SYNTHESIS OF MODEL RANDOM

POLYAMPHOLYTES

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Submitted to the Faculty of the
Graduate College of the
Oklahoma State University
in partial fulfillment of
the requirements for
the Degree of
DOCTOR OF PHILOSOPHY
May, 2008

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POLYAMPHOLYTES

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PREFACE

Polymers are large molecules that are made up of smaller units called monomers. A copolymer is made up of two or more monomers. Polyampholytes are a group of polymers that contain both positively and negatively charged monomers within the same chain. Proteins containing amino acid residues with both acidic and basic functional groups are an example of polyampholytes. A polyampholyte widely used in the food and pharmaceutical industry is gelatin. Polyampholytes may be either neutral (possess equal number of positive and negative charges) or have an overall charge of one sign.

The behavior of polyampholytes in solution is controlled by either attractive or repulsive interactions between the positively and negatively charged groups. If the overall charge is very large, the electrostatic forces between monomers become repulsive, and in a dilute solution, the polymer extends and adopts a necklace-like conformation. A polyampholyte with an equal number of positively and negatively charged groups collapses due to attractive forces within the same polymer chain. At a particular pH value, called the isoelectric point, the overall charge on a polyampholyte will be zero.

Synthetic polymers have molecules with one or more repeating structures and a range of chain lengths. The goal of this research was to prepare water-soluble polyampholytes from copolymers comprised of three neutral monomers, by a controlled method of polymerization, followed by modification of the polymer end groups. The

overall compositions of the copolymers tend to approach the compositions of the initial monomer mixtures, indicating that the copolymers have a homogeneous composition.

The long term goal of this project is to prepare a family of polyampholytes with varying amounts of positively and negatively charged groups that are water-soluble at room temperature, with homogeneous compositions, a narrow distribution of chain lengths, and molecular weights large enough for the purpose of determining the solution properties of these materials in dilute aqueous media.

ACKNOWLEDGEMENTS

I would like to thank my research advisor, Dr. Warren Ford for being an excellent advisor. Dr. Ford, I cannot thank you enough for the valuable education I have received under your guidance all through these years.

I would also like to thank the members of my advisory committee, Dr. Darrell Berlin, Dr. Ziad El-Rassi, Dr. LeGrande Slaughter, and Dr. Gary Foutch for their patience and assistance with my research proposal and thesis. I would also like to thank Dr. Margaret Eastman and Gianna Bell-Eunice for their assistance with the NMR experiments. I would like to specially thank Dr. Richard Bunce, Dr. LeGrande Slaughter and Dr. Loralee Ohrtman for their help with research apparatus. I would also like to express my gratitude to all the members of the Ford group.

I would like to thank the Lord for being my guiding light and watching over me through good times and bad times. I wish to take this opportunity to also thank my parents for their love and support. Although they may not be here physically, they have always been a source of constant motivation for me. I wish to say a big thank you to my youngest sister, Anthea, who has been a great help and inspiration during these last few years. I also wish to thank my sister Glynis, her husband Nitin, my nephew Yash, and my in laws for their prayers and support all through these years.

I would like to thank my husband Frank from the bottom of my heart for his untiring support and belief in me. Thank you Frank for not giving up on me, and for always challenging me to do everything that I took on to the best of my ability. Last but not the least, I would like to thank my two year and four month old son, Ethan, for being such an obedient and understanding child and letting me finish writing up this dissertation in a timely manner. I would like to thank the Department of Chemistry for their financial support during my graduate study at Oklahoma State University. I would also like to thank the National Science Foundation for funding this research.

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CHAPTER I

POLYAMPHOLYTES AND CONTROLLED RADICAL POLYMERIZATION

Charged polymers have attracted much attention both theoretically and experimentally due to their unique properties and their technological importance.[1,2] They are perhaps the most important class of macromolecules due to their wide range of industrial applications in processes involving charged colloids.[3] These types of polymers range from naturally occurring biopolymers such as proteins and polynucleotides to synthetic viscosity modifiers and soaps.[1] Ion containing polymers can be classified into two major categories, namely, polyelectrolytes and polyzwitterions.[4] Polyelectrolytes contain *either* anionic or cationic functional groups along the polymer chain, while polyzwitterions contain *both* anionic and cationic groups. Common polyelectrolytes include polyacrylic and methacrylic acids and their salts, sulfonated polystyrene, and other strong acids and bases.[2]

The aqueous solution properties such as viscosity and hydrodynamic volume of polyelectrolytes and polyzwitterions are primarily governed by the intra- and intermolecular electrostatic interactions that occur among the cations and anions in aqueous media.[4] In dilute, salt-free aqueous solutions, the coulombic repulsions between like charges along a polyelectrolyte chain lead to an expansion in hydrodynamic volume

of the polyelectrolyte coil; however addition of electrolytes like sodium chloride (NaCl) results in coulombic shielding and a decrease in hydrodynamic volume and thus solution viscosity. This solution behavior is termed the *polyelectrolyte effect*.[4]

For polyzwitterions, the charges may be located either on the pendent side chains of different monomer units, or in the case of some polyesters, polyphosphazenes, and polybetaines, one or both of the charges may be located along the polymer backbone.[1] The distinction between zwitterionic polyampholytes and polybetaines is not always clear from literature. The term polyzwitterion includes *all* polymers that possess both cationic and anionic groups. Polyampholytes refers to those polymers that specifically possess charged groups on *different* monomer units, while polybetaines refers to those polymers with anionic and cationic groups on the *same* monomer unit.

In contrast to polyelectrolytes, structure-property relationships of polyampholytes are governed by coulombic attractions between anionic and cationic polymer units.[4] The coulombic interactions between positively and negatively charged repeat units of polyampholytes reduce hydrodynamic volume, as a result of which the polymer adopts a collapsed or globular conformation in dilute, salt-free aqueous media.[4] In some cases, the electrostatic interactions are so strong that the polymer may become insoluble. On adding simple electrolytes like NaCl to a polyampholyte solution in the dilute regime, the hydrodynamic volume of the polymer coil increases due to the screening of the intramolecular charge-charge attractions, allowing the transition from a globule to a random coil conformation. Such a solution behavior is known as the *anti-polyelectrolyte effect* and is evidenced by increased polymer hydrodynamic volume and solution viscosity.[4]

In addition to interactions with small molecule electrolytes, other factors such as charge density and distribution, charge balance, monomer sequence distribution (random, alternating, and block), and the nature of the ionizable groups along the polymer backbone play an important role in determining polymer conformation and rheological behavior of polyzwitterions in aqueous solution.[4] For polyampholytes, the magnitude of the globule-to-coil transition, the extent of polymer solubility, and the hydrodynamic volume are typically governed by the charge density of the system. Larger concentrations of electrolytes are needed to elicit coil expansion as charge density is increased; however the magnitude of hydrodynamic volume increase observed is greater with an increased number of zwitterionic interactions.

