_5), 52.26 (-NH-*C*H_2-Ar), 55.41 (-CH_2-*C*H_2-NH-), 113.23 (*C*H_2=CH-Ar), 125.50, 126.27, 126.83, 127.46, 128.10, 134.71, 135.61, 136.13 (-*C*$_6$H$_4$-, Ar), 135.87 (CH_2=*C*H-Ar), 196.25 (-N-*C*S_2-), FTIR (KBr) 1629 cm^{-1} (CH=CH_2), 1174 cm^{-1} (C=S), 1475 cm^{-1} (C-N), 696 cm^{-1} (C-S). Analysis $C_{21}H_{25}NS_2$, calcd: C, 70.94; H, 7.09; N, 3.94; S, 18.03, found: C, 70.46; H, 7.35; N, 4.03; S, 17.78.

6.11.2 N,N'-bis(4-bibenzyl)-N,N'-dibutyldithiuram disulphide [BBTD]

Because of the light-sensitive features of the molecule the synthesis and purification was performed while excluding light in order to keep the

dithiocarbamate groups intact and to avoid undesirable photochemical polymerisations from occurring.

NVBA (0.508 g, 2.68 mmol) and TEA (1 mL, 7.096 mmol) were dissolved in chloroform (10 mL) at 0°C using an ice / water bath. To this mixture, carbon disulphide (0.35 mL, 5.775 mol) was added drop wise for 30 minutes at 0°C. Once the addition was completed the ice / water bath was removed and the solution stirred at room temperature (water bath) for 3 hours (reaction monitored by TLC: disappearance of the secondary amine spot). After that time iodine dissolved in chloroform (0.750 g in 250 mL) was added dropwise, until the brownish colour of iodine persisted (around two hours). The solution was then washed with a mixture of ice / water and the organic phase was dried over magnesium sulphate, filtered, and concentrated in a rotavapor. The product was purified by column chromatography (10 cm length) on silica gel with hexane / ethyl acetate 9.5:0.5 as eluent giving a dark yellow oil (yield: 65%). Rf = 0.36 (hexane / EtOAc 9:1, silica gel). ^{1}H NMR, 400MHz, DMSO-d_6, 70°C, δ: 0.94 (t, 6H, C*H*$_3$-), 1.38 (m, 4H, CH$_3$-C*H*$_2$-), 1.80 (m, 4H, CH$_3$-CH$_2$-C*H*$_2$-), 3.97 (t, 4H, -CH$_2$-C*H*$_2$-NH-), 5.30 (d, 2H, *H*-CH=CH-Ar, $^{3}J_{cis}$ = 10.79 Hz), 5.34 (s, 4H, -NH-C*H*$_2$-Ar), 5.84 (d, 2H, *H*-CH=CH-Ar, $^{3}J_{trans}$ = 18.42 Hz), 6.77 (dd, 2H, CH$_2$=C*H*-Ar, $^{3}J_{\text{trans}}$ = 10.79 Hz, $^{3}J_{\text{cis}}$ = 18.42 Hz), 7.44 (m, 8H, aryl). ^{13}C NMR, 100.5 MHz, $CDCl_3$, 30°C, δ: 13.93 (*C*H$_3$-), 18.38 (CH$_3$-*C*H$_2$-), 28.28 (CH$_3$-CH$_2$-*C*H$_2$-), 58.32 (-CH$_2$-*C*H$_2$-NH-), 65.93 (-NH-*C*H$_2$-Ar), 113.59(*C*H$_2$=CH-Ar), 126.37, 127.60, 136.41, 136.61, 137.06 (CH$_2$=*C*H-Ar), 211.39 (-N-*C*S$_2$-), FTIR (KBr) 1630 cm^{-1} (CH=CH$_2$), 1174 cm^{-1} (C=S), 1489 cm^{-1} (C-N), 735 cm^{-1} (S-S). Analysis $C_{28}H_{36}N_2S_4$, calcd: C, 63.59; H, 6.86; N, 5.29; S, 24.26, found: C, 63.72; H, 6.70; N, 5.48; S, 24.21.

6.11.3 (S)-Benzyl 1-phenylethyl(4-vinylbenzyl)dithiocarbamate [S-BPVD]

Because of the light-sensitive features of the molecule the synthesis and purification were performed in the dark in order to keep the dithiocarbamate groups intact and to avoid undesirable photochemical polymerisations from occurring.

Carbon disulphide (4.30 mL, 79.22 mmol) and 4-vinylbenzyl bromide (4.30 mL, 36.15 mmol) were added to a 100ml round bottomed flask in an ice / water bath and the mixture was stirred with a magnetic stir bar for 5 minutes. S-VBPE (7.09 g, 29.54 mmol) and TEA (11.46 mL, 82.22 mmol) were mixed in a separate beaker and then added to the reaction flask dropwise. The reaction was stirred at 0ºC for 30 minutes and after that time the mixture was allowed to warm to room temperature and stirred until the reaction was complete (4.5 hours, as monitored by TLC). The reaction mixture was diluted with water (50 mL) and the product extracted with diethyl ether (3 × 15 mL). The organic layers were dried over $MgSO_4$ and the solvent removed. The product was purified by column chromatography on silica (hexane / ethyl acetate, from 9.5:0.5 to pure ethyl acetate) giving a yellow viscous oil that crystallised on standing (yield: 58%). Rf = 0.57 (hexane / EtOAc 9:1, silica gel). ^{1}H NMR, 400MHz, DMSO-d_6, 100°C, δ: 1.57 (d, 3H, C*H*$_3$-CH-C_6H_5), 4.66 (s, 2H, -S-C*H*$_2$-C_6H_5), 5.25 (dd, 2H, -NH-C*H*$_2$-Ar), 5.22 (d, 1H, *H*-CH=CH-Ar, $^{3}J_{cis}$ = 10.79 Hz), 5.69 (d, 1H, *H*-CH=CH-Ar, $^{3}J_{trans}$ = 17.36 Hz), 6.68 (ddt, 1H, CH_2=C*H*-Ar, $^{3}J_{trans}$ = 10.79 Hz, $^{3}J_{cis}$ = 17.36 Hz), 6.77 (m, 1H, -N-C*H*$_2$-C_6H_5), 7.22 (m, 15H, aryl),^{13}C NMR, 100.5 MHz, DMSO-d_6, 150°C, δ: 17.35 (*C*H_3-), 42.42 (S-*C*H_2-C_6H_5), 52.86 (CH_3-*C*H-C_6H_5), 61.63 (-NH-*C*H_2-Ar), 114.19 (*C*H_2=CH-Ar), 136.96-139.80 (Ar, *C*H_2=CH-Ar, -C_6H_5) 199.46 (-N-*C*S_2-), FTIR (KBr) 1629 cm^{-1} (CH=CH_2), 1165 cm^{-1} (C=S), 1449 cm^{-1} (C-N), 696 cm^{-1} (C-S). Analysis $C_{25}H_{25}NS_2$, calcd: C, 74.40; H, 6.24; N, 3.47; S, 15.89, found: C, 74.21; H, 6.46; N, 3.19; S, 14.08.

6.12 Removal of the oxygen in polymerisation systems

For the removal of oxygen from the system two protocols were used depending on the polymerisation. This was achieved either by repeated freeze-evacuate-thaw cycles or the bubbling of inert gas into the polymerisation mixture.

6.12.1 Freeze-evacuate-thaw cycles

1. Firstly the reaction vessel, fitted with a closed stopcock, was immersed in a liquid nitrogen bath until complete solidification of the solution was achieved. The time of this process depended on the volume of the solution but the average time taken was around 3 minutes.

2. With the solution still frozen and the reaction vessel still in the liquid nitrogen bath, the headspace was evacuated by connecting a DD75 JAVAC (Leroy-Somer, France) double stage rotary high vacuum pump (75 l / min flow rate, 0.001 mbar ultimate vacuum) and opening the stopcock. To ensure complete evacuation pumping for a period of 5 minutes was undertaken. The stopcock was again closed.
3. After that time the reaction vessel was removed from the liquid nitrogen bath and the frozen mixture defrosted at room temperature while the system was still under vacuum. A water bath was used to accelerate the process.
4. When the solution had returned to its liquid state, argon was allowed to fill the headspace by gently opening the stopcock while attached to a gas line before again sealing the vessel.

In order to thoroughly degas polymerisation mixtures, the steps 1 – 4 above were repeated at least three times.

6.12.2 Bubbling of inert gas

A pipette was first connected to an inert gas inlet through a plastic tube. The tip of the pipette was then immersed into the system that was to be degassed (**Scheme 6-1**). To avoid evaporation of solvent the system can be kept in a cold water jacket.

Scheme 6-1: Immersion of a Pasteur pipette into the solution to degas it with an inert gas

6.13 Synthesis of the linear polymer

6.13.1 Poly(benzyl N-butyl-N-(4-vinylbenzyl)dithiocarbamate) [Poly(BBVC)]

Because of the light-sensitive features of the molecule the synthesis and purification was performed in the dark in order to keep the dithiocarbamate groups intact and to avoid undesirable photochemical polymerisations from occurring.

BBVC (3 g, 8.44 mmol) and AIBN (10 mg, 0.06 mmol) (ratio initiator / inimer 0.7% mol) were dissolved in (6 mL) ([BBVC] = 0.5 g / mL) and then poured in a glass ampoule sealed with a gas tap. The solution was degassed with the freeze-pump-thaw technique (× 3). The reaction vessel, the gas tap and required glass junctions, were covered completely with aluminium foil. The inimer was then polymerised leaving the tube in the dark at 100ºC for 24 hours. After the reaction time the tube was removed from the oil bath and the system was allowed to cool to room temperature. Once the solution was at room temperature the aluminium foil was removed and it was observed that the solution was more viscous, consistent with the creation of high molar mass material. The polymer was precipitated and purified by pouring the solution into a methanol / ethyl acetate 1:1 vortex (× 3) precipitating a plastic solid which was washed with acetonitrile at 0ºC and dried until an expanded solid structure appeared. Grinding produced the final product as a yellow powder (yield: 50%, 14 KDa). ^{1}H NMR, 400MHz, toluene -d_8, 100ºC, δ: 0.87 (t, 3H, C*H*$_3$-), 1.31 (hex, 2H, CH_3-C*H*$_2$-), 1.66 (pen, 2H, CH_3-CH_2-C*H*$_2$-), 3.85 (t, 2H, -CH_2-C*H*$_2$-NH-), 4.61 (s, 2H, -C*H*$_2$-C_6H_5), 5.20 (s, 2H, -NH-C*H*$_2$-Ar), 5.24 (d, 1H, *H*-CH=CH-Ar), 5.74 (d, 1H, *H*-CH=CH-Ar,), 6.74 (dd, 1H, CH_2=C*H*-Ar), 7.32 (m, 9H, aryl), FTIR (KBr) 1110 cm^{-1} (C=S), 1477 cm^{-1} (C-N), 696 cm^{-1} (C-S). Analysis, calcd: C, 70.94; H, 7.09; N, 3.94; S, 18.03, found: C, 70.93; H, 7.53; N, 4.00; S, 20.38.

6.14 Synthesis of cross-linked polymers

6.14.1 Auto-poly(benzyl N-butyl-N-(4-vinylbenzyl)dithiocarbamate) [Auto-Poly(BBVC)]

Poly(BBVC) (0.485 g) was dissolved in chloroform (40 mL) ([linear polymer] = 0.0121 g / mL). The yellow solution was immersed in an ultrasonic bath until homogeneous and then poured into a glass ampoule sealed with a gas tap. The solution was degassed with the freeze-pump-thaw technique (× 3) and the linear polymer was cross-linked using a 300W UV lamp placed 10 cm from the reaction vessel, irradiating for 4 hours using a water thermostat at 22ºC. After this a precipitate appeared in the solution as well as a gel on the walls of the ampoule in front of the lamp. The heterogeneous solution was poured into a flask and the $CHCl_3$ evaporated using the rotor evaporator. A fresh fraction of chloroform (15 mL) was added to the dried solid and its solution added to a methanol / chloroform 1:1 vortex (× 3) to precipitate the auto-cross-linked polymer and purify it from the starting material and the by-products formed, e.g. bibenzyl. The solid was dried and ground giving a yellow powder that sometimes became greenish in the precipitation suspension. The solid was dried in the oven at 50ºC overnight (yield: 67%). FTIR (KBr) 1110 cm^{-1} (C=S), 1477cm^{-1} (C-N), 696 cm^{-1} (C-S), 750 cm^{-1} (S-S). Analysis, found: C, 65.54; H, 7.01; N, 4.11; S, 19.75.

6.14.2 Poly(ethylene glycol dimethacrylate-*co*-Benzyl N-butyl-N-(4-vinylbenzyl)dithiocarbamate) [Poly(EGDMA-*co*-BBVC)]

Because of the light-sensitive features of the molecule the synthesis and purification was done in the dark in order to keep the dithiocarbamate groups intact and to avoid undesirable photochemical polymerisations from occurring.

BBVC (0.2 g, 0.56 mmol), EGDMA free from inhibitors* (0.444 g, 2.24 mmol) (ratio BBVC:EGDMA = 1:4) and AIBN (23 mg, 0.14 mmol) (ratio initiator / inimer 5% mol) were dissolved in toluene (1 mL) ([BBVC] = 0.2 g / mL) ([EGDMA] = 0.444 g / mL) and the mixture was sonicated in an ultrasonic bath until a homogeneous solution was obtained. The solution was poured into a glass

ampoule sealed with a gas tap. The yellow solution was degassed with the freeze-pump-thaw technique (× 3) and the reaction vessel sealed under argon. The inimer was then polymerised leaving the tube in the dark (covering all the parts of the system with aluminium foil) at 80ºC for 24 hours. After that time the polymerisation was stopped by removing the ampoule from the heat source and the system was allowed to cool to room temperature. Once the solution was cool the aluminium foil was removed and the polymer (solid block) was extracted from the reaction vessel. The block was ground (150 < x < 38 μm), and washed in a Soxhlet apparatus (24 hours, cycle time 2 minutes, solvents: methanol followed by ethyl acetate). The polymer was dried in the oven at 80ºC for 48 hours. The final product was a white yellowish powder (yield: 86%). FTIR (KBr) 945 cm^{-1} (C-H, glycol), 1637 cm^{-1} (C=C). Analysis $C_{61}H_{81}NO_{16}S_2$ calcd: C, 63.80; H, 7.11; N, 1.22; S, 5.58; O, 22.29 found: C, 63.87; H, 7.32; N, 1.57; S, 6.02; O, 21.22.

*To remove the inhibitor the EGDMA was passed through a column of Al_2O_3.

6.14.3 Poly(ethylene glycol dimethacrylate-*co*-N,N'-bis(4-bibenzyl)-N,N'-dibutyldithiuram disulphide) [Poly(EGDMA-*co*-BBTD)]

Because of the light-sensitive features of the molecule the synthesis and purification was done in the dark in order to keep the dithiocarbamate groups intact and to avoid undesirable photochemical polymerisations from occurring.

BBTD (1 g, 1.89 mmol), EGDMA free from inhibitors (1.2 g, 6.05 mmol) (ratio BBTD:EGDMA = 0.31) and AIBN (50 mg, 0.30 mmol) (ratio initiator / inimer 16% mol) were mixed in toluene (1 mL) ([BBTD] = 1 g / mL) ([EGDMA] = 1.2 g / mL) in a 4 mL vial. The solution was degassed with an argon flow for 5 minutes, then the vial sealed with a PTFE cap, covered with aluminium foil and placed in an oil bath at 65ºC for 24 hours. After that time the polymerisation was stopped by removing the vessel from the heat source and the system was allowed to cool to room temperature. Once the solution was cool the aluminium foil was removed and the polymer (solid block) was extracted from the reaction vessel. The block was ground (150 < x < 38 μm), and washed with a Soxhlet apparatus

(24 hours, cycle time 2 minutes, solvent: chloroform). The polymer was dried in the oven at 50ºC for 1 hour. The final product was a yellow powder (yield: 85%). FTIR (KBr) 945 cm^{-1} (C-H, glycol), 1637 cm^{-1} (C=C). Analysis calcd: C, 62.00; H, 7.00; N, 2.49; S, 11.42; O, 17.09 found: C, 61.55; H, 7.02; N, 1.02; S, 10.69; O, 19.72.

6.15 Purification of the polymers

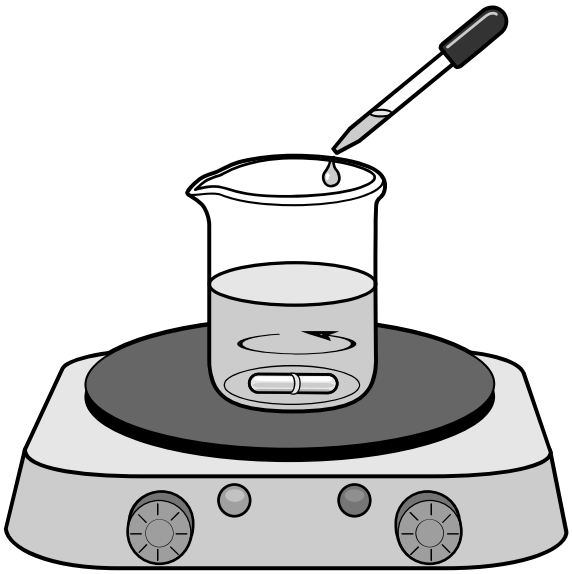
6.15.1 Soluble polymers

Precipitation of soluble polymers is not trivial (Hayes & Rannard, 2004). This is achieved by injecting solution of the created polymer using a Pasteur pipette into large volumes of solvent or mixtures of solvents (the non-solvent). The non-solvent must be chosen such that the starting material is soluble but the polymer is insoluble in it. The volume of non-solvent should be stirred rapidly enough to form a vortex. The solution of polymer has to be dropped onto the sides of the vortex at a suitable speed in order to precipitate the polymer in the desired particle size range. This protocol produces a precipitate of the polymer, meanwhile unreacted starting materials and low molecular weight byproducts remain in the non-solvent (**Scheme 6-2**). The precipitated polymer is removed from the solution by filtration or centrifugation and washed. At this stage it can be re-dissolved for further reprecipitation to remove any remaining impurities. By repeating this process several times a satisfactory purification is achieved.

6.15.2 Insoluble polymers

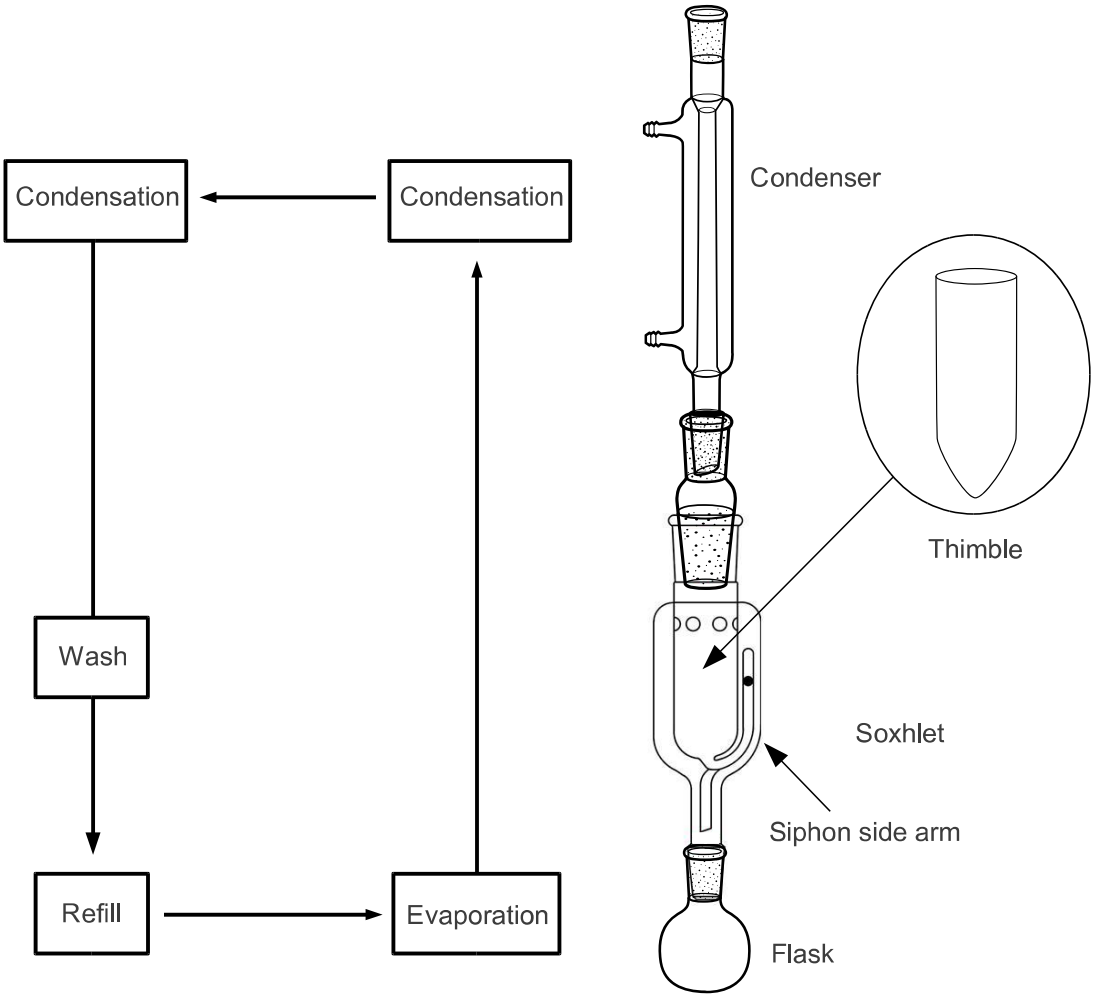
When the polymers have a high degree of cross-linking they are insoluble in any solvent and they appear as a solid in the reaction vessel once the reaction is finished. To remove the impurities that the polymer may contain, the solid is ground to a fine powder (in this way the impurities will be more accessible to solvent). Then the powder is suspended in a solvent / mixture of solvents that can dissolve the unreacted starting material or low molecular weight macromolecules. The suspension is stirred and then the polymer is removed by filtration or centrifugation. The solution will contain the impurities. By repeating this process several times a satisfactory purification is achieved. If the amount

of polymer is large enough to make the previous protocol very time-consuming a Soxhlet technique is used instead.



Scheme 6-2: Stirring the solvent to create a vortex and precipitate the polymer by dropping in the solution of the polymer

In the Soxhlet technique (**Scheme 6-3**) the polymer is encapsulated into a thimble made of filter paper. Then a solvent (or mixture of solvents) is poured into the flask, then the Soxhlet extractor is connected to the flask and the thimble is placed inside the Soxhlet apparatus. Lastly a condenser is connected on top of the Soxhlet apparatus. The solvent in the flask is heated, then it evaporates and when it reaches the condenser it falls as a liquid filling the space where the thimble with the polymer is. The solvent will wash out and dissolve the impurities. Once the solvent inside the Soxhlet reaches a certain level, the solvent is evacuated through the siphon side arm and it returns into the flask. The solvent from the flask will evaporate again, condense and return to the flask in a continuous cycle that will wash the polymer quite effectively. That is because the condensed solvent that washes the polymer is always a clean fraction of solvent. Meanwhile, as the solvent evaporates, impurities with higher boiling points are retained in the flask.

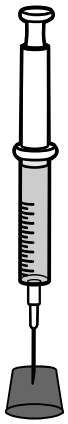


Scheme 6-3: Soxhlet system to purify cross-linked polymers through washing cycles

6.16 Swelling studies

For the swelling studies a glass syringe with a fitted needle inserted in a cork was used as a measurement system (**Scheme 6-4**). The syringe allows controlling the volume of the polymer. The weighed amount of polymer was suspended in $CHCl_3$ in the dark, allowing the polymer to swell. After defined periods of time the excess of solvent was removed and the system (syringe, needle, cork) was weighed. In the second part of the swelling studies the experiment was repeated under irradiation. The UV light source used here was

a 300W lamp. During UV exposure the system was kept at 22ºC using a water jacket.



Scheme 6-4: Syringe, needle, cork and plunger used to measure the swelling of the polymers

The swelling percentage, *S*, was calculated from the **Equation 6-1** where W_d and W_s represent the weight of the dry and swollen polymer respectively (Sokker *et al.*, 2009).

$$S(\%) = \frac{W_s - W_d}{W_d}\ x\ 100$$

Equation 6-1: Calculation of the swelling percentage

6.17 Calculation of the degree of cross-linking in polymers with ethylene glycol dimethacrylate as cross-linker

To calculate the degree of cross-linking (H. N. Kim & Spivak, 2003) in the cross-linked polymers by analysis of the FTIR spectrum, the area of a C=C stretching band was determined in absorbance mode between 1621 cm^{-1} and 1650 cm^{-1}, and this area was normalised against a reference with integration limits between 910 cm^{-1} and 985 cm^{-1} *(***Appendix C***)*.

6.18 De-cross-linking of the auto-cross-linked polymer

6.18.1 De-cross-linking of auto-poly(benzyl N-butyl-N-(4-vinylbenzyl)dithiocarbamate) [De-cross-Poly(BBVC)]

Auto-Poly(BBVC) (17.5 mg) was suspended in chloroform (5 mL) in a glass vial and an excess of TETD (450 mg) was added. The solution was degassed with a flow of Argon for 5 minutes and irradiated for 6 hours using a 300W UV lamp placed 10 cm from the reaction vessel which was kept at 22ºC during the process using a water jacket. The yellow suspension was left in the dark for 42 hours to yield a clear yellow solution. The de-cross-linked polymer was precipitated from the solution using the vortex technique (× 2) with a mixture of methanol and acetonitrile 1:1 as non-solvent. ^{1}H NMR, 400MHz, $CDCl_3$, 30ºC, δ: 0.90 (m, 3H, C*H*$_3$-), 1.31 (hex, 2H, CH_3-C*H*$_2$-), 1.66 (pen, 2H, CH_3-CH_2-C*H*$_2$-), 3.85 (t, 2H, -CH_2-C*H*$_2$-NH-), 4.61 (s, 2H, -C*H*$_2$-C_6H_5), 5.20 (s, 2H, -N-C*H*$_2$-Ar), 5.24 (d, 1H, *H*-CH=CH-Ar), 5.74 (d, 1H, *H*-CH=CH-Ar), 6.74 (dd, 1H, CH_2=C*H*-Ar), 7.32 (m, 9H, aryl).

6.19 General protocol for the synthesis of macrocycles

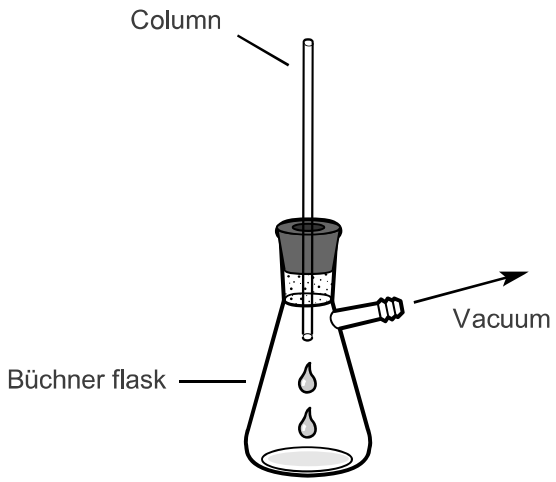
6.19.1 Packing of chromatography glass columns to connect to HPLC systems

Custom-cut SPE frits (Sigma Aldrich, UK) were put at each end of the glass column (6.4 mm o.d. with 1.5 mm wall, 70 mm length), purchased from SGE Analytical Science (Milton Keynes, UK), and it was filled with the polymer suspended in solvent. The column was inserted into a cork connected to a Büchner flask (**Scheme 6-5**). Connecting the vacuum caused the polymer to settle in a compact and homogeneous manner.

6.19.2 Connecting the column to the HPLC system

The column was fitted into two PEEK™ adapters 10-32 TO M6 (0.020 inch. hole, Sigma-Aldrich, UK), previously machined to fit the column and equipped with a custom-made rubber gaskets. The column was then mounted on a

custom-made aluminium frame (**Figure 6-1**) and connected to an HPLC system.



Scheme 6-5: Packing the column using vacuum

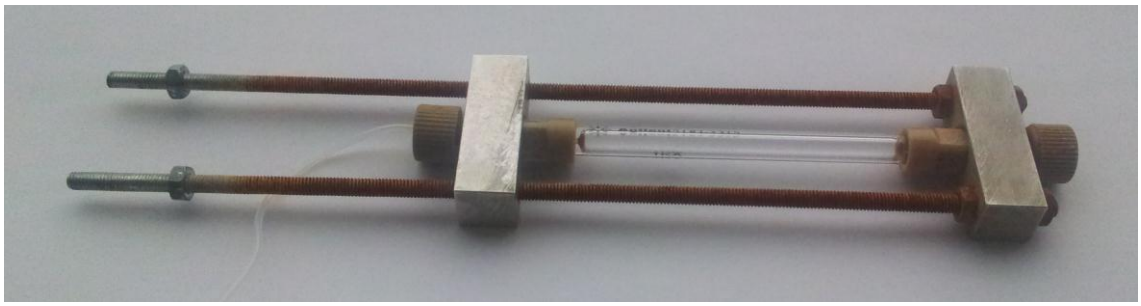
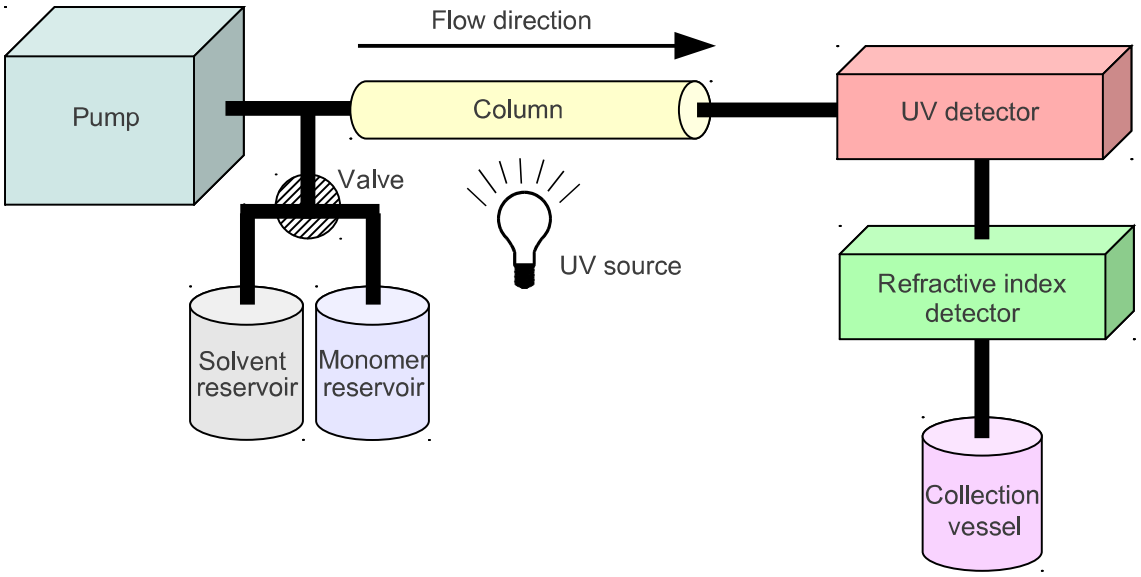


Figure 6-1: Glass column fitted into two PEEK™ adapters and mounted on a custom-made aluminium frame

6.19.3 Protocol of the synthesis of macrocycles using a HPLC photo-polymerisation system

The protocol has several steps which differ depending on the polymer used to pack the column. However, the system used in both cases is the same (**Scheme 6-6**).



Scheme 6-6: HPLC photo-polymerisation system to synthesise macrocycles

6.19.3.1 Protocol for Poly(BBVC-*co*-EGDMA)

1) Activation: The pump was connected and the flow of solvent passes through the column without irradiation to remove unreacted material. After some time the UV source was turned on and flow of solvent passes through the column to remove possible byproducts from the initial stages of irradiation.
2) Feed: The UV source was turned off. The valve was changed to pass a flow of a mixture of monomer / solvent through the column. In this step the molecules of monomer would react with the reactive sites of the polymer.
3) Polymerisation: The UV source was turned off, the flow was stopped and the system was left to allow the oligomers to be created.
4) Wash: The valve was changed and a flow of only solvent was passed through the column in the dark to remove unreacted material.
5) Collection: The UV source was turned on to liberate the oligomers formed and to allow them to rearrange into macrocycles. The flow

of solvent was kept turned on to push out the material and collect it to subsequent analysis.

6.19.3.2 Protocol for Poly(BBTD-*co*-EGDMA)

1. Activation: The pump was connected and the flow of solvent passed through the column without irradiation to remove unreacted material. After some time the UV source was turned on and flow of solvent passed through the column to remove possible byproducts from the initial stages of irradiation.
2. Feed: The UV source was kept turned on. The valve was changed to pass a flow of a mixture of monomer / solvent through the column. In this step the molecules of monomer would react with the reactive sites of the polymer.
3. Polymerisation: The UV source is kept turned on, the flow is stopped and the system is left to allow the oligomers to be created.
4. Wash: The UV source was turned off. The valve was changed and a flow of only solvent was passed through the column in the dark to remove unreacted material.
5. Collection: The UV source was turned on to liberate the oligomers formed and to allow them to rearrange into macrocycles. The flow of solvent was kept turned on to push out the material and collect it to subsequent analysis.