As the degree of charge imbalance on a polyampholyte chain increases, the polymer tends to behave in a manner that is more characteristic of a conventional polyelectrolyte.[4] Typically, polymers that have random incorporation of charged species exhibit more profound antipolyelectrolyte behavior than polyampholytes with alternating incorporation of anionic and cationic groups. This is due to long range electrostatic interactions in the random moieties versus the alternating ones, which are governed by short-range interactions.

The solution properties of polyampholytes also depend on the chemical nature of the charged groups.[4] Polyampholytes bearing strong acids or salt-like functionalities such as sulfonic acids and quaternary ammonium ions, are generally insensitive to changes in solution pH; thus the charge balance and charge density are determined solely by the relative incorporation of the anionic and cationic monomers. However, in polyampholytes containing weak acid/base functionalities such as carboxylic acid and/or

primary, secondary, or tertiary amine groups, the charge density and charge balance of the polymer are determined by the relative incorporation of the ionizable monomers, the pK_a of the amphoteric species, and the solution pH. An example is that of a polyampholyte containing equimolar amounts of a carboxylic acid and quaternary ammonium functional groups.[4] At low pH, this polymer behaves as a cationic polyelectrolyte due to an overall net charge that is a result of virtually no ionization of the acidic groups. As the solution pH is raised, these groups are ionized, eventually establishing a charge balance, at which point the polymer exhibits polyampholyte behavior. For polyampholytes in which the amphoteric repeat units (for example in monomers containing carboxylic acid units) are present in excess of permanently charged repeat units, polyampholyte behavior is observed at the isoelectric point (IEP). The isoelectric point (IEP) is defined as the pH at which the number of cationic and anionic groups are equal. As the solution behavior is adjusted from the IEP, polyelectrolyte behavior is observed due to the increase in the net charge.[4]

Examples of Polyampholytes

The first study of synthetic polyampholytes was reported by Alfrey, Morawetz, Fitgerald, and Fuoss in their 1950 article "Synthetic Electrical Analog of Proteins."[5] Polyampholytes are interesting for several reasons, not the least of which is the fact that they are synthetic analogs of naturally occurring biological molecules such as proteins, and find applications in areas such a lithographic film, formulation of emulsions and drag reduction.[1] Polyampholytes can be grouped into four subclasses, based on their responses to changes in pH, as shown in Figure 1.[1] First, the polyampholyte may contain both

anionic and cationic species that may be neutralized (**1a**). Secondly, the anionic group may be neutralized, but the cationic groups are insensitive to pH changes, for example, quaternary alkyl ammonium groups (**1b**). Thirdly, the cationic species may be neutralized, with the anionic groups showing no response to pH changes, for example, sulfonate groups (**1c**), and finally both the anionic and cationic species may be insensitive to changes in the pH of the solution throughout the useful range (**1d**).

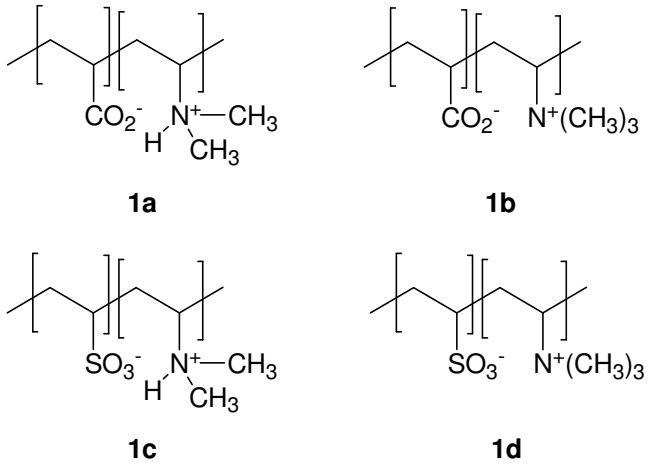


Figure 1. Representative structures of the four subclasses of polyampholytes

More reports on the synthesis of polyampholytes were first published in the 1950s.[1] These polyampholytes were synthesized via conventional free radical polymerization. Some examples include methacrylic acid-*stat*-2(dimethylamino)ethyl methacrylate copolymers, synthesized by Ehrlich and Doty, acrylic acid-*stat*-2-vinyl pyridine copolymers, synthesized by Alfrey and Morawetz, and acrylic acid-*stat*-2-(dimethylamino)ethyl methacrylate copolymers reported by Alfrey and Pinner.[6-8] Since then, numerous researchers have reported on the synthesis and properties of a variety of statistical polyampholytes (Figure 2).

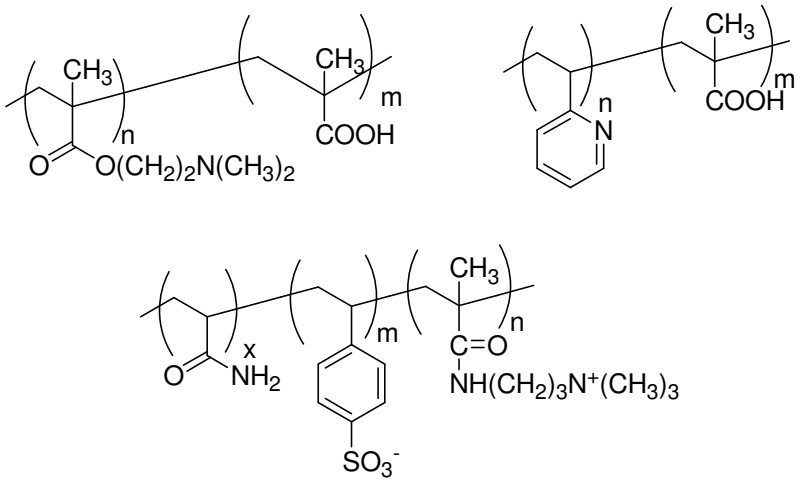


Figure 2. Examples of synthetic statistical polyampholytes

In the early 1970s, Stille's research group was the first to report the synthesis of block polyampholytes by anionic polymerization.[9] These were block copolymers of 2-vinylpyridine and trimethylsilyl methacrylate (TMSMA). Poly(TMSMA) was readily hydrolyzed to poly(methacrylic acid) using a water/methanol mixture. Subsequently, Varoqui and co-workers synthesized AB diblock polyampholytes from styrenesulfonate and 2-vinyl pyridine.[10] Later, Morishima and co-workers reported the synthesis of block copolymers of TMSMA and p-*N,N*-dimethylaminostyrene.[11] Creutz and co-workers have developed the synthesis of block copolymers of methacrylic acid with co-monomers like dimethylaminoalkyl methacrylates.[12] These were synthesized by anionic polymerization using *tert*-butyl methacrylate (tBMA) as the protected precursor to poly(methacrylic acid) groups.