6.20 Screening of dormant radical reactivity

6.20.1 Preparative

The tetraethylthiuram disulphide (TETD) (Acros, Loughborough, UK) was recrystallised from ethanol prior use. The benzyl N,N-diethyldithiocarbamate (BDD) was used as purchased (TCI, Oxford, UK) and also synthesised following a published protocol for this compound (Guan & DeSimone, 1994) with minor alterations (yield: 51%).

6.20.2 Irradiation

The iniferter molecule and the target molecule were dissolved in a suitable solvent and degassed by bubbling argon through the solution for 5 minutes. The solutions were then irradiated with a 300W UV lamp for 60 minutes. The solution was kept at 22°C during the irradiation using a water jacket.

6.20.3 Analysis

The solutions were analysed with thin layer chromatography using silica gel plates, developed with a mixture of hexane / ethyl acetate 9:1. The spots were visualised by placing the plates under short wavelength (254 nm) 4W UV light.

6.20.4 Irradiation of the BDD solution and purification of the products

BDD was dissolved in acetonitrile (25 mL) and degassed with a flow of argon for 5 minutes. The solution was irradiated with a 300W UV light for 3.5 hours with the temperature maintained at 22°C (water jacket). The yellow solution was concentrated in rotavapor and the crude material purified by preparative column chromatography on silica gel with mixtures of hexane / ethyl acetate (9.5:0.5 to 1:1) as eluent.

6.21 Protocol for the separation of mixtures using dormant radicals

6.21.1 Packing of chromatography glass columns to connect to HPLC systems

Custom-cut SPE frits (Sigma Aldrich, UK) were put at each end of the glass column (6.4 mm o.d. with 1.5 mm wall, 70 mm length), purchased from SGE Analytical Science (Milton Keynes, UK), and it was filled with the polymer suspended in acetonitrile. The column was inserted into a cork connected to a Büchner flask (**Scheme 6-5**). Connecting the vacuum caused the polymer to settle in a compact and homogeneous manner.

6.21.2 Connecting the column to the HPLC system

The column was fitted into two PEEK™ adapters 10-32 TO M6 (0.020 inch. hole, Sigma-Aldrich, UK), previously machined to fit the column and equipped with a custom-made rubber gaskets. The column was then mounted on a custom-made aluminium frame (**Figure 6-1**) and connected to an HPLC system.

6.21.3 Separation of mixtures

6.21.3.1 Protocol for Poly(BBVC-*co*-EGDMA)

The column was connected to an Alliance 2795 Separations Module (Waters, Hertfordshire, UK) equiped with a Waters Micromass Quattro Micro API Triple Quad Benchtop Mass Spectromete. The column was irradiated with a flow of acetonitrile of 0.2 mL / min.

Once the first experiment was finished the column was connected to an Agilent 1100 HPLC system equipped with a G1313A Autosampler, a G1316A Column Compartment, aG1311A Quaternary Pump, a G1365B Multiple Wavelength Detector, a G1322A Vacuum Degasser and a G1321A Fluorescence Detector. The analytes were analysed at a flow rate of 0.5 mL / min using acetonitrile as eluent. The injections consisted on 20 µL of solutions of 10mg / mL of benzene, acetic acid, phenol, aniline, acetone, benzoic acid, (2,2,6,6-Tetramethylpiperidin-1-yl)oxyl (TEMPO), methyl methacrylate, and styrene (Sigma Aldrich, UK). The analytes were analysed in the dark and with the UV irradiation of the 14W UV lamp. The different retention times were recorded.

6.21.3.2 Protocol for Poly(BBVC-*co*-EGDMA)

The column was connected to an Agilent 1100 HPLC system equipped with a G1313A Autosampler, a G1316A Column Compartment, aG1311A Quaternary Pump, a G1365B Multiple Wavelength Detector, a G1322A Vacuum Degasser and a G1321A Fluorescence Detector. The analytes were analysed at a flow rate of 0.5 mL / min with acetonitrile as the eluent. The injections consisted on 20 µL of solutions of 10mg / mL of benzene, acetic acid, phenol, aniline, acetone, benzoic acid, TEMPO, methyl methacrylate, and styrene (Sigma

Aldrich, UK). The analytes were analysed in the dark and with the UV irradiation of the 14W UV lamp. The different retention times were recorded.

6.22 Synthesis of the hyper-branched polymer

6.22.1 Synthesis of branched poly(3-(trimethoxysilyl)propyl methacrylate-*co*-(S)-Benzyl 1-phenylethyl(4-vinylbenzyl)dithiocarbamate) [branched poly(TMSPMA-*co*-BPVD)]

BPVD (216 mg, 0.54 mmol) and 3-(trimethoxysilyl)propyl methacrylate (TMSPMA) (Sigma–Aldrich, Gillingham, UK) (27 mg, 0.11 mmol) were mixed in a clear vial and dissolved in toluene (360 mg) using an ultrasonic bath for 5 minutes. The solution was degassed using a flow of Nitrogen and the vial was closed using a PTEF cap. The vial was rotated at 33 rpm with a Stuart analogue tube roller mixer and irradiated at 35°C for 5 hours with a 14W UV light. The high molecular mass material was precipitated by pouring the reaction mixture into EtOH and purified from the low molecular mass material using the vortex technique with the EtOH / THF system (× 3). The white powder was dried in the oven at 60°C for 30 minutes and stored at room temperature in the dark (yield: 31%, 3 KDa). 1H NMR, 400 MHz, CDCl3, 30°C, δ: 0.40-0.80 (m, 0.7 H, -CH_2-C*H*$_2$-CH_2), 1.25-2.75 (m, 7H, H_2C=C-C*H*$_3$, -Si-C*H*$_2$-), 3.5-4.0 (s, 2.3H, -Si-O-C*H*$_3$-), 4.5-4.75 (m, 1.77H, -S-C*H*$_2$-, -N-C*H*$_2$-), 5.25-5.50 (m, 0.5H, *H*$_{cis}$-CH=CH-Ar, -N-C*H*$_2$-), 5.65-5.80 (m, 0.3H, *H*$_{trans}$-CH=CH-Ar, *H*$_{cis}$-CH=CH-CO-), 6.15-6.30 (m, 0.22H, CH_3-C*H*-C_6H_5, *H*$_{trans}$-CH=CH-CO-), 6.50-8.00 (m, 14H, -C_6*H*$_5$, -Ar-). FTIR (KBr) 1085 cm^{-1}, 1142 cm^{-1}, 1200 cm^{-1} (O-CH_3, glycol), 1475 cm^{-1} (C-N),1722 cm^{-1} (C=O). Analysis calcd: C, 72.20; H, 7.07; N, 2.81; S, 10.71; Si, 1.88; O, 5.34 found: C, 70.32; H, 6.35; N, 3.04; S, 13.57; Si, 1.75; O, 4.97.

6.23 Modifications of the glass beads

6.23.1 Activation of the glass beads.

To activate the beads, 125 mL of 9-13 µm hollow spherical non-porous glass beads (Sigma-Aldrich, Gillingham, UK)) were suspended in 100 mL NaOHaq (4M) and refluxed for 20 minutes, as was previously reported (X. D. Liu *et al.*,

2002). After that time the beads were allowed to cool to room temperature and then washed several times with deionised water, followed by one wash with acetone to accelerate the drying process (in the oven at 75°C overnight). In the washing process the paper filter was changed three times, as due the high polydispersity of the beads small particles were blocking the filter. This proved necessary in order to avoid obstructing the columns.

To activate the 75 µm glass beads Supelco (Sigma-Aldrich, Gillingham, UK) the same process was used except that the polydispersity was less, consequently blocking of the filter was less of a problem, resulting in an easier protocol.

6.23.2 Derivatisation of the 9-13 µm glass beads with branched poly(TMSPMA-*co*-BPVD)

The glass beads (2.5 g) were suspended in a solution of (branched poly(TMSPMA-*co*-BPVD)) (400 mg) in toluene (10 mL) inside a clear vial. The suspension was degassed with a flow of nitrogen for 15 minutes and closed with a PTFE cap. The vial was covered with aluminium foil and it was rotated at 33 rpm with a Stuart analogue tube roller mixer (Bibby Scientific Limited, Staffordshire, UK) in the dark at room temperature for 20 hours. The beads were washed with THF (× 4), dried in the oven at 75°C for 60 minutes, and stored at room temperature in the dark.

6.23.3 Derivatisation of the 75 µm glass beads with branched poly(TMSPMA-*co*-BPVD)

The glass beads (10.84 g) were suspended in a solution of (branched poly(TMSPMA-*co*-BPVD)) (335 mg) in toluene (10 mL) inside a clear vial. The suspension was degassed with a flow of nitrogen for 10 minutes and closed with a PTFE cap. The vial was rotated at 33 rpm with the analogue tube roller mixer in the dark at room temperature for 20 hours. The beads were washed with THF (× 6), dried at room temperature in the dark. The beads were stored at room temperature in the dark.

6.24 General protocol for the separation of enantiomers

6.24.1 Packing of chromatography stainless steel columns

A stain-steel column (250 x 4.6 mm) (Phenonenex, Macclesfield, UK) equipped with stainless steel frits (Phenonenex, Macclesfield, UK) was filled with a suspension of the hyper-branched-modified-glass beads in acetonitrile. The column was inserted into a cork connected to a Büchner flask (**Scheme 6-5**). Connecting the vacuum caused the polymer to settle in a compact and homogeneous manner.

6.24.2 Separation of enantiomers

The column was connected to an Agilent 1100 HPLC system equipped with a G1313A Autosampler, a G1316A Column Compartment, aG1311A Quaternary Pump, a G1365B Multiple Wavelength Detector, a G1322A Vacuum Degasser and a G1321A Fluorescence Detector and the analytes were analysed at a flow rate of 0.3 mL / min using acetonitrile as eluent. The injections consisted on 20 µL of solutions of 1mg / mL and 0.1 mg / mL of the (+) and (–) forms of ephedrine (Sigma Aldrich, UK) in acetonitrile. The different retention times were recorded; the retention factors and the separation factors were calculated.

7 REFERENCES

Agrawal, R.C., Shukla, Y. & Mehrotra, N.K. (1997) Assessment of mutagenic potential of thiram. *Food and Chemical Toxicology*, 35 (5), pp.523-525.

Akhond, M., Absalan, G., Sheikhian, L., Eskandari, M.M. & Sharghi, H. (2006) Di (n-propyl) thiuram disulfide bonded on silica gel as a new sorbent for separation, preconcentration, and measurement of silver ion from aqueous samples. *Separation and Purification Technology*, 52 (1), pp.53-59.

Al-Malaiaka, S., Marogi, A. & Scott, G. (1987) Mechanisms of antioxidant action: Time-controlled stabilisation of polypropylene by transition metal dithiocarbamates. *Polymer Degradation and Stability*, 18 (1), pp.89-98.

Al-Malaika, S. (1997) *Reactive modifiers for polymers*. 1st ed. London, Chapman & Hall.

American chemical Society (1994) *Chemical technology*. American Chemical Society.

Arvanitis, N., Kotzamanidis, C.Z., Skaracis, G.N. & Karagouni, A.D. (2004) The effectiveness of commercial antimicrobial compounds against saccharolytic microorganisms isolated from a beet sugar production line. *World Journal of Microbiology and Biotechnology*, 20 (3), pp.291-296.

Azizi, N., Aryanasab, F. & Saidi, M.R. (2006) Straightforward and highly efficient catalyst-free one-pot synthesis of dithiocarbamates under solvent-free conditions. *Organic Letters*, 8 (23), pp.5275-5277.

Baikenova, G.G., Abdulina, G.A., Gazaliev, A.M., Fazylov, S.D. & Kudaibergenova, S.Z. (2004) Synthesis and antimicrobial activity of anabasine, piperidine, and morpholine dithiocarbamates. *Pharmaceutical Chemistry Journal*, 38 (1), pp.19-20.

Balzani, V., Credi, A., Raymo, F. & Stoddart, J. (2000) Artificial Molecular Machines. *Angewandte Chemie (International ed. in English)*, 39 (19), pp.3348-3391.

Barriga, S. (2001) 2,2,6,6-Tetramethylpiperidin-1-oxyl (TEMPO). *Synlett*, 2001 (04), p.563.

Beer, P.D. & Gale, P.A. (2001) Anion Recognition and Sensing: The State of the Art and Future Perspectives. *Angewandte Chemie (International ed. in English)*, 40 (3), pp.486-516.

Bharathi, P. & Moore, J.S. (1997) Solid-supported hyperbranched polymerization: Evidence for self-limited growth. *Journal of the American Chemical Society*, 119 (14), pp.3391-3392.

Blau, K. & King, G.S. (1993) *Handbook of Derivatives for Chromatography*. 2nd ed. K. Blau & G. S. King eds. Chichester, Wiley.

Van Boi, L. (2000) Thiocarbamoylation of amine-containing compounds. *Russian Chemical Bulletin*, 49 (2), pp.335-343.

Bolm, C. & Fey, T. (1999) TEMPO oxidations with a silica-supported catalyst. *Chemical Communications*, (18), pp.1795-1796.

Bowden, S.T., Harris, W.E. & Roberts, D.I. (1939) 68. Free radicals and radical stability. Part III. Diphenylpiperonylmethyl and phenyl-p-anisyldiphenylylmethyl. *J. Chem. Soc.*, pp.302-307.

Bower, J.J., Leonard, S.S. & Shi, X. (2005) Conference overview: Molecular mechanisms of metal toxicity and carcinogenesis. *Molecular and Cellular Biochemistry*, 279 (1-2), pp.3-15.

Brenner, I.B., Zander, A., Plantz, M. & Zhu, J. (1997) Characterization of an ultrasonic nebulizer-membrane separation interface with inductively coupled plasma mass spectrometry for the determination of trace elements by solvent extraction: Invited lecture. *Journal of Analytical Atomic Spectrometry*, 12 (3), pp.273-279.

Bryant, J.J.L. & Semlyen, J.A. (1997) Cyclic polyesters: 7. Preparation and characterization of cyclic oligomers from solution ring-chain reactions of poly(butylene terephthalate). *Polymer*, 38 (17), pp.4531-4537.

Cary, R., Dobson, S. & Delic, J. (1999) 1,2-Diaminoethane (ethylenediamine). *IPCS Concise International Chemical Assessment Documents*, (15), pp.1-30.

Caughley, F.G. & Robertson, P.W. (1933) 308. The system allyl alcohol-iodine-di-iodopropyl alcohol. *Journal of the Chemical Society (Resumed)*, pp.1323-1326.

Cavell, K.J., Hill, J.O. & Magee, R.J. (1979) Synthesis and characterisation of some secondary amine-dithiocarbamate salts. *Journal of Inorganic and Nuclear Chemistry*, 41 (9), pp.1277-1280.

Cervantes, G., Moreno, V., Molins, E. & Miravitlles, C. (1997) Reactions of Pd(II) and Pt(II) complexes with tetraethylthiouram disulfide. *Metal-Based Drugs*, 4 (6), pp.317-325.

Chakraborty, K.B. & Scott, G. (1986) Mechanisms of antioxidant action: Effect of amine complexing on the photo-antioxidant activity of zinc diethyldithiocarbamate in polypropylene. *Polymer Degradation and Stability*, 16 (1), pp.1-12.

Chakraborty, K.B., Scott, G. & Poyner, W.R. (1984) Mechanisms of antioxidant action: Concentration effects of zinc dialkyldithiocarbamates in the uv stabilisation of polypropylene. *Polymer Degradation and Stability*, 8 (1), pp.1-11.

Chatterjee, P.K. & Gupta, B.S. (2002) *Absorbent technology*. Elsevier Science.

Chaturvedi, D. & Ray, S. (2006) Triton-B catalyzed efficient one-pot synthesis of dithiocarbamate esters. *Monatshefte fur Chemie*, 137 (3), pp.311-317.

Chen, D., Cui, Q.C., Yang, H. & Dou, Q.P. (2006) Disulfiram, a clinically used anti-alcoholism drug and copper-binding agent, induces apoptotic cell death in breast cancer cultures and xenografts via inhibition of the proteasome activity. *Cancer Research*, 66 (21), pp.10425-10433.

Chen, K., Richter, J.M. & Baran, P.S. (2008) 1,3-Diol synthesis via controlled, radical-mediated C-H functionalization. *Journal of the American Chemical Society*, 130 (23), pp.7247-9.

Chen, Q.-Y., Yang, Z.-Y., Zhao, C.-X. & Qiu, Z.-M. (1988) Studies on fluoroalkylation and fluoroalkoxylation. Part 28. Palladium(0)-induced addition of fluoroalkyl iodides to alkenes: an electron transfer process. *Journal of the Chemical Society, Perkin Transactions 1*, (3), p.563.

Chiefari, J., Chong, Y.K., Ercole, F., Krstina, J., Jeffery, J., Le, T.P.T., Mayadunne, R.T.A., Meijs, G.F., Moad, C.L., Moad, G, Rizzardo, E. & Thang, S.H. (1998) Living free-radical polymerization by reversible addition - Fragmentation chain transfer: The RAFT process. *Macromolecules*, 31 (16), pp.5559-5562.

Clementi, M., Causin, R., Marzocchi, C., Mantovani, A. & Tenconi, R. (2007) A study of the impact of agricultural pesticide use on the prevalence of birth defects in northeast Italy. *Reproductive Toxicology*, 24 (1), pp.1-8.

Costantini, C., d' Ischia, M., Palumbo, A. & Prota, G. (1994) Photochemistry of 5-S-cysteinyldopa. *Photochemistry and photobiology*, 60 (1), pp.33-7.

Demis, D.J. (1994) *Clinical dermatology*. J.B. Lippincott.

Denisov, E.T., Denisova, T.G. & Pokidova, T.S. (2003) *Handbook of free radical initiators*. 1st ed. Moscow, John Wiley & Sons, Inc.

Desai, R.M., Dodiya, D.K., Trivedi, A.R. & Shah, V.H. (2008) Simple and efficient synthetic routes to bioactive s-triazinyl dithiocarbamate derivatives. *Medicinal Chemistry Research*, 17 (8), pp.495-506.

Devi, K.R.G., Sathyanarayana, D.N. & Manogaran, S. (1981) Molecular vibrations and conformation of primary dithiocarbamate ester. Infrared and NMR studies on S-methyl dithiocarbamate. *Spectrochimica Acta Part A: Molecular Spectroscopy*, 37 (1), pp.31-36.

Dika Manga, J., Polton, A., Tardi, M. & Sigwalt, P. (1998) Mechanism of the polymerization of n-butyl acrylate initiated by N,N-diethyldithiocarbamate derivatives. Part 1. Photolysis of butyl-2-(N,N-diethyldithiocarbamyl)propionate and oligomerization of butyl acrylate. *Polymer International*, 45 (1), pp.14-21.

England, R.M. & Rimmer, S. (2010) Hyper/highly-branched polymers by radical polymerisations. *Polymer Chemistry*, 1 (10), p.1533.

Fawcett, A.H., Mee, R.A.W. & McBride, F.V. (1995) A Monte-Carlo Study of Ring Formation and Molecular Configurations during Step Growth on a Lattice in Three Dimensions. *Macromolecules*, 28 (5), pp.1481-1490.

Ferry, J.D. (1980) *Viscoelastic properties of polymers*. Wiley.

Fletcher, D.A., McMeeking, R.F. & Parkin, D. (1996) The United Kingdom chemical database service. *Journal of Chemical Information and Computer Sciences*, 36 (4), pp.746-749.

Ford, L. & Jahn, U. (2009) Radicals and transition-metal catalysis: an alliance par excellence to increase reactivity and selectivity in organic chemistry. *Angewandte Chemie (International ed. in English)*, 48 (35), pp.6386-9.

Frank, R.L., Smith, P.V., Woodward, F.E., Reynolds, W.B. & Canterino, P.J. (1948) Mercaptan structure and regulator activity in emulsion polymerizations. *Journal of Polymer Science*, 3 (1), pp.39-49.

Gao, C. & Yan, D. (2004) Hyperbranched polymers: from synthesis to applications. *Progress in Polymer Science*, 29 (3), pp.183-275.

Garcia, J.I. & Humeres, E. (2002) Mechanisms of acid decomposition of dithiocarbamates. 4. Theoretical calculations on the water-catalyzed reaction. *Journal of Organic Chemistry*, 67 (9), pp.2755-2761.

García-Con, L.M., Whitcombe, M.J., Piletska, E.V. & Piletsky, Sergey A (2010) A sulfur--sulfur cross-linked polymer synthesized from a polymerizable dithiocarbamate as a source of dormant radicals. *Angewandte Chemie (International ed. in English)*, 49 (24), pp.4075-8.

Gergaly, Š. (1985) Investigation of thermal decomposition of ethylenebisdithiocarbamate acid, its diammonia salt and β-amino-ethyl-dithiocarbamate. *Thermochimica Acta*, 93 (C), pp.137-140.

Gomberg, M. (1932) A survey of the chemistry of free radicals. *Journal of Chemical Education*, 9 (3), pp.439-451.

Gomberg, M. (1900) An instance of trivalent carbon: triphenylmethyl. *Journal of the American Chemical Society*, 22 (11), pp.757-771.

Gruber, H.F. (1992) Photoinitiators for free radical polymerization. *Progress in Polymer Science*, 17 (6), pp.953-1044.

Guan, Z. & DeSimone, J.M. (1994) Fluorocarbon-Based Heterophase Polymeric Materials. 1. Block Copolymer Surfactants for Carbon Dioxide Applications. *Macromolecules*, 27 (20), pp.5527-5532.

Hawker, Craig J. (1997) “Living” Free Radical Polymerization: A Unique Technique for the Preparation of Controlled Macromolecular Architectures. *Accounts of Chemical Research*, 30 (9), pp.373-382.

Hayes, W. & Rannard, S. (2004) Polymer chemistry: a practical approach. In: F. J. Davis ed. New York, Oxford University Press, pp.99-125.

Hedrick, J.L., Hawker, C J, Miller, R.D., Twieg, R., Srinivasan, S.A. & Trollsås, M. (1997) Structure control in organic-inorganic hybrids using hyperbranched high-temperature polymers. *Macromolecules*, 30 (24), pp.7607-7610.

Hicks, R.G. (2007) What’s new in stable radical chemistry? *Organic & biomolecular chemistry*, 5 (9), pp.1321-38.

Hoffman, R.E. (2006) Standardization of chemical shifts of TMS and solvent signals in NMR solvents. *Magnetic Resonance in Chemistry*, 44 (6), pp.606-616.

Holloway, C.E. & Gitlitz, M.H. (1967) Rotational barrier in dithiocarbamate esters. *Canadian Journal of Chemistry*, 45, pp.2659-2663.

Houeto, P., Bindoula, G. & Hoffman, J.R. (1995) Ethylenebisdithiocarbamates and ethylenethiourea: Possible human health hazards. *Environmental Health Perspectives*, 103 (6), pp.568-573.

Hu, J.Q., Wei, X.Y., Dai, G.L., Fei, Y.W., Liu, C.C., Zong, Z.M. & Yao, J.B. (2007) Synergistic antioxidation of organic molybdenum complex with dithiocarbamate antioxidant evaluated by differential scanning calorimetry and thin film micro oxidation test. *Thermochimica Acta*, 453 (1), pp.21-26.

Ishizu, K & Mori, A. (2001) Novel synthesis of branched polystyrenes by quasi-living radical copolymerization using photofunctional inimer. *Polymer International*, 50 (8), pp.906-910.

Ishizu, K & Mori, A. (2002) Solution properties of hyperbranched polymers and synthetic application for amphiphilic star-hyperbranched copolymers by grafting from hyperbranched macroinitiator. *Polymer International*, 51 (1), pp.50-54.

Ishizu, K & Mori, A. (2000) Synthesis of hyperbranched polymers by self-addition free radical vinyl polymerization of photo functional styrene. *Macromolecular Rapid Communications*, 21 (10), pp.665-668.

Ishizu, K & Ochi, K. (2006) Architecture of star - Block copolymers consisting of triblock arms via a N,N-diethyldithiocarbamate-mediated living radical photo-polymerization and application for nanocomposites by using as fillers. *Macromolecules*, 39 (9), pp.3238-3244.

Ishizu, K, Kobayakawa, N., Takano, S., Tokuno, Y. & Ozawa, M. (2007) Synthesis of polymer particles possessing radical initiating sites on the surface by emulsion copolymerization and construction of core-shell structures by a photoinduced atom transfer radical polymerization approach. *Journal of Polymer Science, Part A: Polymer Chemistry*, 45 (9), pp.1771-1777.

Ishizu, K, Kojima, T., Ohta, Y. & Shibuya, T. (2004) Nanopattern formation on polymer substrate using star-hyperbranched nanospheres. *Journal of Colloid and Interface Science*, 272 (1), pp.76-81.

Ishizu, K, Ochi, K., Uchida, S. & Odoi, K. (2006) Two-dimensional regular nanopatterning on block copolymer substrate having lamellar morphology using star-hyperbranched nanospheres by electrostatic interaction. *Journal of Applied Polymer Science*, 101 (6), pp.4206-4210.

Ishizu, K, Park, J., Tanimura, K., Uchida, S. & Tamura, T. (2004) Architecture of shell-crosslinked polymer nanoparticles via a living radical mechanism and modification to hollow nanocapsules. *Journal of Materials Science*, 39 (13), pp.4353-4357.

Ishizu, K, Shibuya, T. & Kawauchi, S. (2003) Kinetics on formation of hyperbranched poly(ethyl methacrylate) via a controlled radical mechanism of photofunctional inimer. *Macromolecules*, 36 (10), pp.3505-3510.

Ishizu, Koji & Kanno, H. (1996) Novel synthesis and characterization of cyclic polystyrenes. *Polymer*, 37 (8), pp.1487-1492.

Iwata, Y., Araki, Y., Honna, K., Miki, Y., Sato, K. & Shimada, H. (2001) Hydrogenation active sites of unsupported molybdenum sulfide catalysts for hydroprocessing heavy oils. *Catalysis Today*, 65 (2-4), pp.335-341.

Jiang, J., Bekaroglu, O.C.O.N. & Bian, Y.C.O.N. (2010) *Functional Phthalocyanine Molecular Materials*. Springer.

Jones, D. (2004) *Pharmaceutical Applications of Polymers for Drug Delivery*. Rapra Technology.

Joris, S.J., Aspila, K.I. & Chakrabarti, C.L. (1970) On the mechanism of decomposition of dithiocarbamates. *The Journal of Physical Chemistry*, 74 (4), pp.860-865.

Kannurpatti, A.R., Lu, S., Bunker, G.M. & Bowman, C.N. (1996) Kinetic and mechanistic studies of iniferter photopolymerizations. *Macromolecules*, 29 (23), pp.7310-7315.

Kaplancikli, Z.A., Turan-Zitouni, G., Revial, G. & Iscan, G. (2004) Synthesis of some dithiocarbamate derivatives and their antimicrobial activity. *Phosphorus, Sulfur and Silicon and the Related Elements*, 179 (7), pp.1449-1454.

Kim, H.N. & Spivak, D.A. (2003) New insight into modeling non-covalently imprinted polymers. *Journal of the American Chemical Society*, 125 (37), pp.11269-11275.

Kim, Y.H. (1998) Hyperbranched polymers 10 years after. *Journal of Polymer Science, Part A: Polymer Chemistry*, 36 (11), pp.1685-1698.

Kim, Y.H.O. & Webster, O.W. (1992) Hyperbranched polyphenylenes. *Macromolecules*, 25 (21), pp.5561-5572.

Kim, Y.H.O. & Webster, O.W. (1990) Water-soluble hyperbranched polyphenylene: “A unimolecular micelle”? *Journal of the American Chemical Society*, 112 (11), pp.4592-4593.

Kimura, K., Yokoyama, K., Sato, H., Nordin, R.B., Naing, L., Kimura, S., Okabe, S., Maeno, T., Kobayashi, Y., Kitamura, F. & Araki, S. (2005) Effects of pesticides on the peripheral and central nervous system in tobacco farmers in Malaysia: Studies on peripheral nerve conduction, brain-evoked potentials and computerized posturography. *Industrial Health*, 43 (2), pp.285-294.

Koo, S.P.S., Stamenović, M.M., Prasath, R.A., Inglis, A.J., Du Prez, F.E., Barner-Kowollik, C., Van Camp, W. & Junkers, T. (2010) Limitations of radical thiol-ene reactions for polymer-polymer conjugation. *Journal of Polymer Science Part A: Polymer Chemistry*, 48 (8), pp.1699-1713.

Krenn, B.M., Holzer, B., Gaudernak, E., Triendl, A., Van Kuppeveld, F.J. & Seipelt, J. (2005) Inhibition of polyprotein processing and RNA replication of human rhinovirus by pyrrolidine dithiocarbamate involves metal ions. *Journal of Virology*, 79 (22), pp.13892-13899.

Krzysztof, M. (2005) A Commentary on “Role of Initiator-Transfer Agent-Terminator (Iniferter) in Radical Polymerizations: Polymer Design by Organic Disulfides as Iniferters” by T. Otsu, M. Yoshida (Macromol. Rapid Commun.1982,3, 127-132). *Macromolecular Rapid Communications*, 26 (3), pp.135-142.

Kubo, M., Hayashi, T., Kobayashi, H. & Itoh, T. (1998) Syntheses of Tadpole- and Eight-Shaped Polystyrenes Using Cyclic Polystyrene as a Building Block. *Macromolecules*, 31 (4), pp.1053-1057.

Kubo, M., Hibino, T., Tamura, M., Uno, T. & Itoh, T. (2002) Synthesis and Copolymerization of Cyclic Macromonomer Based on Cyclic Polystyrene: Gel Formation via Chain Threading. *Macromolecules*, 35 (15), pp.5816-5820.

Kunz, T.K. & Wolf, M.O. (2011) Electrodeposition and properties of TEMPO functionalized polythiophene thin films. *Polymer Chemistry*, 2 (3), p.640.

Kurata, M. (1982) *Thermodynamics of polymer solutions*. Harwood Academic Publishers.

Labarre, D.J., Ponchel, G. & Vauthier, C. (2010) *Biomedical and Pharmaceutical Polymers*. Pharmaceutical Press.

Lakshmi, S. & Jayakrishnan, A. (1998) Photocross-linking of dithiocarbamate-substituted PVC reduces plasticizer migration. *Polymer*, 39 (1), pp.151-157.

Lambrinos, P., Tardi, M., Polton, A. & Sigwalt, P. (1990) The mechanism of the polymerization of n.butyl acrylate initiated with N,N-diethyl dithiocarbamate derivatives. *European Polymer Journal*, 26 (10), pp.1125-1135.

Lee, H.J., Nakayama, Y. & Matsuda, T. (1999) Spatio-resolved, macromolecular architectural surface: Highly branched graft polymer via photochemically driven quâsiliving polymerization technique. *Macromolecules*, 32 (21), pp.6989-6995.

Lepoittevin, B. & Hémery, P. (2002) Synthesis of high-molecular-weight cyclic and multicyclic polystyrenes. *Polymers for Advanced Technologies*, 13 (10-12), pp.771-776.

Leyden, D.E. & Luttrell, G.H. (1975) Preconcentration of trace metals using chelating groups immobilized via silylation. *Analytical Chemistry*, 47 (9), pp.1612-1617.

Lindström, U.M. (2007) *Organic reactions in water: principles, strategies and applications*. Blackwell Pub.

Liu, X.D., Tokura, S., Haruki, M., Nishi, N. & Sakairi, N. (2002) Surface modification of nonporous glass beads with chitosan and their adsorption property for transition metal ions. *Carbohydrate Polymers*, 49 (2), pp.103-108.

Lorentz, L.J. (1991) High-performance liquid chromatography. In: R. E. Schirmer ed. *Modern methods of pharmaceutical analysis.* Boca Raton, CRC Press, pp.239-391.

Lowell, S. (2004) *Characterization of porous solids and powders: surface area, pore size, and density*. Kluwer Academic Publishers.

M Izatt, R., L Bruening, R. & B Borup, M. (2011) Heavy Metal Removal Using Bound Macrocycles.

M. E. Simonsen and E. G. Soegaard (2008) Photocatalytic degradation of chloroform using a new type of photo-reactor. In: P. Innocenzi and Y. L. Zub and V. G. Kessler ed. *Sol-Gel Methods for Materials Processing. Focusing on Materials for Pollution control, Water Purification and Soil Remedation*. Dordrecht, Springer, pp.421-426.

Merna, J., Cihlar, J., Kucera, M., Deffieux, A. & Cramail, H. (2005) Polymerization of hex-1-ene initiated by diimine complexes of nickel and palladium. *European Polymer Journal*, 41 (2), pp.303-312.

Meyer, V. (2004) *Practical high-performance liquid chromatography*. Cornwall, Wiley.

Mishra, M.K. & Yagci, Y. (1998) *Handbook of radical vinyl polymerization*. New York, Marcel Dekker.

Moad, Graeme & Solomon, D.H. (2006) *The chemistry of radical polymerization*. 1st ed. London, Elsevier Ltd.

Moriyama-Gonda, N., Igawa, M., Shiina, H., Urakami, S. & Terashima, M. (2003) Decreased survival of prostate cancer cells in vitro by combined treatment of heat and an antioxidant inhibitor diethyldithiocarbamate (DDC). *Experimental and Toxicologic Pathology*, 55 (4), pp.251-256.