Until recently, classical anionic polymerization was the most attractive route to the synthesis of block polyampholytes. Patrickios and co-workers, in 1994, reported on

the synthesis of diblock, triblock, and statistical methacrylic polyampholytes by employing group transfer polymerization (GTP).[13,14] Similar to anionic polymerization, monomers with labile protons, namely methacrylic acid could not be directly polymerized and protected acid monomers were required. Patrickios and co-workers selected TMSMA and 2-tetrahydropyranyl methacrylate (THPMA) as protected methacrylic acid (MAA) monomers. TMSMA was chosen because it is commercial and can easily be converted to MAA, and THPMA can be converted to MAA under very mild acidic conditions. They copolymerized the protected monomers with 2-(dimethylamino)ethyl methacrylate (DMAEMA), and in the synthesis of the triblock copolymers, methyl methacrylate (MMA) was introduced as the third hydrophobic co-monomer. Subsequently, Lowe, Billingham, and Armes synthesized AB diblock copolymers of DMAEMA with MAA using THPMA as a protected precursor.[15]

The recent developments in controlled free radical polymerization techniques, such as nitroxide-mediated polymerization (NMP)[16], atom-transfer radical polymerization (ATRP)[17], and reversible addition-fragmentation chain transfer (RAFT)[18] polymerization, allow for direct synthesis of many polyampholytic block copolymers without the need for protecting group chemistry. McCormick and co-workers have prepared AB diblock copolymers of DMAEMA with acrylic acid (AA) via RAFT.[19] They also accomplished the polymerization of sodium acrylate directly in aqueous solution via RAFT as well as the anionic acrylamido monomers, 2-acrylamido-2-methylpropanesulfonic acid (AMPS) and 3-acrylamido-3-methylbutanoic acid (AMBA).[20]

Studies of Polyampholyte Solutions

The five basic findings for dilute polyampholyte solutions are as listed below:[21] (1) The conductivity, viscosity and coil size of weakly hydrophobic polyampholytes have minima at the isoelectric pH. This is due to the collapse of the polymer coil because of intramolecular electrostatic attractions between cationic and anionic repeat units. (2) Hydrophobic polyampholytes precipitate close to the isoelectric pH. (3) The addition of salt to a nearly charge-balanced polyampholyte increases the viscosity and coil-size. (4) For polyampholytes with a large net charge, the viscosity and coil-size decrease as salt is added. In this case the polyampholyte behaves as a polyelectrolyte. (5) The viscosity and coil-size in pure water display a strong minimum as a function of copolymer composition, where positive and negative charges are balanced.

Katchalsky and Miller studied the influence of oppositely charged groups on dissociation, and they found that increasing the acid content of their copolymers, caused a larger fraction of the basic monomers to dissociate at a given pH.[22] As expected, the addition of salt screens the electrostatic interactions and thus reduces the inductive influence of neighboring groups. McCormick and co-workers have confirmed many of the classical findings for dilute polyampholyte solutions as described above.[23,24] Copolymers of sodium 2-(acrylamido)-2-methylpropanesulfonate (NaAMPS) and [2-(acrylamido)-2-methylpropyl]trimethylammonium chloride (AMPTAC) and (2-acrylamido-2-methylpropyl)dimethylammonium chloride (AMPDAC) were synthesized in these studies. They also discovered that in the case of polyampholytes with balanced stoichiometry, the electrostatic interactions between oppositely charged ions predominates, and the addition of salt allows chain expansion. At feed ratios that were far

off from stoichiometric balance, the repulsive forces between like ions predominates and typical polyelectrolyte behavior is observed with the addition of salt. Modern theories of polyampholytes also expect this behavior, as salt first screens the charge repulsion on large scales that extends the chain, and only at higher salt concentration the charge attraction, which compresses the polyampholyte locally, is screened, causing the chain to swell.[21] The composition distribution of randomly prepared polyampholytes was explored in detail by Candau and coworkers.[25] This paper reports the study of a low charge density terpolymer prepared using microemulsion polymerization by incorporating acrylamide (AM) as a neutral water soluble monomer, along with sodium 2-(acrylamido)-2-methylpropanesulfonic acid (NaAMPS) and [2-(methacryloyloxy)ethyl]-trimethylammonium chloride (MADQUAT) as the charged monomers. In a medium of high salt content, the electrostatic interactions are screened out and all the chains are soluble. Below a critical salt content, attractive electrostatic interactions are dominant, and the chains with a zero or small net charge precipitate, due to the polyampholyte effect. The supernatant contains highly swollen oppositely charged polyampholyte molecules. The polymer concentration in the supernatant decreases with decreasing salt content, with an increased swelling of chains.[25] Thus, salt can in some cases provide a means of fractionation, in which the neutral chains precipitate.

Theory of Polyampholyte Solutions

The properties of polyampholyte chains in solutions depend not only on the fractions of positively and negatively charged monomers, but also on the distribution of charged monomers along the polymer backbone.[21] Theoretical models as well as

computer simulations of charge-balanced polyampholytes usually consider ensemble average properties. This corresponds to averaging over all possible charge sequences along the polymer backbone with fixed fractions of charged groups and charge asymmetry. Consequently, the properties of the whole ensemble of chains are often represented by the properties of the most probable member, which may not always be valid. It is for this reason, that model random polyampholytes having a random distribution of compositions are needed to test the theory of polyampholyte solutions.

Synthetic polyampholytes are produced by random polymerization reactions. Such samples contain chains with different fractions of positively and negatively charged groups.[21] The overall size and shape of polyampholytes in dilute salt-free solutions is determined by the balance of four factors: (1) the fraction of positive and negative charges on the chain, (2) the charge sequence, (3) the degree of polymerization, and (4) the ratio of the Bjerrum length to the monomer size. The Bjerrum length is the distance at which the electrostatic interaction energy between two elementary charges is equal to the thermal energy in a medium of a given dielectric constant. As the polyampholyte chain approaches charge balance, it collapse into a globule due to intrachain electrostatic attractions. In polyampholytes with a net charge, the globule elongates and forms a charge balanced necklace.

For synthetic polyampholytes prepared by copolymerization reactions, one only has control over the composition of the initial monomeric mixture.[21] Even for a symmetric mixture with equal concentrations of positive and negative monomers, the individual polymer molecules produced will have an excess of positively charged groups or negatively charged groups, or be neutral. The width of the charge asymmetry

distribution is determined by the propagation reaction rate constants between monomers that could favor alternating, random, or blocky charge sequences. The charge sequence of a polyampholyte chain consisting of weakly acidic or basic groups can be adjusted by either changing the pH of the aqueous solution, or by imposing an external electrostatic potential, for example, by placing chains near charged surfaces. Such polyampholytes are called annealed polyampholytes.[21] A qualitative study of the properties of polyampholyte solutions was reported by Katchalsky and co-workers.[22] The effect of net charge on the shape of a polyampholyte chain was studied independently by Kantor, Gutin and Dobrynin.[26-28] They found that excess charge deforms the polyampholyte chain into an elongated globule, whereas fluctuation-induced attraction collapses the chain into a globule. However, the interplay of globule surface energy and repulsion of the net unbalanced charge elongates the globule.