Nakayama, Y., Sudo, M., Uchida, K. & Matsuda, T. (2002) Spatio-resolved hyperbranched graft polymerized surfaces by iniferter-based photograft copolymerization. *Langmuir*, 18 (7), pp.2601-2606.

Neelakantan, L. (1958) Disulfides. *Journal of Organic Chemistry*, 23 (6), pp.938-939.

Nichols, P.J. & Grant, M.W. (1983) Thermal dissociation of thiuram disulfides in solution; an electron spin resonance and kinetic study. *Australian Journal of Chemistry*, 36 (7), pp.1379-1386.

Nieuwenhuizen, P.J., Ehlers, A.W., Haasnoot, J.G., Janse, S.R., Reedijk, J. & Baerends, E.J. (1999) The mechanism of zinc(II)-dithiocarbamate-accelerated vulcanization uncovered; theoretical and experimental evidence. *Journal of the American Chemical Society*, 121 (1), pp.163-168.

Oki, M. & Nakanishi, H. (1971) Conformations of the Esters. IV. The Conformations of Carbamates. *Bulletin of the Chemical Society of Japan*, 44 (11), pp.3148-3151.

Osburn, C.L. & Morris, D.P. (2003) UV effects in aquatic organisms and ecosystems. In: E. W. Helbling & H. E. Zagarese eds. Cambridge, Royal Society of Chemistry, pp.188-194.

Otsu, T. (2000) Iniferter concept and living radical polymerization. *Journal of Polymer Science, Part A: Polymer Chemistry*, 38 (12), pp.2121-2136.

Otsu, T. & Nayatani, K. (1958) Vinyl polymerization XXVIII. The polymerization of styrene initiated by tetralkyl thiuram disulfides. *Die Makromolekulare Chemie*, 27 (1), pp.149-156.

Otsu, T., Matsunaga, T., Doi, T. & Matsumoto, A. (1995) Features of living radical polymerization of vinyl monomers in homogeneous system using N,N-diethyldithiocarbamate derivatives as photoiniferters. *European Polymer Journal*, 31 (1), pp.67-78.

Otsu, T., Nayatani, K., Muto, I. & Imai, M. (1958) Vinyl polymerization XXVII. Organic polysulfides as polymerization initiators. *Die Makromolekulare Chemie*, 27 (1), pp.142-148.

Otsu, T., Yamashita, K. & Tsuda, K. (1986) Synthesis, reactivity, and role of 4-vinylbenzyl N,N-diethyldithiocarbamate as a monomer-iniferter in radical polymerization. *Macromolecules*, 19 (2), pp.287-290.

Ottenbrite, R.M. (1972) Preparation of aryl lsothiocyanates by pyrolysis of N-aryldithiocarbamates. *Journal of the Chemical Society, Perkin Transactions 1*, pp.88-90.

Palau, J., Penya-Roja, J.M., Gabaldón, C., Álvarez-Hornos, F.J. & Martínez-Soria, V. (2011) Effect of pre-treatments based on UV photocatalysis and photo-oxidation on toluene biofiltration performance. *Journal of Chemical Technology & Biotechnology*, p.n/a-n/a.

Parker, S.P. (1997) *McGraw-Hill encyclopedia of science & technology: MET-NIC.* McGraw-Hill.

Patel, A. & Mequanint, K. (2008) Syntheses and characterization of physically crosslinked hydrogels from dithiocarbamate-derived polyurethane macroiniferter. *Journal of Polymer Science, Part A: Polymer Chemistry*, 46 (18), pp.6272-6284.

Patel, S.I., Davis, F.J., Roberts, P.M.S., Hasson, C.D., Lacey, D., Hall, A.W., Greve, A. & Finkelmann, H. (2004) Liquid crystalline polymers. In: F. J. Davis ed. *Polymer chemistry, a practical approach*. Oxford, New York, Oxford University Press, p.248.

Paunikallio, T., Suvanto, M. & Pakkanen, T.T. (2008) Grafting of 3-(trimethoxysilyl)propyl methacrylate onto polypropylene and use as a coupling agent in viscose fiber/polypropylene composites. *Reactive and Functional Polymers*, 68 (3), pp.797-808.

Piletsky, S A, Mijangos, I., Guerreiro, A., Piletska, E., Chianella, I., Karim, K. & Turner, A. (2005) Polymer Cookery: Influence of Polymerization Time and Different Initiation Conditions on Performance of Molecularly Imprinted Polymers. *Macromolecules*, 38 (4), pp.1410-1414.

Pişkin, E., Kesenci, K., Şatiroğlu, N. & Geŋ, Ö. (1996) Dithiocarbamate-incorporated monodisperse polystyrene microspheres as specific sorbents: Adsorption of cadmium ions. *Journal of Applied Polymer Science*, 59 (1), pp.109-117.

Poole, C.F. (2003) *The essence of chromatography*. Amsterdam, Elsevier Science.

Pudovik, A.N., Khairullin, V.K., Il'yasov, A.V., Vasyanina, M.A., Aleksandrova, I.A., Ismayev, I.E. & Ovcharov, V.I. (1988) Mechanism of action of phosphorylated dithiocarbamates on the vulcanization of rubbers. *Polymer Science U.S.S.R.*, 30 (3), pp.475-480.

Quiclet-Sire, B. & Zard, S.Z. (1997) Riding the tiger: Using degeneracy to tame wild radical processes. *Pure and Applied Chemistry*, 69 (3), pp.645-650.

Rabek, J.F. (1995) *Polymer photodegradation: mechanisms and experimental methods*. 1st ed. New Delhi, Cambridge, Chapman & Hall.

Reghunadhan Nair, C.P. & Clouet, G. (1990) Block copolymers via thermal polymeric iniferters. Synthesis of silicone-vinyl block copolymers. *Macromolecules*, 23 (5), pp.1361-1369.

Reichardt, C. & Welton, T. (2011) *Solvents and Solvent Effects in Organic Chemistry*. John Wiley & Sons.

Robinson, J.W., Frame, E.M.S. & George M. Frame II (2005) *Undergraduate Instrumental Analysis*. New York, Marcel Dekker.

Rogachev, I., Kampel, V., Gusis, V., Cohen, N., Gressel, J. & Warshawsky, A. (1998) Synthesis, properties, and use of copper-chelating amphiphilic dithiocarbamates as synergists of oxidant-generating herbicides. *Pesticide Biochemistry and Physiology*, 60 (3), pp.133-145.

Roovers, J. & Charleux, B. (1999) *Branched polymers*. Springer.

Rudorf, W.D. (2007) Reactions of carbon disulfide with N-nucleophiles. *Journal of Sulfur Chemistry*, 28 (3), pp.295-339.

Ryu, I., Kreimerman, S., Araki, F., Nishitani, S., Oderaotoshi, Y., Minakata, S. & Komatsu, M. (2002) Cascade Radical Reactions Catalyzed by a Pd/Light System: Cyclizative Multiple Carbonylation of 4-Alkenyl Iodides. *Journal of the American Chemical Society*, 124 (15), pp.3812-3813.

Salvatore, R.N., Sahab, S. & Jung, K.W. (2001) Mild and efficient synthesis of thiocarbonates and thiocarbamates via a three-component coupling utilizing Cs2CO3 and TBAI. *Tetrahedron Letters*, 42 (11), pp.2055-2058.

Salvatore, R.N., Yoon, C.H. & Jung, K.W. (2001) Synthesis of secondary amines. *Tetrahedron*, 57 (37), pp.7785-7811.

Sandström, J. (1967) Barriers to internal rotation in thioamides. Experimental results and molecular orbital calculations. *Physical Chemistry*, 71 (7), pp.2318-2325.

Sato, T., Yutani, Y. & Otsu, T. (1983) Long-lived polymer radicals: 5. Synthesis of block copolymer by the reaction of living poly(N-phenylmethacrylamide) radical with vinyl monomers. *Polymer*, 24 (8), pp.1018-1022.

Schreck, R., Meier, B., Mannel, D.N., Droge, W. & Baeuerle, P.A. (1992) Dithiocarbamates as potent inhibitors of nuclear factor κB activation in intact cells. *Journal of Experimental Medicine*, 175 (5), pp.1181-1194.

Scozzafava, A., Mastrolorenzo, A. & Supuran, C.T. (2000) Arylsulfonyl-N,N-diethyl-dithiocarbamates: A novel class of antitumor agents. *Bioorganic and Medicinal Chemistry Letters*, 10 (16), pp.1887-1891.

Segovia, N., Crovetto, G., Lardelli, P. & Espigares, M. (2002) In vitro toxicity of several dithiocarbamates and structure - Activity relationships. *Journal of Applied Toxicology*, 22 (6), pp.353-357.

Si, X., McManus, B.M., Zhang, J., Yuan, J., Cheung, C., Esfandiarei, M., Suarez, A., Morgan, A. & Luo, H. (2005) Pyrrolidine dithiocarbamate reduces coxsackievirus B3 replication through inhibition of the ubiquitin-proteasome pathway. *Journal of Virology*, 79 (13), pp.8014-8023.

Silverstein, R.M., Webster, F.X. & Kiemle, D.J. (2005) *Spectrometric Identification Of Organic Compounds*. 7th ed. Hoboken, John Wiley & Sons, Inc.

Smith, M. & March, J. (2007) *March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*. 6th ed. New Jersey, Wiley-Interscience.

Sokker, H.H., Abdel Ghaffar, A.M., Gad, Y.H. & Aly, A.S. (2009) Synthesis and characterization of hydrogels based on grafted chitosan for the controlled drug release. *Carbohydrate Polymers*, 75 (2), pp.222-229.

Song, Q., Wang, Z. & Sanghvi, Y.S. (2003) A short, novel, and cheaper procedure for oligonucleotide synthesis using automated solid phase synthesizer. *Nucleosides, Nucleotides and Nucleic Acids*, 22 (5-8), pp.629-633.

Stefan, C., Nobel, I., Kimland, M., Lind, B., Orrenius, S. & Slater, A.F.G. (1995) Dithiocarbamates induce apoptosis in thymocytes by raising the intracellular level of redox-active copper. *Journal of Biological Chemistry*, 270 (44), pp.26202-26208.

Stoker, T.E., Cooper, R.L., Goldman, J.M. & Andrews, J.E. (1996) Characterization of pregnancy outcome following thiram-induced ovulatory delay in the female rat. *Neurotoxicology and Teratology*, 18 (3), pp.277-282.

Struble, R.G., Husain, K. & Somani, S.M. (1999) Response of the olfactory bulb antioxidant system following diethyldithiocarbamate (DDTC) administration in rats. *Journal of Applied Toxicology*, 19 (4), pp.221-228.

Svec, F. & Fréchet, J.M.J. (1996) New designs of macroporous polymers and supports: From separation to biocatalysis. *Science*, 273 (5272), pp.205-211.

Teegarden, D.M. (2004) *Polymer chemistry: introduction to an indispensable science*. NSTA Press, National Science Teachers Association.

Timoshin, A.A., Drobotova, D.Y., Lakomkin, V.L., Ruuge, E.K. & Vanin, A.F. (2008) Estimation of nitric oxide level in vivo by microdialysis with water-soluble iron-N-methyl-d-dithiocarbamate complexes as NO traps: A novel approach to nitric oxide spin trapping in animal tissues. *Nitric Oxide - Biology and Chemistry*, 19 (4), pp.338-344.

Tinkler, J., Gott, D. & Bootman, J. (1998) Risk assessment of dithiocarbamate accelerator residues in latex-based medical devices: Genotoxicity considerations. *Food and Chemical Toxicology*, 36 (9-10), pp.849-866.

Tiwari, S. & Bajpai, A. (2005) Metal ion extraction by dithiocarbamate function supported on polyacrylamide. *Reactive and Functional Polymers*, 64 (1), pp.47-54.

Todorovi, Z., Poli, P., Sabo, T. & Caki, M. (2002) Preconcentration method for trace metals in natural waters using 4-morpholine dithiocarbamate. *Journal of the Serbian Chemical Society*, 67 (12), pp.879-885.

Turner, S.R. & Blevins, R.W. (1990) Photoinitiated block copolymer formation using dithiocarbamate free radical chemistry. *Macromolecules*, 23 (6), pp.1856-1859.

United States Environmental Protection Agency (2001) European Commission/Disulfiram Robust Summary [Internet]. Available from: <http://www.epa.gov/HPV/pubs/summaries/thiurmct/c13348rs.pdf> [Accessed 7 December 2010].

Valentine, W.M., Amarnath, V., Amarnath, K., Rimmele, F. & Graham, D.G. (1995) Carbon disulfide mediated protein cross-linking by N,N-diethyldithiocarbamate. *Chemical Research in Toxicology*, 8 (1), pp.96-102.

Vancotthem, W., Beel, C., Danneels, P., Dekeyzer, J. & Vyvey, Q. (1991) Restoring the natural vegetation on strong eroded volcanic soils of Cape Verde (West-Africa). *Soil Technology*, 4 (2), pp.183-189.

Various (1988) Dithiocarbamate pesticides, ethylenethiourea, and propylenethiourea: A general introduction. *Environmental Health Criteria*, (78), pp.1-140.

Vollhardt, K.P.C. & Schore, N.E. (2002) *Organic Chemistry*. 4th ed. New York, Freeman.

Wang, F., Rauh, R.D. & Rose, T.L. (1997) An electrically conducting star polymer. *Journal of the American Chemical Society*, 119 (45), pp.11106-11107.

Watanabe, I., Otake, M., Yoshimoto, M., Sakanishi, K., Korai, Y. & Mochida, I. (2002) Behaviors of oil-soluble molybdenum complexes to form very fine MoS2 particles in vacuum residue. *Fuel*, 81 (11-12), pp.1515-1520.

Wen, B., Shan, X.Q., Liu, R.X. & Tang, H.X. (1999) Preconcentration of trace elements in sea water with poly (acrylaminophosphonic - dithiocarbamate) chelating fiber for their determination by inductively coupled plasma mass spectrometry. *Fresenius' Journal of Analytical Chemistry*, 363 (3), pp.251-255.

Wood, B.R., Semlyen, J.A. & Hodge, P. (1997) Cyclic polyesters: 4. Cyclics prepared by poly(decamethylene adipate) ring-chain reactions. *Polymer*, 38 (1), pp.191-194.

Wünchs, J.R. (2000) *Rapra Review Reports - Expert overviews covering the science and technology of rubber and plastics*. R. Dolbey & Rapra Technology Limited eds. Volume 10, Number 4, Rapra Technology Limited.

Yamase, T., Kokado, H. & Inoue, E. (1970) The Photolysis of Sodium N,N-Dimethyldithiocarbamate and Hexamethyleneammonium Hexamethylenedithiocarbamate. *Bulletin of the Chemical Society of Japan*, 43 (3), pp.934-935.

Yan, Z., Lu, Y. & Li, X. (2007) Silver ion-selective electrodes based on bis(dialkyldithiocarbamates) as neutral ionophores. *Sensors and Actuators B: Chemical*, 122 (1), pp.174-181.

Yokoyama, K. (2007) Our recent experiences with sarin poisoning cases in Japan and pesticide users with references to some selected chemicals. *NeuroToxicology*, 28 (2), pp.364-373.

Young, R.J. & Lovell, P.A. (1991a) *Introduction to polymers*. 2nd ed. London, Chapman & Hall.

Young, R.J. & Lovell, P.A. (1991b) *Introduction to polymers*. 2nd ed. London, Chapman & Hall.

Young, R.J. & Lovell, P.A. (1991c) *Introduction to polymers*. 2nd ed. London, Chapman & Hall.

Young, R.J. & Lovell, P.A. (1991d) *Introduction to polymers*. 2nd ed. London, Chapman & Hall.

Zanger, M. & Rabinowitz, J.L. (1975) A nuclear magnetic resonance investigation of the iodination of 1,2-disubstituted ethylenes. Evidence for a trans addition-cis elimination. *Journal of Organic Chemistry*, 40 (2), pp.248-250.

Zverev, A.N., Vinogradova, V.G. & Maizus, Z.K. (1980) Mechanism of the synergistic action of mixtures of metal dithiocarbamates with thiuram bisulfide in the inhibition of the oxidation of hydrocarbons. *Bulletin of the Academy of Sciences of the USSR Division of Chemical Science*, 29 (11), pp.1745-1749.

8 APPENDICES

Appendix A Calculation of the degree of cross-linking (DC) of the auto-cross-linked polymer

In order to find the % of cross-linking in this polymer we needed to know which proportion of the original linear polymer (fragment **D** in **Scheme_Apx A-1**) was still uncross-linked and which proportion of the linear polymer had made bonds forming cross-links (fragment **CL** in **Scheme_Apx A-1**) inside the polymer. When the linear polymer is irradiated, radical cross-over reactions can occur (**Scheme_Apx A-2**). Formation of each molecule of bibenzyl means that two new dithiocarbamate radicals have been formed which have the potential to form one new cross-link. The amount of bibenzyl produced will therefore represent the maximum number of cross-links that could have been formed; hence we can calculate the maximum degree of cross-linking in the polymer.

Table_Apx A-1: Elemental analysis of the photochemically auto-cross-linked polymer

Photochemically auto-cross-linked polymer	C	H	N	S
Theory(considering 100% of cross-linking)	64.70	7.24	5.03	23.03
Experimental	65.54	7.01	4.11	19.75

First we will calculate the moles of C in the sample and then the moles of C with the theoretical data considered for 0% of cross-linking using the values from **Table_Apx A-1**.

Sample

C) $\frac{65.54}{12.01} = 5.46$

H) $\frac{4.11}{1.01} = 6.94$

N) $\frac{4.11}{14.01} = 0.29$

S) $\frac{19.75}{32.06} = 0.62$

Normalising →

C) 18.83

H) 29.93

N) 1.00

S) 2.14

Theoretical

C) $\frac{70.94}{12.01} = 5.91$

H) $\frac{7.09}{1.01} = 7.02$

N) $\frac{3.94}{14.01} = 0.28$

S) $\frac{18.03}{32.06} = 0.56$

Normalising →

C) 21.11

H) 25.07

N) 1.00

S) 2.00

We will subtract the moles of carbon in the theoretical data from the moles of carbon in the sample (**Table_Apx A-1**) in order to obtain the moles of carbon from the bibenzyl formed when the cross-links are produced because in the theoretical data we had all the benzyl segments attached to the linear polymer but in the sample some of them have been lost:

21.11 moles of C in the polymer with 0% of cross-links (theoretical)

18.83 moles of C in the cross-linked polymer (sample)

21.11 – 18.83 = 2.28 moles of C in the bibenzyl

We will figure out the moles of bibenzyl and then the moles of the cross-links in the polymer. In this case it is the same value because it is equimolecular:

1 molecule of bibenzyl was created because 1 cross-link was made

$$2.28 \text{ mol C bibenzyl} \times \frac{1.00 \text{ mol bibenzyl}}{14.00 \text{ mol C}} = 0.16 \text{ mol of bibenzyl}$$

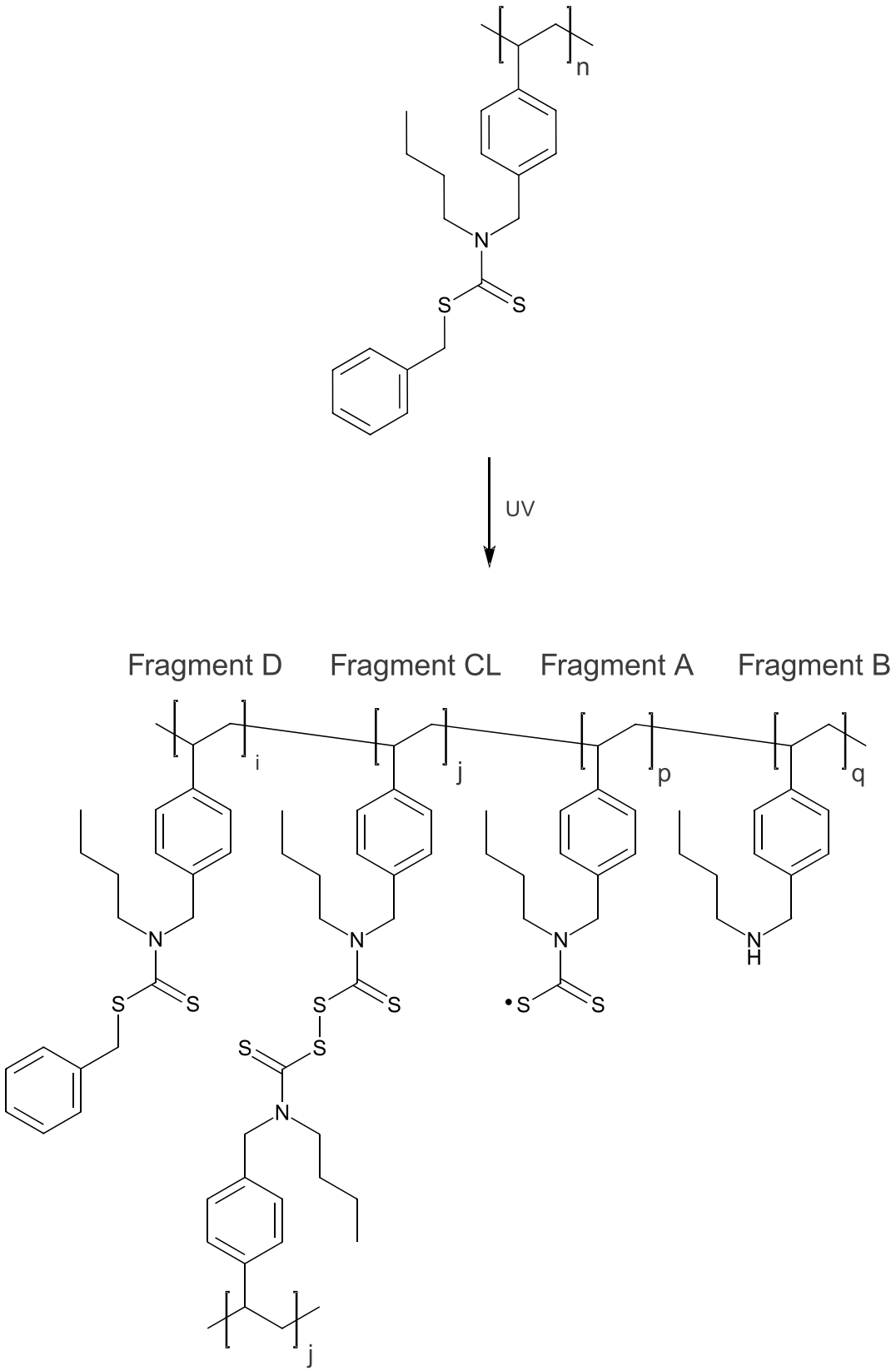
$$= 0.16 \text{ mol of cross-link}$$

We have considered 0% of cross-linking so in that case all the side-chains are like those in the original linear polymer and there are no cross-links. If this is true then the 21.11 moles of carbon come exclusively from the initial monomer added and we can calculate the amount of fragments **D** that have been converted into fragments **CL** in **Scheme_Apx A-1**:

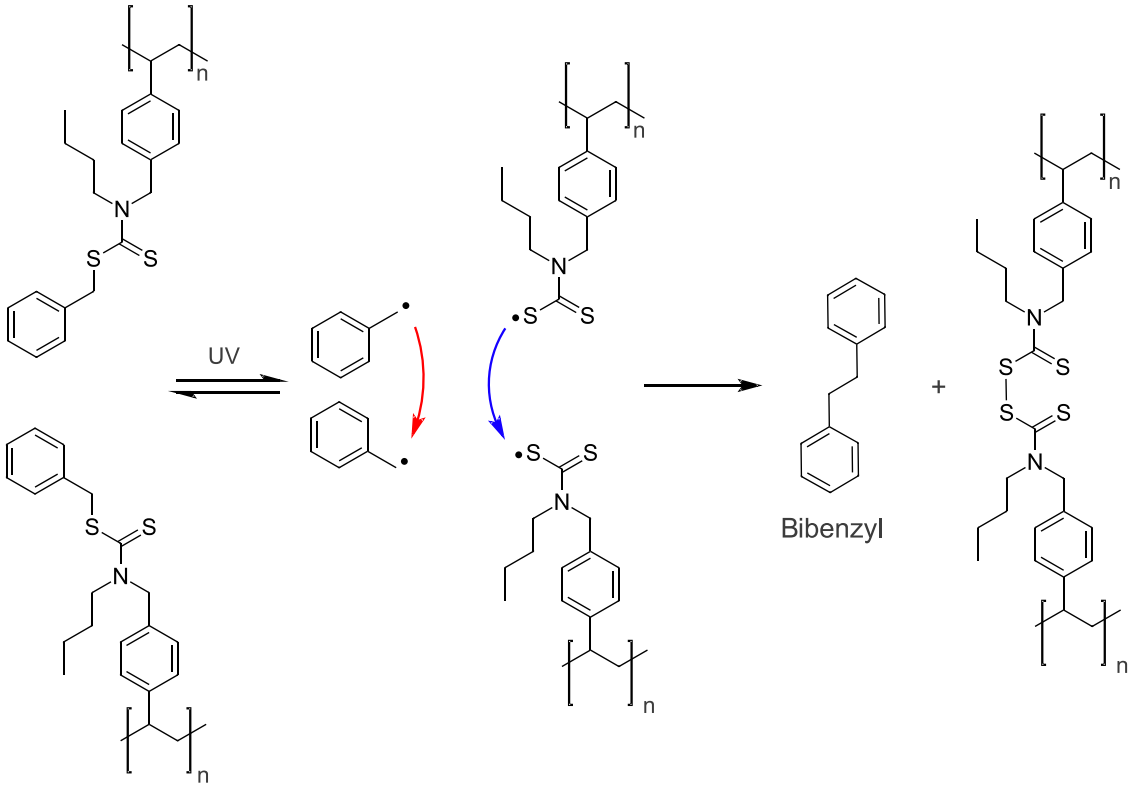
$$21.11 \text{ mol C (theoretical)} \times \frac{1.00 \text{ mol fragment D}}{21.00 \text{ mol C}} =$$

$$= 1.01 \text{ mol of fragment D (initial)}$$

$$\frac{0.16 \text{ mol of cross-linker}}{1.01 \text{ mol of fragment D (initial)}} = 0.16 \times 100 = \boxed{16\%}$$



Scheme_Apx A-1: Calculating the degree of cross-linking in the auto-cross-linked polymer



Scheme_Apx A-2: The irradiation of the linear polymer poly(BBVC) generates the photodissociation and the cross-over reaction of radicals, creating a cross-linked polymer and bibenzyl as subproduct

Appendix B Calculation of the degree of cross-linking (DC) of the de-cross-linked polymer

There are three different fragments that compound the structure of the macromolecule **Figure_Apx B-1**:

1. The fragment with the original monomer with dithiocarbamate functionality that still remains intact from the linear polymer (fragment **D**)
2. The fragment that has a thiuram structure due to the cross reaction of the TETD with the auto-cross-linked polymer (fragment **T**)
3. And the fragment that remains intact from the auto-cross-linked polymer and has a thiuram structure that generated the cross-links between chains (fragment **CL**).

Knowing the ratio between the fragments we can know how successful was the interchange of thiuram groups and we could know as well the degree of cross-linking in the new polymer. We can calculate the proportion of those fragments inside the macromolecule using the information that the ^{1}H NMR analysis provides due the integrals of the peaks assigned to particular groups of atoms, telling us the number of protons involved in that group.

The protons marked as ***d*** and ***t*** in the **Figure_Apx B-1** have an environment that can be only found in the fragments **D** and **T** respectively. There is a slight overlap between those peaks and with others in the spectrum but their shape is still recognisable to find their approximate value. There is no a proton with a unique environment that can only be found in the fragment **CL**. To find the proportion of this fragment we had to use a peak assigned to a group of atoms that existed in the three fragments. Consequently the three peaks, one for every fragment, will coalescence in one peak in the spectrum and we will have to do calculations to extract the information from that single peak. The chosen group of atoms in the structure is due to its peak (represented as s in the spectrum) is isolated from the rest of the spectrum. The integral of that chosen peak in the spectrum will be then the sum of the integrals for the protons of that group of atoms along the macromolecule:

$$s_d + s_t + s_{cl} = s$$

We can find the values $\mathbf{s_d}$ and $\mathbf{s_t}$ respect the signals **d** and **t** based on the number of protons of the groups:

$$\frac{d}{2} = s_d \qquad\qquad \frac{t}{4} = s_t$$

There is an added difficulty in this procedure that it is reflected in those equations: the peak of the proton ***s*** in the spectrum splits in two below 100°C because of the effect explained before in **Section 1.9.3**. The problem can be easily resolved as the peak always splits to the same proportions at the same temperature: the chosen peak always has the half of the original value at 25°C in CH_3Cl and that is the reason why the peak ***d*** has the double the integral value of peak $\boldsymbol{s_d}$ although the peaks correspond to the same number of protons, and the same happens in the fragment **T**. Substituting parameters we will find the final expression:

$$\frac{d}{2} + \frac{t}{4} + s_{cl} = s$$

Using the peak ***d*** as the reference peak with a value of 2 we will find the value of $\boldsymbol{s_{cl}}$, the peak corresponding to the fragment **CL**:

Peak ***d*** → integral value: 2.00

Peak ***t*** → integral value: 5.00

Peak ***s*** → integral value: 2.44

$$\frac{d}{2} + \frac{t}{4} + s_{cl} = s$$

$$1.00 + 1.25 + s_{cl} = 2.44$$

$$s_{cl} = 0.19$$

Calculating the values of every integral for one proton we will find the proportion between fragments:

Peak ***d*** (2H) → integral value: 2.00

Peak ***t*** (4H) → integral value: 5.00

Peak $\boldsymbol{s_{cl}}$ (2H) → integral value: 0.19

↓ Values for 1H

Peak ***d***: $\frac{2.00}{2} = 1.00$

Peak ***t***: $\frac{5.00}{4} = 1.25$

Peak $\boldsymbol{s_{cl}}$: $\frac{0.19}{2} = 0.01$

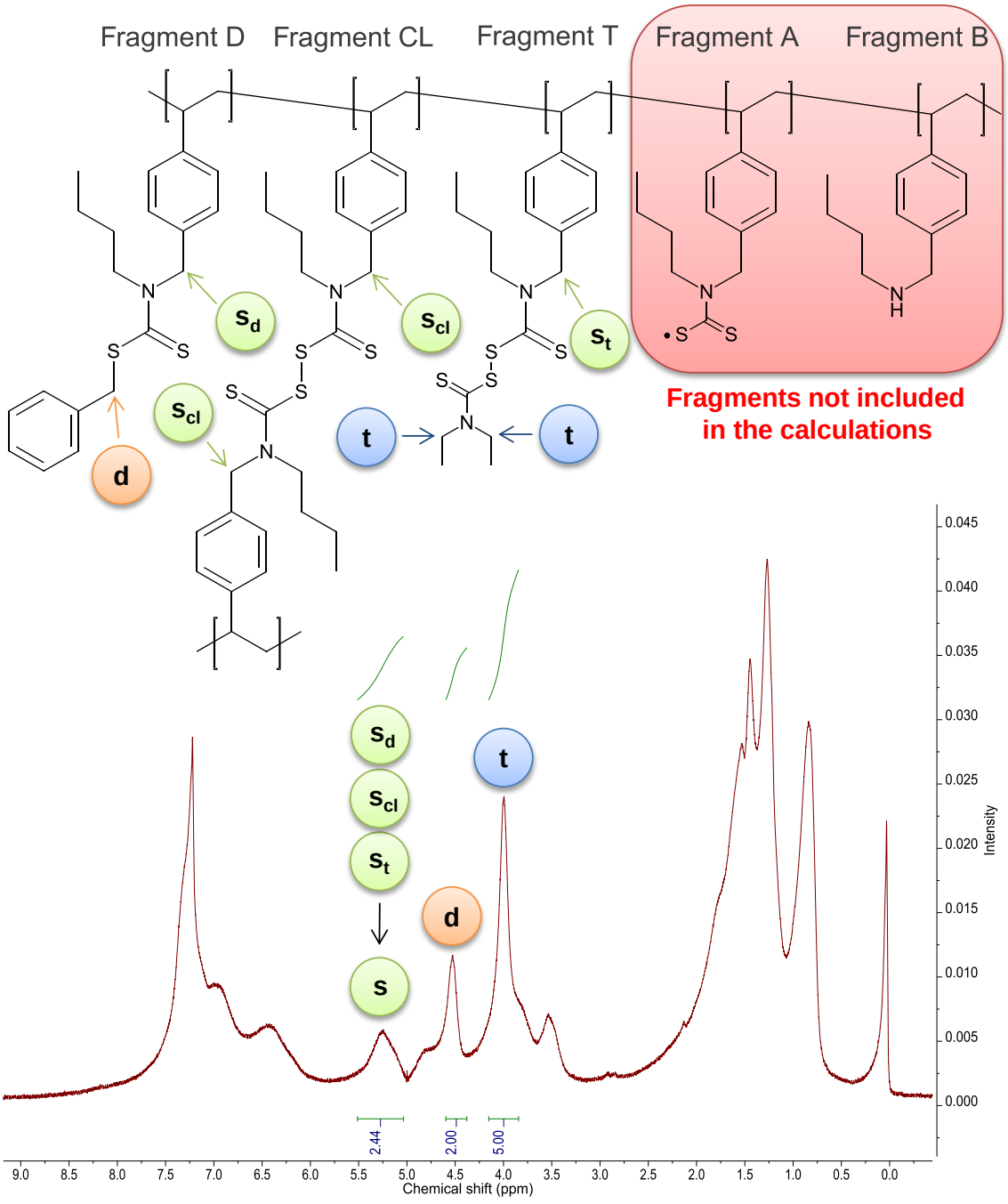
Fragment D 44%

Fragment T 55%

Fragment CL 1%

↓

Degree of cross-linking



Figure_Apx B-1: Calculating the degree of cross-linking using the ^{1}H NMR spectrum of the de-cross-linked polymer

This method it is not very exact, because the value of the integrals depends on the area of the peak that it is selected which is always very subjective when there is an overlap of peaks. Also, the remaining TETD molecules in the

polymer will contribute to the % of the fragment **T**. We could even have fragments like fragment **S** and fragment **N**, with only a dithiocarbamate dormant radical in the pendant group of the chain and a side-chain residue with only a secondary amine in it (a product of decomposition of the dithiocarbamate radical) might be possible. Those groups would be difficult to estimate and we believe that their number is not really relevant so we will not calculate them and we will include them in the fragment **CL**. The lack of accuracy can be represented carrying other calculations using different peaks: the methyl and the aromatic. Those calculations produced values for the fragment **CL** of 18% and 40% respectively, something that it was impossible as the product was soluble. In any case, regardless the different final values for the proportions between fragments the exchange of the groups in the thiuram and the de-cross-linking process is evident.