Applications of Polyampholytes

Although polyampholytes have not been extensively used in commercial applications, their unusual solution properties present unique opportunities for formulation in the presence of electrolytes. These include areas such as personal care, enhanced oil recovery, and flocculation. Water-soluble and water-swelling polyampholytes could be used in desalination of water, sewage treatment, flocculation, coagulation, drilling fluids and enhanced oil recovery.[29]

The ability of polyampholytes to swell and be effective viscosity enhancers in high salinity media plays a crucial role in enhanced oil recovery (EOR) processes. In the recovery of oil from oil-bearing reservoirs, an important component is the formulation of

drilling muds. A conventional water-based drilling mud formulation includes water, clay such as bentonite, lignosulfonate, a weighting agent such as $BaSO_4$ and a caustic material such as sodium hydroxide to adjust the pH between 10 and 10.5. Amphoteric terpolymers have been found to act as viscosity control additives for water-based drilling muds. They are chemically and thermally stable in high ionic strength environments. The solution viscosity remains essentially invariant to temperature changes. Terpolymers composed of acrylamide, metal styrenesulfonate and methacrylamidopropyltrimethylammonium chloride show improved drag reduction in water, while efficient drag reduction in a variety or organic solutions was exhibited by terpolymers of styrene, metal styrenesulfonate and 4-vinylpyridine.[30]

Protein-polyelectrolyte complexes have found application for protein separation and enzyme immobilization.[21] The interaction of proteins with DNA is central to the control of gene expression and nucleic acid metabolism. One method for protein separation by water soluble polyampholytes that have random sequences is based on a selective complexation of a polyampholyte with a protein that has a net complementary charge. A prerequisite of the process is that the latter interaction is stronger than that between other proteins in the same solution. Thus, only one of the proteins will form a complex with the polyampholyte and phase separate, while the other proteins remain in the supernatant phase. The resultant protein/polyampholyte assembly can be removed from the system and redissolved at a different pH. Finally, the polyampholyte can be separated at its pI, when precipitation occurs. The phenomenon of adsorption of polyampholytes on a charged surface has great potential because many biological and technological processes are closely connected with the adsorption phenomenon.[29]

Capillary electrophoresis (CE) is being widely used for the separation of biopolymers such as proteins, peptides or DNA fragments, as a result of the possibilities provided by this technique in terms of analysis speed, high efficiency, and low sample consumption.[31] CE allows separation of these materials based on differences in molecular size, charge/mass ratio and isoelectric point. These modes of separation can also prove valuable for the characterization of synthetic polymers based on the fact that properties like size and molecular dispersion of synthetic macromolecules have a great influence on their applications.

Free Radical Polymerization

Free radical polymerization can be used with a large variety of monomers including (meth)acrylates, styrenes, (meth)acrylamides, 1,3-dienes, and vinyl acetate. The process is tolerant to a wide range of functional groups, for example, OH, NH_2, COOH and $CONR_2$. Moreover, these polymerizations can be economically performed in bulk and in suspension, which are distinct advantages from an industrial point of view.[32] Free radical polymerization methods do not allow for precise control over molar masses and tend to give broad molecular weight distributions or polydispersity indices (M_w/M_n).[33] The polydispersity index (PDI) is a measure of the distribution of molecular mass in a given polymer sample.[34]

Controlled Free Radical Polymerization (CRP) Methods

In order to prepare well-defined polymers by free radical polymerization, it is necessary to reduce termination reactions. Because free radicals terminate at nearly

diffusion controlled rates, termination reactions can only be reduced by employing very low radical concentrations. Controlled free radical polymerizations attain very low radical concentrations via an exchange process between the dormant and active propagating chains. The equilibrium in these systems strongly favors the dormant species to minimize radical concentration. While the lower radical concentration reduces the rate of polymerization, the rate of termination which is second order with respect to radical concentration, is suppressed to a greater degree, yet not completely eliminated.[33] The various copolymer architectures that can be achieved by controlled radical polymerization include alternating and statistical, AB diblock, ABC triblock, graft and star copolymers (Figure 3).

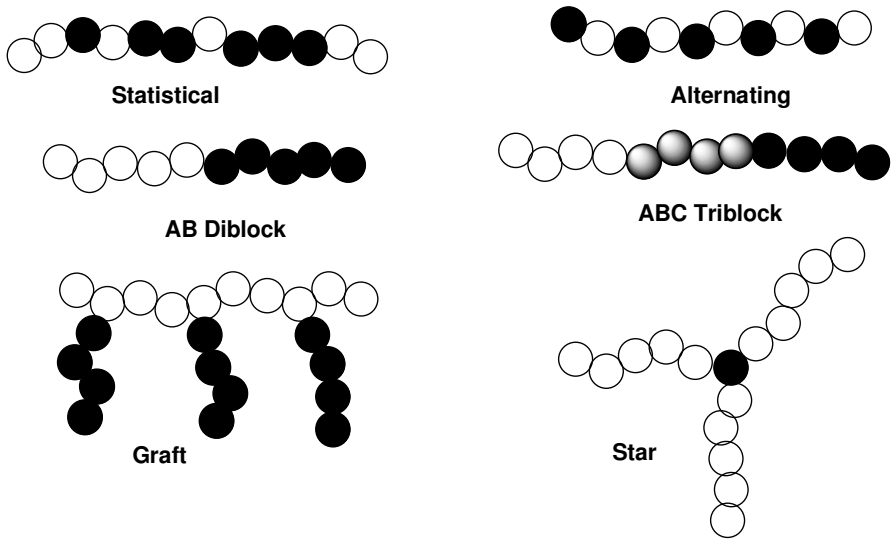


Figure 3. Copolymer architectures attainable via controlled radical polymerization

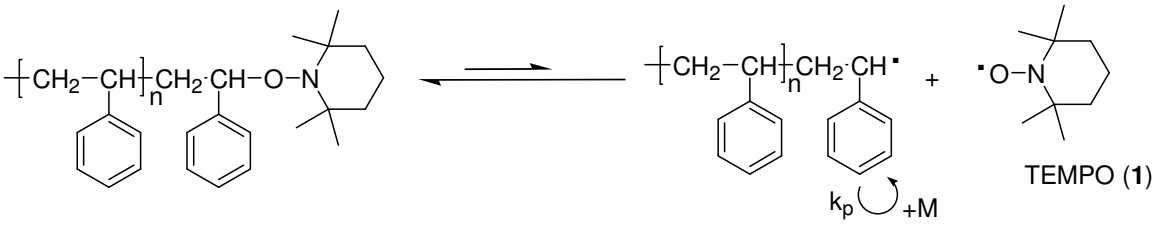
In recent years, the development of CRP techniques, including, nitroxide-mediated polymerization (NMP), atom transfer radical polymerization (ATRP), and reversible addition-fragmentation chain transfer (RAFT) polymerization, have received a

great deal of attention due to the fact that radical processes are more tolerant of functional groups and impurities as compared with traditional anionic and cationic polymerization methods.[32,35-36] Several criteria including fast initiation relative to propagation, a low concentration of propagating radicals, and a fast exchange between the dormant species and the growing radicals must be satisfied in order to achieve an efficient controlled radical polymerization.[37]

Nitroxide-Mediated Polymerization

Mechanistically, NMP operates on the principle of reversible end-capping of propagating polymer chains by a nitroxide stable free radical.[38] The equilibrium is such that at any given time, most of the polymer chains exist as dormant non-propagating species. This maintains an extremely low concentration of radicals and thus significantly reduces the occurrence of bimolecular termination reactions. The use of such species as end-capping agents was explored by Solomon and co-workers, and subsequently by Georges et. al.[16,39] Homolytic dissociation of the alkoxyamine end-group yields a polymeric radical, which is capable of undergoing subsequent propagation, and a stable nitroxide free radical. NMP is best exemplified by *2,2,6,6*-tetramethylpiperidinyloxyl (TEMPO, **1**) mediated polymerization of styrene (Scheme 1).

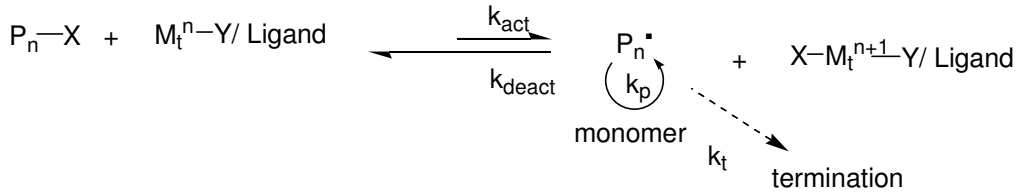
Scheme 1. Tempo-mediated polymerization of Styrene



Atom Transfer Radical Polymerization (ATRP)

The term "atom transfer radical polymerization" was first coined by Wang and Matyjaszewski in 1995 to describe the controlled polymerization of styrene by employing Cu(I) complexes.[17] ATRP is based on the same principle as NMP, in this case the reversible homolytic cleavage of the terminal covalent bond in the dormant species. However, in the case of ATRP, activation of the dormant chain is catalyzed by a redox process involving a transition metal species in a low oxidation state and the terminal functional group X, which is typically Cl or Br. A general mechanism for ATRP is shown in Scheme 2. The propagating species $P_n^{\cdot}$, are generated through a reversible redox process, catalyzed by a transition metal complex (activator**,** M_t^n-Y/ ligand) (symbols defined in Scheme 2), where Y may be another ligand or counterion) which undergoes a one-electron oxidation with concomitant abstraction of a (pseudo) halogen atom, X, from a dormant species, P_n-X.

Scheme 2. General scheme of transition-metal catalyzed ATRP



P_n-X = dormant propagating species

X = Cl, Br

M^t_n = transition metal

P_n ▪ = propagating radical species

k_{act} = rate constant of activation

k_{deact} = rate constant of deactivation

k_p = rate constant of propagation

k_t = rate constant of termination

The rate of polymerization is determined by the product of the propagation rate constant, k_p, the equilibrium constant, K_{eq} ($K_{eq} = k_{act}/k_{deact}$), and the concentration of monomer.[33] ATRP will occur too slowly if the equilibrium constant is too small. In contrast, too large equilibrium constant will lead to a large amount of termination, because of a high radical concentration.

ATRP has been successfully employed for the controlled free radical polymerizations of monomers such as dienes, (meth)acrylates, styrene, acrylates, acrylamides, acrylonitrile, and methacrylic acid.[35] ATRP can be conducted over wide temperature ranges (-40 ^oC to 160 ^oC), an obvious advantage over NMP. The well-known drawback of ATRP is the presence of the transition metal catalyst, which must be removed following polymerization. This drawback alone limits the industrialization of the ATRP technique.

Reversible Addition-Fragmentation Chain Transfer (RAFT) Polymerization

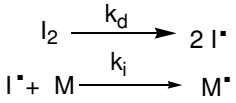
RAFT polymerizations were first introduced by Rizzardo and Moad in 1998.[18,40] RAFT polymerization is one of the most recent entrants in the field of controlled radical polymerization (CRP) and arguably the most convenient and versatile.[36] Although the acronym RAFT can be used in a more general sense, it has come to be closely associated with radical polymerizations carried out in the presence of thiocarbonylthio compounds, which react by reversible addition-fragmentation chain transfer.[32] The same process involving xanthate RAFT agents is sometimes also called MADIX (macromolecular design by interchange of xanthate).[41]

RAFT polymerizations are performed by adding an appropriate quantity of a suitable RAFT agent to a conventional free radical polymerization mixture. The RAFT process offers the same versatility and convenience as conventional free radical polymerization, being applicable to the same range of monomers, (for example, (meth)acrylates, styrenes, acrylamides), solvents, functional groups, (for example, OH, CO_2H, NR_2) and reaction conditions (for example, bulk, solution, suspension and emulsion), but provides polymers with narrow polydispersity and predetermined chain length.[32]

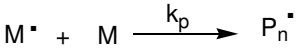
The RAFT process is compatible with a broad range of reaction media, including protic solvents like water,[42] and alcohols.[43] Moreover, RAFT polymerizations have been carried out in supercritical carbon dioxide[44] and ionic liquids.[45] RAFT polymerizations can also be conducted in the presence of Lewis acids.[46] The mechanism for RAFT polymerization is shown in Scheme 3.[33]

Scheme 3. Proposed mechanism of the RAFT process

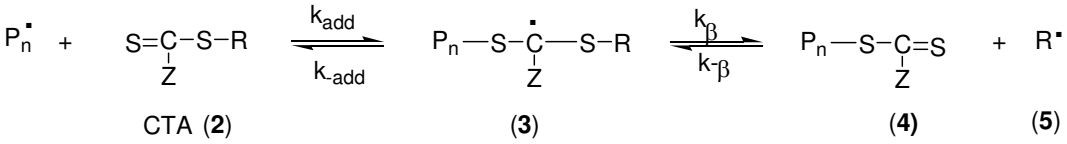
I. **Initiation**



II. **Propagation**

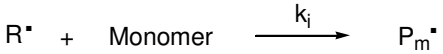


III. **Chain Transfer**



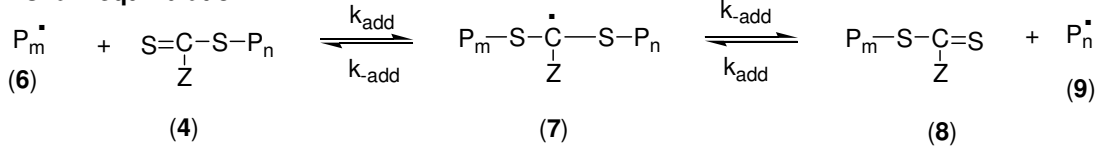
CTA (**2**) (**3**) (**4**) (**5**)