Appendix C Calculation of the degree of cross-linking (DC) of the cross-linked polymer poly(EGDMA-*co*-BBVC)

To calculate the degree of cross-linking (*DC*) in the cross-linked in this polymer (H. N. Kim & Spivak, 2003) we need to know the ratio between the units of monomer that are cross-linked (*CL*) to the whole units of monomer present in the polymer (*M*):

$$\text{Degree of cross-linking: } \frac{CL}{M}$$

To find out those numbers we used the FTIR of the cross-linked polymer (**Figure_Apx C-1**) and of the cross-linker alone (**Figure_Apx C-2**). To make the values valid we have to find an internal standard, a peak that it is not altered in the polymerisation process, and create a ratio with it. The selected peak is the C-H peak from the glycol unit of EGDMA at 950 cm^{-1} since that glycol part is not involved in the reaction. The peak that we will look in the FTIR as a measurement of the amount of cross-linker in the sample will be the one correspondent to the C=C of the vinyl part.

We calculate the areas of the peaks of EGDMA alone:

C=C (vinyl), 1637.349 cm^{-1}
Area: 2.003
Area Normalized: 6.476

C-H (glycol), 943.067 cm^{-1}
Area: 3.214
Area Normalized: 9.913

And then the ratios of the areas for the peaks of the EGDMA alone:

Area: 0.623
Normalize Area: 0.653

This value will correspond to a 0% of cross-linking since it is just the molecule of cross-linker, with all the double bonds intact.

The same calculations were done for the peaks of the cross-linked polymer:

C=C (vinyl), 1637.349 cm^{-1}
Area: 1.857
Area Normalized: 3.410

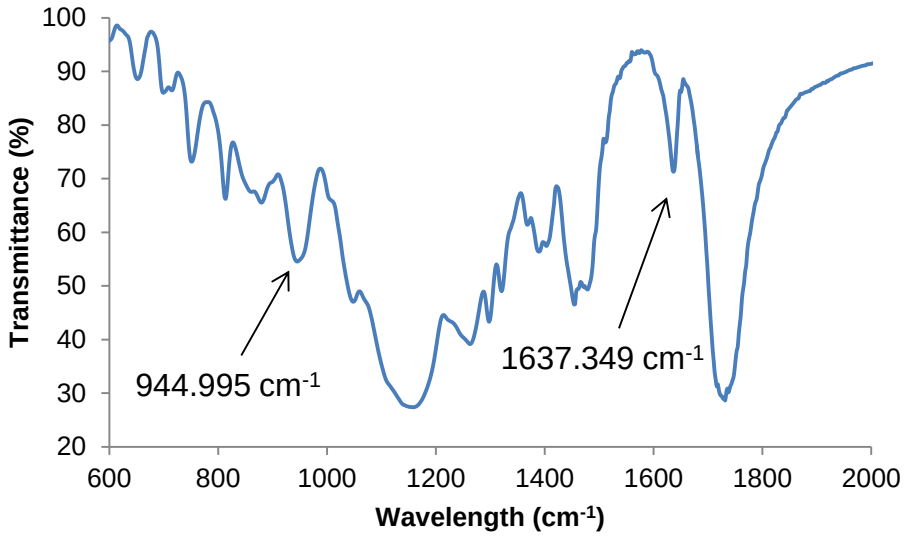
C-H (glycol), 944.995 cm^{-1}
Area: 4.714
Area Normalized: 7.669

And the ratios of the areas for the peaks for the cross-linked copolymer:

Area: 0.394
Normalize Area: 0.445

There is one clear piece of evidence so far: the ratios were calculated dividing the normalised area of the C=C peaks by the corresponding to the C-H of the glycol part and since the number of double bonds should decrease in the

polymer corresponding to the values of the cross-linker alone also the ratios for the polymer should be lower, and that is exactly what is happening, from 0.653 to 0.445.



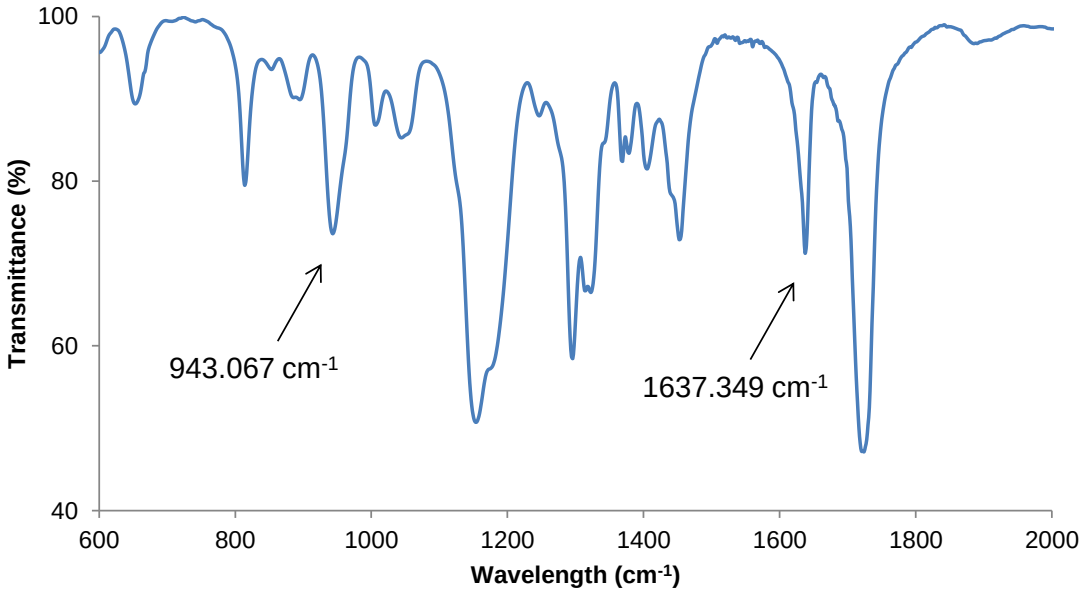
Figure_Apx C-1: FTIR of the polymer poly(EGDMA-co-BBVC)

To calculate now the DC we will consider in those calculations that the wash of the polymer was ideal and there are no inimer and cross-linker left. In that case all the double bonds found in the FTIR of the polymer will correspond to the cross-linkers that only reacted with one of the two double bonds available. If we subtract that value from that of the total of double bonds from the molecules of cross-linker we would have the value of cross-links in the polymer:

$$0.653 - 0.445: 0.208$$

Now we can calculate the degree of cross-linking:

Degree of cross-linking: $\frac{0.208}{0.653}$ = 32%



Figure_Apx C-2: FTIR of the EGDMA molecule

Appendix D Calculation of the proportion of BBVC, secondary amine and EGDMA in the cross-linked polymer Poly(EGDMA-*co*-BBVC)

We will take the values of the elemental analysis for that polymer (**Table_Apx D-1**).

Table_Apx D-1: Elemental analysis of the cross-linked polymer Poly(EGDMA-*co*-BBVC)

Thermally cross-linked polymer	C	H	N	S	O
Theory	62.55	7.07	0.74	3.37	26.28
Experimental	61.73	7.16	1.32	1.84	27.91

We will assume that the oxygen in the polymer comes from the EGDMA fragments, that the sulphur represent the fragments of inimer in the polymer with the dithiocarbamate functionality intact and the nitrogen content will represent the fragments of inimer that have the dithiocarbamate functionality intact and also the dithiocarbamates that decomposed leading to amine groups:

$$\frac{27.91 \text{ mg of O}}{100 \text{ mg total}} \; 1 \text{ mg total} = 0.2791 \text{ mg of O}$$

$$0.2791 \text{ mg of O} \times \frac{1 \text{ mmol O}}{16 \text{ mg O}} \times \frac{1 \text{ mmol EGDMA}}{4 \text{ mmol O}} =$$

$$= 4.3609735 \times 10^{-3} \text{ mmol EGDMA}$$

$$\frac{1.32 \text{ mg of N}}{100 \text{ mg total}} \quad 1 \text{ mg total} = 0.0132 \text{ mg of N}$$

$$0.0132 \text{ mg of N} \times \frac{1 \text{ mmol N}}{14 \text{ mg N}} \times \frac{1 \text{ mmol inimer}}{1 \text{ mmol N}} =$$

$$= 9.4285714 \times 10^{-4} \text{ mmol total inimer}$$

$$\frac{1.84 \text{ mg of S}}{100 \text{ mg total}} \quad 1 \text{ mg total} = 0.0184 \text{ mg of S}$$

$$0.0184 \text{ mg of S} \times \frac{1 \text{ mmol S}}{32 \text{ mg S}} \times \frac{1 \text{ mmol inimer}}{2 \text{ mmol S}} =$$

$$= 2.875 \times 10^{-4} \text{ mmol of inimer intact}$$

With the last two values we can calculate the number of inimers that have suffered decomposition and now are amines; we will subtract the number of inimer fragments with the dithiocarbamate functionality intact from the total number of inimer fragments:

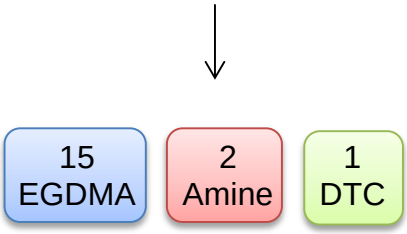
$$9.4285714 \times 10^{-4} - 28.75 \times 10^{-4} = 6.5535714 \times 10^{-4} \text{ mmol of amine}$$

With those values we can now have the proportion of fragments within the polymer:

4.3609375×10^{-4} mmol of EGDMA

6.5535714×10^{-4} mmol of amine

2.875×10^{-4} mmol of dithiocarbamate (DTC)

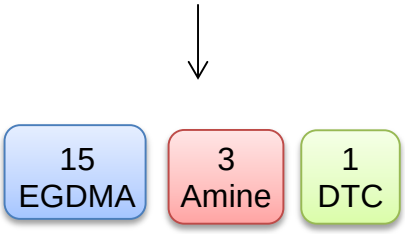


Those are the experimental values, to compare with the theoretical values we have to follow the same calculations using the theoretical values obtained from the elemental analysis. Doing the same steps we have these results:

0.44 mmol of EGDMA

0.09 mmol of amine

0.03 mmol of dithiocarbamate (DTC)



Therefore the values do not deviate much from the real ones.

Appendix E Calculation of the ratio between the inimer BVPD and the monomer TMSPMA in the hyperbranched polymer Branched-poly(TMSPMA-*co*-BVPD).

In the ^{1}H NMR the peaks corresponding to the benzyl parts of the inimer BVPD and the methoxysilyl in the monomer 3-(Trimethoxysilyl) propyl methacrylate (TMSPMA) were found and measured (**Figure_Apx E-1**). The integral of the aromatic part were normalised to 14 to get a value of 2.34 in the methoxy part. Both values were divided by the number of protons that they represent:

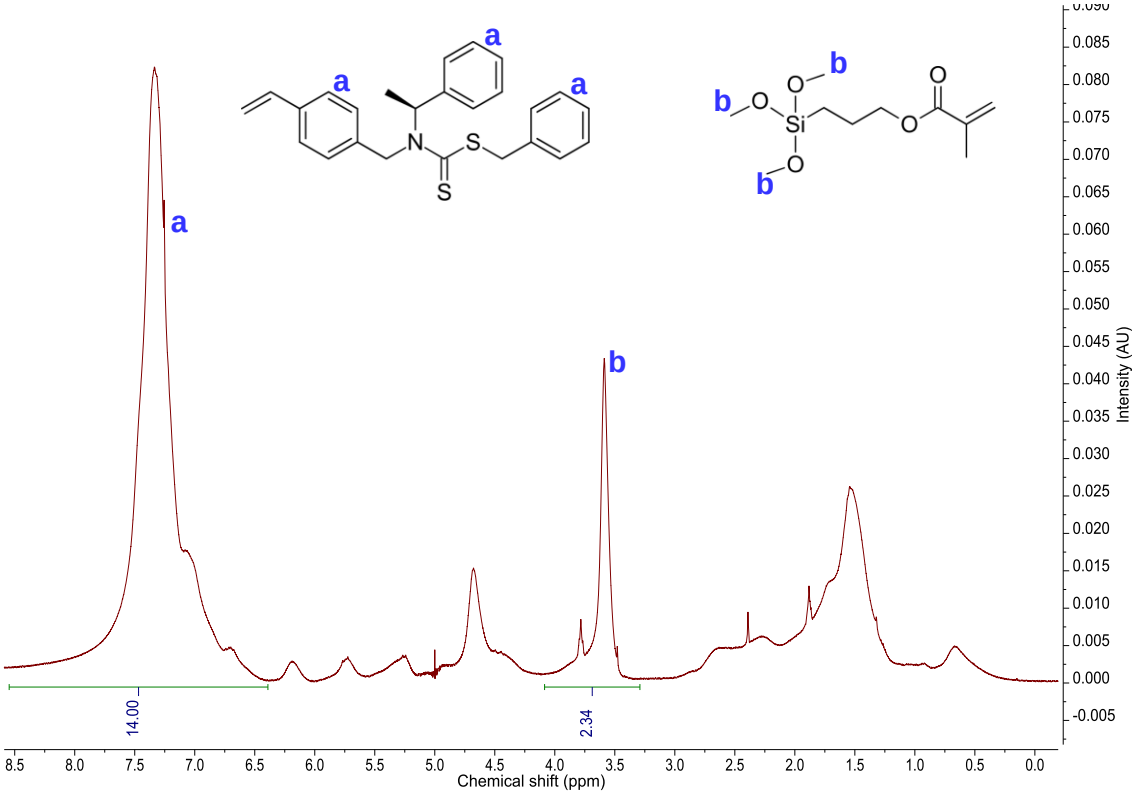
$$\text{Aromatic part of the BVPD: } \frac{14 \text{ AU}}{14 \text{ protons}} = 1 \text{ AU/Protons}$$

$$\text{Methoxy part of the TMSPMA: } \frac{2.34 \text{ AU}}{9 \text{ protons}} = 0.26 \text{ AU/Protons}$$

We will obtain the ratio dividing the results by the lower value:

$$\frac{1 \text{ AU/Protons BVPD}}{0.26 \text{ AU/protons TMSPMA}} = \frac{3.85 \text{ BVPD}}{1 \text{ TMSPMA}}$$

That result tells us that there are 4 molecules of BVPD to one of the TMSPMA in the hyperbranched polymer. Since the initial ratio was 4.25 to 1 the result matches quite well the expected value.