IV. **Re-initiation**



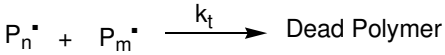
(**6**)

V. **Chain equilibration**



(**4**) (**7**) (**8**) (**9**)

VI. **Termination**



I = initiator

M = monomer

$P_n^{\bullet}$, $P_m^{\bullet}$ = propagating radical species

(**4**), (**7**) = dormant polymeric species

k_t= rate constant of termination

k_d= rate constant of decomposition

k_i = rate constant of initiation

k_p = rate constant of propagation

k_{add} = rate constant of addition of $P_n^{\bullet}$ to CTA

k_{-add}= rate constant of fragmentation of adduct radical (**3**) to original reactants

k_{β} = rate constant of fragmentation of adduct radical (**3**) to a new radical species $R^{\bullet}$

$k_{-\beta}$ = rate constant of addition of $R^{\bullet}$ with macro-CTA (**4**)

The overall RAFT polymerization is generally divided into two sets of reactions, namely, the pre-equilibrium or initiation, which includes the initiation of the living

process, and the main equilibrium or propagation between the growing and dormant polymer chains.[47]

Initiation. A crucial feature of RAFT polymerization is the establishment of a sequence of addition-fragmentation equilibria in order to impart control as shown in Scheme 3. As in conventional free radical polymerization, radical sources such as peroxides and azo compounds can be used as initiators. The initiator (I_2) splits homolytically to produce two free radicals ($I^{\cdot}$). The initiator-derived free radical adds to monomer (M) to form a monomer ended radical ($M^{\cdot}$).

Propagation. The propagation in a RAFT-mediated polymerization proceeds as in a conventional free radical polymerization. An initiator–derived radical adds to monomer, followed by propagation to yield propagating macroradicals ($P_n^{\cdot}$).

Chain Transfer. The propagating macroradicals ($P_n^{\cdot}$) add to the carbon–sulfur double bond of the RAFT chain transfer agent (CTA) (**2**) with a rate constant k_{add}, resulting in a carbon-centered intermediate radical species (**3**).[47] The adduct radical (**3**) may fragment to either the original reactants with a rate constant k_{-add}, or to a new dormant macroCTA (**4**) and a new radical species $R^{\cdot}$ (**5**), with a rate constant k_{β}. The new radical species $R^{\cdot}$ (**5**) can react with the macroCTA (**4**) with a rate constant $k_{-\beta}$, or re-initiate polymerization by adding to monomer to form the propagating species $P_m^{\cdot}$ (**6**).

The time period necessary for all $R^{\cdot}$ fragments to undergo addition to monomer is determined by the relative magnitudes of the rate constants, k_{add}, k_{-add}, k_{β} and $k_{-\beta}$. A rapid k_{add} step is crucial to ensure that the propagating chains grow for only a short duration before being converted to the dormant state. Moreover, the quick formation of $R^{\cdot}$ ensures that the majority of the chains are initiated nearly at the same time, allowing for the

preparation of polymers with narrow molecular weight distribution. Assuming that the number of initiator-derived radicals is significantly less than the number of radicals derived from CTA in solution, a factor controlled by the initial [CTA]/[I] ratio, most of the polymer chains will be initiated by R-fragments. The leaving ability of R· must, however, must be balanced by the ability of R· to reinitiate polymerization.

R· adds to monomer to give propagating species (P_m·) (**6**). The propagating species, (P_m·) undergoes addition to either CTA (**2**) or a macro-CTA (**4**). The main equilibrium signifies a period of rapid exchange of the dithioester end-groups between the dormant adduct radical species (**7**) and the propagating species (**9**), thus imparting a living character to the polymerization. Under the conditions of the main equilibrium, the fragmentation of the intermediate radical species (**7**) to either side of the equilibrium results in the production of identical polymeric species or in other words, the chain transfer process becomes degenerate.

Chain Termination. Similar to all CRP processes, termination reactions in RAFT polymerizations cannot be completely avoided. The two types of termination reactions, termination by radical coupling and termination by disproportionation, also occur in RAFT polymerizations, and the rate of formation of radicals by the initiator equals the rate of termination of radicals. When the primary mode of termination is due to radical coupling, the number of dead chains is equal to half the initiator-derived chains. For systems that terminate primarily by disproportionation, the number of dead chains is equal to the number of initiator derived chains.[18]

Evidence in Support of the RAFT Mechanism

The proposed RAFT mechanism is supported by the retention of the dithiocarbonyl end-groups during the RAFT polymerization. To this effect, end-group analysis by ^{1}H NMR spectroscopy,[18] UV-Vis spectroscopy,[18] matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectrometry, and ESI (electrospray ionization mass spectrometry)[32] have shown that the majority of the polymer chains synthesized by the RAFT method retain the dithioester end-groups. Further evidence of retention of the dithioester end-groups is the chain extension of recovered polymers to form block copolymers.[32]

Choice of RAFT Chain Transfer Agent

The effectiveness of dithiocarbonyl compounds as CTAs for RAFT polymerization was first demonstrated by Moad et. al.[18] Since then, a variety of other classes of compounds have been explored including dithioesters,[48,49] xanthates,[47] dithiocarbamates,[50] and trithiocarbonates[51] as shown in Figure 4. The effectiveness of the above RAFT agents for a specific monomer depends on both the nature of the free radical leaving group ($R^{\cdot}$) and the Z-group, which activates or deactivates the dithiocarbonyl double bond.[52]

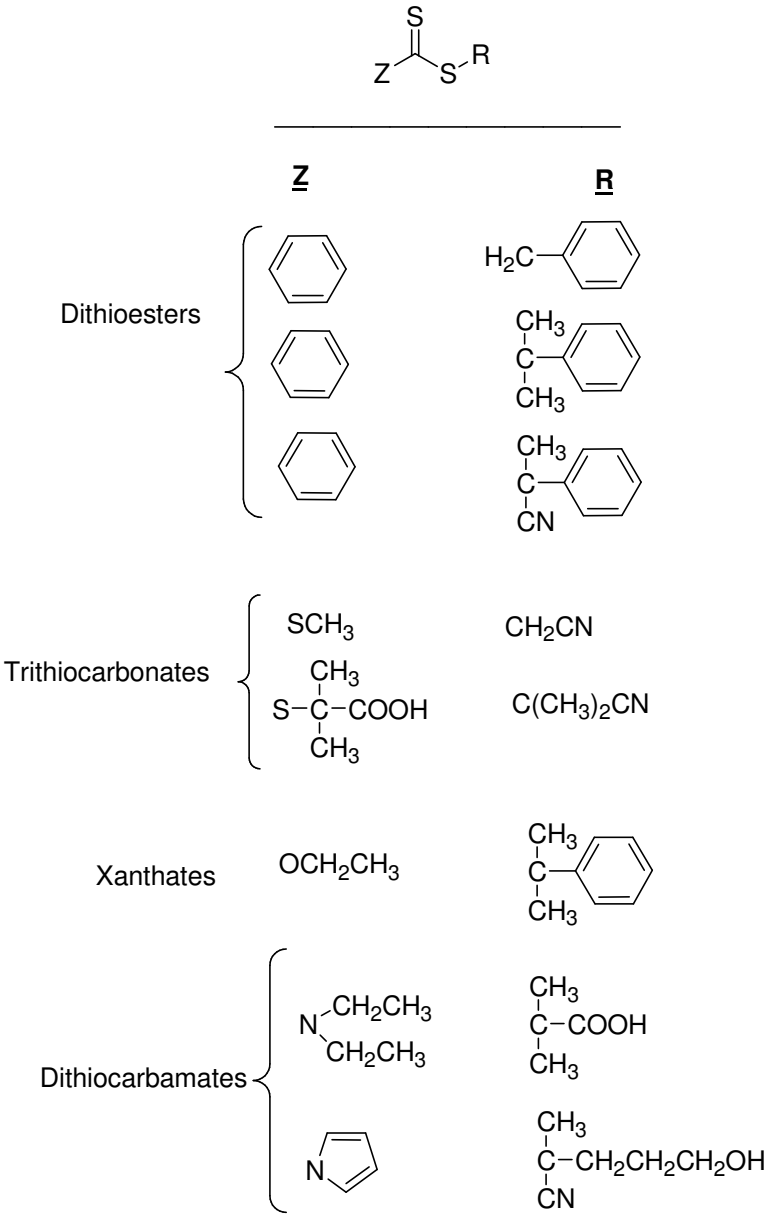


Figure 4. Examples of the different classes of thiocarbonylthio compounds

Control over molecular weight and polydispersity for a given monomer system depend on the structure of the CTA. Thus, it is crucial to select the appropriate CTA for the synthesis of well-defined polymers. The generic structure of a RAFT CTA is shown in Figure 5.[32]

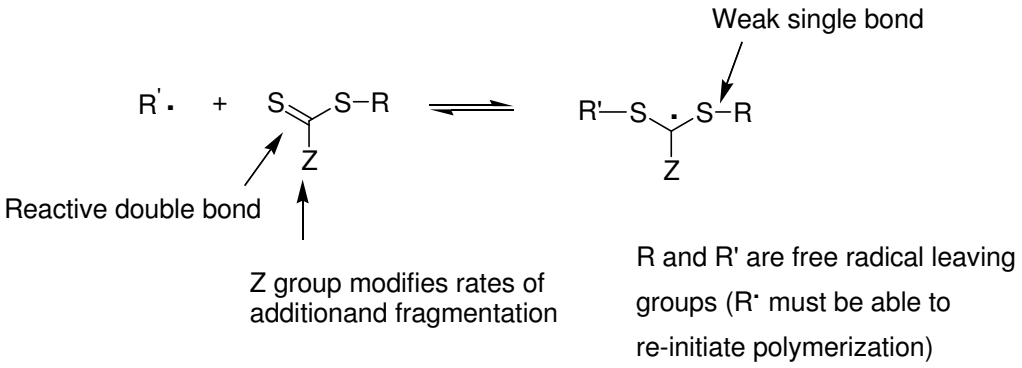


Figure 5. Structural characteristics of a RAFT CTA

The R-group must be a good homolytic free radical leaving group, relative to the propagating macro-radical ($P_n^{\cdot}$), while the rate of addition of radicals to C=S is strongly influenced by the Z-substituent. For an efficient RAFT polymerization, following are the structural prerequisites:[32]

1. The reactivity of the C=S bond in RAFT agent (**2**) and macroCTA (**4**) should be high to facilitate radical addition (high k_{add}).

2. The intermediate radical species (**3**) and (**7**) should rapidly fragment and undergo no side reactions (a weak S-R bond, high k_{β}).

3. The radical intermediate species (**3**) should partition in favor of products ($k_{\beta} \geq k_{-add}$).

4. The expelled radicals ($R^{\cdot}$) must be able to re-initiate efficiently.

Effect of Z and R-Substituents

Since the Z-group is retained at the growing chain end of the polymer, it strongly influences not only the reactivity of the thiocarbonyl group toward radical addition, but also the stability of the derived adduct radical.[49] The rapid addition of propagating species to the carbon sulfur double bond is crucial to ensure the complete consumption of

the CTA in the early stages of polymerization and to limit propagation in between chain transfer events.[48,49] Since the Z-group influences the stability of the intermediate radical, excessive stabilization could result in pronounced retardation and long inhibition periods, by reducing the rate of fragmentation.[33] Commonly employed Z-substituents include alkyl, aryl, and heterocyclic groups. The electronic nature of the Z-group has a dramatic effect on the reactivity of the CTA. Electron-withdrawing Z-groups, which confer a greater electrophilic character to the thiocarboxylic sulfur, enhance radical addition to the C=S double bond, yielding polymers with narrower polydispersities from the initial stages of polymerization.[49] The opposite is true for electron-donating Z-groups, which reduce the double bond character of the thiocarbonyl group.[49]

Although the Z-group influences the polymerization throughout the course of the reaction, the R-group has its most pronounced effect during the pre-equilibrium period. As mentioned earlier, ($R^{\cdot}$) should be an excellent free radical leaving group. While the R-group does not necessarily affect the rate of addition to the thiocarbonyl bond, it can have a significant effect on the lifetime of the intermediate radical species (**3**). Chong and co-workers found that the leaving ability of the R-group depends on the stability, polarity, and the steric bulk of the radical species.[48] They demonstrated the more stable, bulky, and polar groups fragment at a higher rate effectively reducing the lifetime of the intermediate radical species in the pre-equilibrium stage. However, the leaving ability of ($R^{\cdot}$) must also be balanced with its potential to re-initiate the polymerization to ensure that the majority of polymer chains are initiated by the ($R^{\cdot}$) fragment rather than initiator-derived radicals. For example, in the polymerization of MMA, the propagating polymeric radicals have a high fragmentation efficiency. In this case, cyanoisopropyl and cumyl R-

groups, which also have high fragmentation efficiencies, are effective in mediating the polymerization.[48]