Figure_Apx E-1: ^{1}H NMR of the branched-poly(BVPD-*co*-TMSPMA)

9 PUBLICATIONS

Polymer Cross-Linking/De-Linking

DOI: 10.1002/anie.200906676

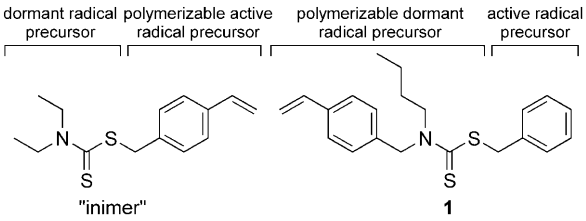
A Sulfur–Sulfur Cross-Linked Polymer Synthesized from a Polymerizable Dithiocarbamate as a Source of Dormant Radicals**

Luis Miguel García-Con, Michael J. Whitcombe, Elena V. Piletska, and Sergey A. Piletsky*

The dithiocarbamates (DTCs) have a special place within polymer chemistry due to their versatile role as thermal and photochemical initiators.[1] In particular the role of dithiocarbamate esters as "iniferters" in "living" radical polymerizations has practical significance.[2] The living nature of DTC ester-initiated photopolymerization derives from the extreme difference in reactivity of the radicals created by homolytic cleavage of the DTC ester bond. This gives rise to a reactive carbon-centered radical and a much less reactive, or dormant, dithiocarbamate radical, in which the unpaired electron is delocalized over the DTC structure. The chemistry of the dithiocarbamate radical is dominated by recombination to reform covalent bonds. It is the ability of dormant radicals to recapture the carbon-centered radical after addition of monomer to form a new DTC ester that imparts living character to DTC ester-initiated photopolymerization. Compounds of this type have been used in the synthesis of telechelic polymers,[3] block,[4,5] or graft copolymers[5,6] and hyperbranched polymers.[7] In the latter context, Otsu et al.[8] synthesized the first example of a DTC ester of a polymerizable derivative, the 4-vinylbenzyl ester of *N*,*N*-diethyldithiocarbamic acid, creating "inimer"—a compound that combines iniferter and monomer functionalities. Inimer could be polymerized photochemically to form hyperbranched polymers or by conventional thermal initiation to form linear polymers with pendant DTC ester groups. These polymers are macro-iniferters, which allow the photochemical grafting of a range of other monomers. As well as the inimer of Otsu et al.,[8] similar compounds, based on methacrylates, have been reported.[9]

In polymers of these compounds, irradiation will generate active macroradicals and dormant dithiocarbamyl radicals as low molar mass fragments. The macroradicals will react rapidly with monomer, oxygen, or with dithiocarbamyl radical to reform DTC esters. The situation will be different, however, if the dithiocarbamyl radical is part of the polymeric system and the active radical is the low molar mass fragment. A likely scenario under these circumstances is that during prolonged irradiation, the more readily diffusible carbon-centered radicals will dimerize, forming stable low-molar mass by-products, leading to an excess of dithiocarbamyl radicals attached to the polymer. This will result in the creation of a relatively stable population of polymeric dormant radicals. The physics and chemistry of immobilized dithiocarbamyl dormant radicals is expected to be an exciting field of investigation, since materials containing stable radicals may possess useful photoresponsive magnetic, mechanical, and electrical properties. Polymers with other stable radical functionalities, such as nitroxy radicals, have been reported as novel battery materials[10] and alkoxamines in the side chain[11] or main chain[12] and have been used as thermally activated systems for the reorganization of polymeric materials through radical crossover reactions. Similarly, reversible "de-linking" to radical fragments has been shown to occur in response to light or pressure in the case of triphenylimidazole dimers present as cross-links on a methacrylate backbone.[13]

In order to develop new materials to explore the properties of polymeric dithiocarbamyl radicals, we designed a monomer, superficially similar to inimer,[8] but reversing the orientation of the molecule, as shown in Scheme 1, such that the dithiocarbamyl residue is the polymerizable part of the molecule.



Scheme 1. The structure of Otsu's "inimer"[8] (left) and of the monomer used in this work: benzyl *N*-butyl-*N*-(4-vinylbenzyl) dithiocarbamate (**1**), or "reversed inimer" (right), showing the differences between the two structures with respect to the active and dormant radical precursor sites and the position of the polymerizable functionality.

The monomer, **1** (Scheme 1), was prepared by reaction of CS_2 with amine in the presence of base,[14] following the one-pot method proposed by Azizi et al.[15] A nominally linear polymer, **2**, was prepared in toluene by AIBN-initiated thermal polymerization in the dark.

UV irradiation of solutions of **2** is expected to result in cleavage of the C–S bond, creating benzyl radicals and

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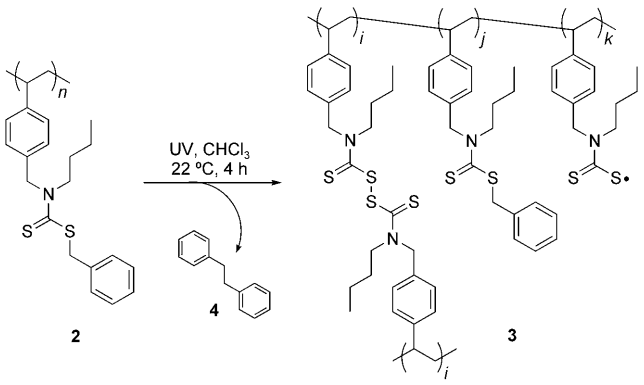
Supporting information for this article, including the synthesis of all compounds and polymers and of the irradiation experiments, is available on the WWW under http://dx.doi.org/10.1002/anie.200906676.

polymeric sulfur radicals. While recombination of the radical pair will reform the initial DTC ester groups, recombination of "like" radicals will result in cross-linking due to the formation of S–S bonds and, as frustrations due to cross-linking increase, isolated sulfur radicals, which are expected to be relatively long-lived. This process will be aided by benzyl radical recombination to form 1,2-diphenylethane (**4**) as by-product (Scheme 2). Irradiation of **2** was performed in



Scheme 2. Photocross-linking of **2** to **3**, with elimination of 1,2-diphenylethane (**4**).

chloroform solution. While this solvent is not ideal for performing photochemical studies, due to the possibility of side-reactions from photolysis of the solvent, nevertheless it was used on account of the greater solubility of the polymer in $CHCl_3$ than in other solvents (such as acetonitrile) which do not suffer from these problems.

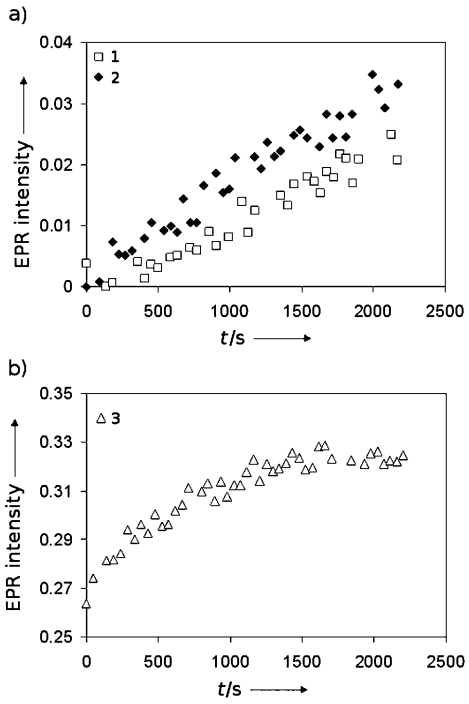


Figure 1. Intensity of the EPR signal against irradiation time for: a) **1** and **2**; and b) **3**.

The kinetics of radical formation during irradiation of **1** and **2** was investigated by EPR spectroscopy (Figure 1 a). In these two cases the DTC ester group is intact at the start of the experiment. The intensity of the EPR signal was seen to increase linearly as a function of irradiation time over the first 2000 s, starting from zero intensity at time $t = 0$ s. This is a characteristic of a system in which the formation of active species is fast compared to other processes (such as polymer propagation) and where the rate of termination can be considered to be negligible until relatively high conversions.[16] The auto cross-linked polymer, **3**, showed different behavior, possessing a significant EPR signal before irradiation due to the presence of isolated dormant radical species (Figure 1 b). Since this sample had been prepared more than 2 weeks previously, it shows the remarkable longevity of dormant radicals in this system. The generation of additional radical species is expected to occur as a result of dissociation of thiuram groups, present as cross-links between polymer chains. The rate of development of the EPR signal in the case of **3** was not linear with time. The signal did not increase after ca. 1500 s, suggesting that the rates of radical formation and loss were approximately equal.

In order to investigate the early stages of photochemical cross-linking, samples of **2** were irradiated for 1, 3, or 5 min only and the solutions examined by GPC. The non-irradiated **2** (Figure 2 a, curve A) showed a monomodal peak centered at

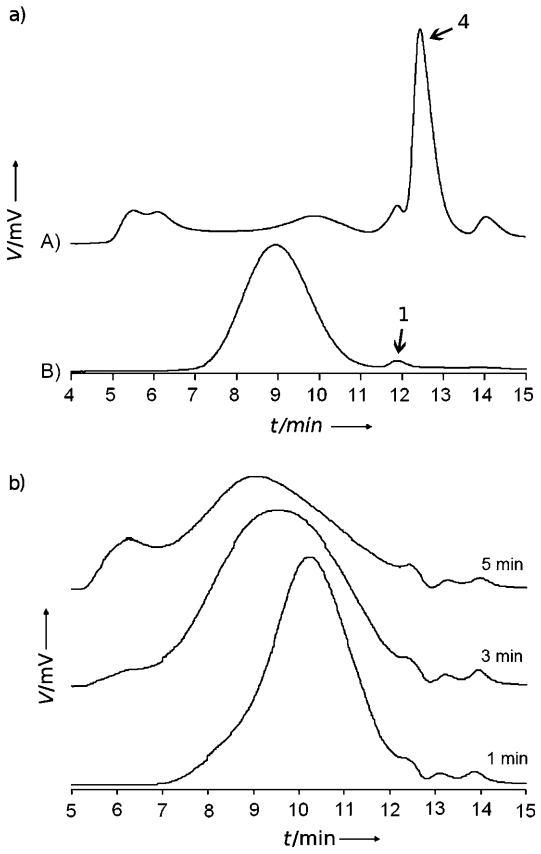


Figure 2. GPC curves for: a) **2** (A) and **3** supernatant (B); b) samples taken from the initial stages of the photochemical cross-linking reaction.

a molecular weight (MW) of 18000. During irradiation, the solution viscosity increased rapidly due to increases in molar mass. The average MW of the polymeric fraction produced after 5 min irradiation was 20000 (Figure 2b, upper line). The solution also contained a growing fraction with a much higher MW, estimated to be >150000, which is most likely formed during the initial stages of gel formation.

UV irradiation for around 4 h was required to create **3** which was no longer soluble in either $CHCl_3$ or THF and appeared as a swollen gel. Precipitation into methanol was performed to separate the gel fraction from soluble material and the supernatant analyzed by GPC. The result (Figure 2a, curve B) showed complete disappearance of **2** (MW = 18000) and formation of both high and low molecular weight products, proving that cross-linking had occurred between polymer chains. The by-product of active radical recombination, 1,2-diphenylethane (**4**), was also detected, the peak in the GPC having the same retention time as an authentic sample. Identification of the by-product was confirmed by HPLC-MS and NMR spectroscopy. Evidence for the proposed mechanism of cross-linking can also be seen in the FT-IR spectrum. The spectrum of **3** (Figure 3, upper curve)

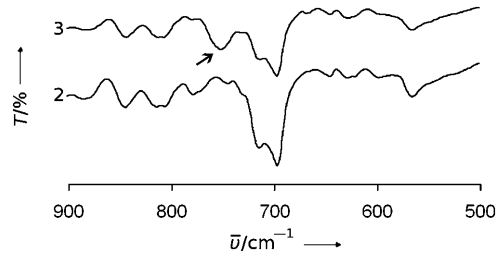
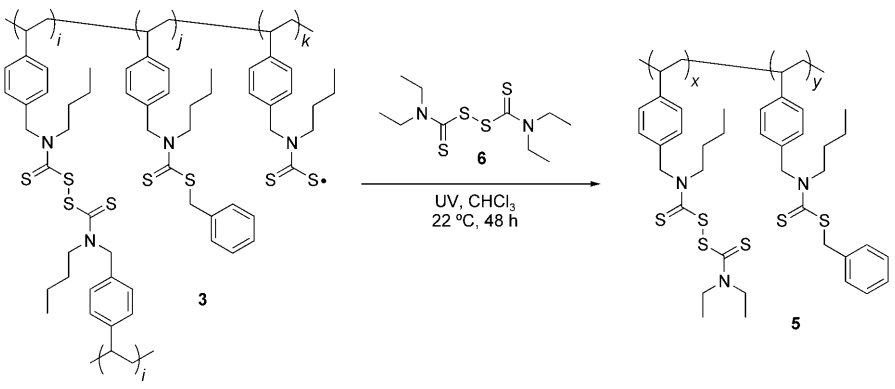


Figure 3. IR spectra of the linear (**2**) and cross-linked polymers (**3**), showing the appearance of a new band due to S–S bond formation.

showed a strong peak due to S–S stretching at 750 cm^{-1},[17] which was absent from the spectra of **1** and **2** (Figure 3, lower curve). Signals due to C=S and C–N stretching vibrations, at 1174 and 1477 cm^{-1} respectively, were found in the spectra of all three compounds.



Scheme 3. De-linking of **3** (to **5**) by photochemical treatment with tetraethyl dithiuram disulfide (**6**).

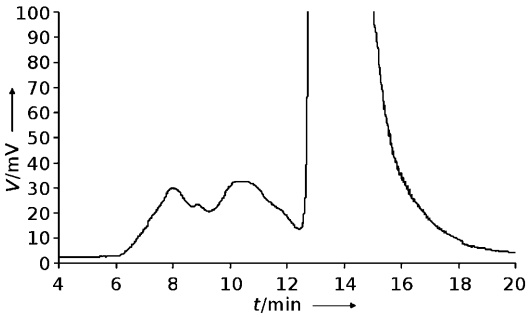


Figure 4. GPC of **5**, showing re-formation of soluble polymeric products.

As a final demonstration that the cross-links in **3** were due to reversible formation of S–S bonds, **3** was irradiated with an excess of tetraethyl dithiuram disulfide (**6**) (Scheme 3). Under these conditions the polymer was rendered completely soluble after 6 h irradiation, followed by 42 h in the dark, the GPC (Figure 4) and NMR spectra (Supporting Information, Figure S2) being consistent with the change.

We have presented an efficient approach to the synthesis of a new range of photoresponsive DTC-containing polymeric materials. We believe that the ability to generate a high concentration of stable radicals under controlled conditions has the potential to be used in many application areas. These may include engineering adhesives, UV filters, separation materials, sensors for radicals, trapping of reactive oxygen species and as antioxidants, thermoplastic vulcanizates, and as new materials for microelectronics.

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[1] a) R. J. Kern, *J. Am. Chem. Soc.* **1955**, *77*, 1382–1383; b) T. E. Ferington, A. V. Tobolsky, *J. Am. Chem. Soc.* **1955**, *77*, 4510–4512; c) T. Otsu, K. Nayatani, *Makromol. Chem.* **1958**, *27*, 149–156; d) T. Otsu, K. Nayatani, I. Muto, M. Imai, *Makromol. Chem.* **1958**, *27*, 142–148; e) C. P. Reghunadhan Nair, G. Clouet, *Polymer* **1988**, *29*, 1909–1917.
[2] T. Otsu, *J. Polym. Sci. Part A* **2000**, *38*, 2121–2136.
[3] R. Jerome, M. Henrioulle-Granville, B. Boutevin, J. J. Robin, *Prog. Polym. Sci.* **1991**, *16*, 837–906.
[4] T. Otsu, A. Kuriyama, *Polym. J.* **1985**, *17*, 97–104.
[5] T. Otsu, *J. Polym. Sci.* **1957**, *26*, 236–239.
[6] P. K. Bhuyan, D. K. Kakati, *J. Appl. Polym. Sci.* **2009**, *112*, 64–71.
[7] K. Ishizu, A. Mori, *Macromol. Rapid Commun.* **2000**, *21*, 665–668.
[8] T. Otsu, K. Yamashita, K. Tsuda, *Macromolecules* **1986**, *19*, 287–290.

[9] a) S. H. Qin, K. Y. Qiu, *Eur. Polym. J.* **2001**, *37*, 711 – 717; b) N. Luo, J. B. Hutchison, K. S. Anseth, C. N. Bowman, *J. Polym. Sci. Part A* **2002**, *40*, 1885 – 1891.
[10] T. Suga, H. Konishi, H. Nishide, *Chem. Commun.* **2007**, 1730 – 1732.
[11] Y. Higaki, H. Otsuka, A. Takahara, *Macromolecules* **2006**, *39*, 2121 – 2125.
[12] a) H. Otsuka, K. Aotani, Y. Higaki, A. Takahara, *Chem. Commun.* **2002**, 2838 – 2839; b) H. Otsuka, K. Aotani, Y. Higaki, A. Takahara, *J. Am. Chem. Soc.* **2003**, *125*, 4064 – 4065.
[13] T. Iwamura, M. Sakaguchi, *Macromolecules* **2008**, *41*, 8995 – 8999.
[14] W. D. Rudorf, *J. Sulfur Chem.* **2007**, *28*, 295 – 339.
[15] N. Azizi, F. Aryanasab, M. R. Saidi, *Org. Lett.* **2006**, *8*, 5275 – 5277.
[16] J. Merna, J. Cihlar, M. Kucera, A. Deffieux, H. Cramail, *Eur. Polym. J.* **2005**, *41*, 303 – 312.
[17] A. Patel, K. Mequanint, *J. Polym. Sci. Part A: Polym. Chem.* **2008**, *46*, 6272 – 6284.