Control of Molecular Weight in RAFT Polymerization

In RAFT polymerization, a high [CTA]:[I] ratio and the choice of the appropriate chain transfer agent (CTA) is crucial. The total number of polymer chains, as indicated by the RAFT mechanism, is equal to the sum of the chains derived from the RAFT CTA and that derived from the initiator. Under conditions where a high molar ratio of RAFT CTA is used relative to initiator, and the chain transfer process if efficient, the assumption that the number of chains derived from the CTA is in a large excess over the chains derived from the initiator. In this case, the theoretical number average molecular weight ($M_{n,th}$) is given by the following equation:

$$(M_{n,th}) = \{([M]_o M_M \text{Conversion})/ [CTA]\} + M_{CTA} \quad (1)$$

where $[M]_o$, [CTA], M_M and M_{CTA} represent the initial monomer concentration, the initial CTA concentration, the molecular weight of the monomer, and the molecular weight of the RAFT CTA respectively.[49,50]

In some cases, where the number of initiator derived chains cannot be neglected, ($M_{n,th}$) can be obtained from the following equation:

$$M(_{n,th}) = \{([M]_o M_M \text{Conversion})/ ([CTA]+2f[I]X)\} + M_{CTA} \quad (2)$$

where "2" is a factor used for thermal initiators, since their decomposition produces 2 free radicals, "f" is the initiator efficiency and "X" is the fraction of initiator

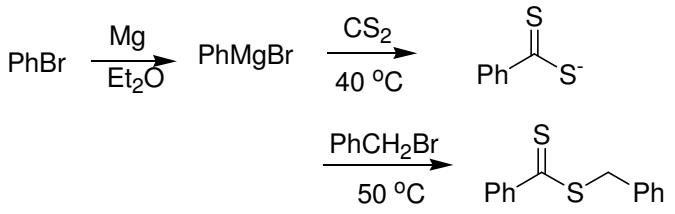
decomposition at a given temperature and time. The term "2f[I]X" together corresponds to the concentration on initiator-derived chains.

Synthetic Methodologies for RAFT Chain Transfer Agents

Currently few RAFT agents are commercially available. However, it is possible to synthesize RAFT agents in moderate-to-excellent yields by a variety of methods, and the syntheses are generally straightforward.[32] Some of the methods employed in recent work include:

1) Reaction of a carbodithioate salt with an alkylating agent (Scheme 4).[18,48,49] This method often involves sequential treatment of an anionic species with carbon disulfide and an alkylating agent in a one-pot reaction. This method has been used to synthesize benzyl dithiobenzoate, 2-(ethoxycarbonyl)prop-2-yl dithiobenzoate, and 2-cyanoprop-2-yl dithiobenzoate.[49]

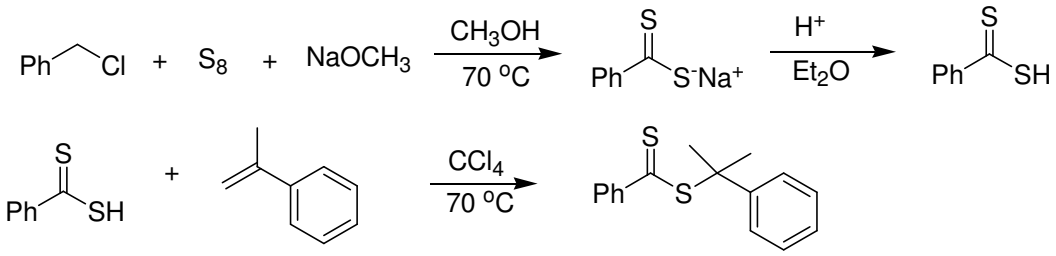
Scheme 4. Reaction of a carbodithioate salt with an alkylating agent



2) Addition of a dithio acid across an olefinic double bond.[48] This procedure has been used in the synthesis of cumyl dithiobenzoate (Scheme 5).[40] Electron-rich olefins (vinyl acetate) give Markovnikov addition, namely sulfur at substituted positions, while

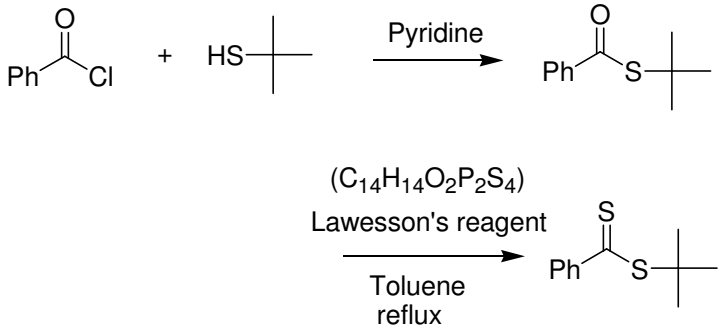
electron-deficient olefins (MMA, methacrylic acid, acrylonitrile) give Michael-like addition, namely sulfur at the unsubstituted position.

Scheme 5. Addition of a dithio acid across an olefinic double bond



3) Sulfuration of a thioloester, a carboxylic acid and an alcohol,[53] or a carboxylic acid with a halide or an olefin with P_4S_{10},[54] or Lawesson's reagent (Scheme 6).

Scheme 6. Sulfuration using Lawesson's reagent



Limitations of the RAFT Process

RAFT polymerization has emerged as one of the most important methods for controlled radical polymerization.[32] As mentioned earlier, this method is robust and versatile and can be applied to the majority of the polymers prepared by radical

polymerization. The drawbacks of this technique arise mainly from conditions that modify the stability of the thiocarbonylthio functionality. The destabilization of the CTA can limit the ability to synthesize more complex architectures. Most RAFT polymerizations are carried out in the absence of oxygen. Thus oxidation is not a major concern. Hydrolysis and aminolysis of the RAFT end groups, however, can cause significant problems for aqueous based RAFT polymerizations. As demonstrated by McCormick's research group, RAFT polymerizations in water have proven to be a versatile approach for the synthesis of a variety of water-soluble polymers.[55]

Another limitation of the RAFT process is the utilization of highly colored and often foul-smelling nature of chain-transfer agents employed in these polymerizations. As a result, most polymers synthesized by the RAFT method have a color ranging from pink to yellow, depending on the type of CTA used in the polymerization. Perrier and co-workers recently reported a method for the removal of the dithioester end-group and recovery of the CTA by treating the RAFT polymers with an excess of azo-compounds.[56] The resulting polymers are colorless and odorless and contain end-groups derived from the respective azo-compound. This technique might prove valuable for large scale utilization of the RAFT process.

OBJECTIVES OF THIS RESEARCH

Polymers containing ionic groups are among the most important classes of macromolecules.[1] Synthetic polyampholytes based on polyacrylamide (PAM) have been the focus of intense research, both academically and industrially, because of their potential applications in the production of petroleum, water treatment, cosmetics and personal care items.[57] Low-charge density polyampholytes derived from the terpolymerization of acidic and basic monomers with acrylamide (AM) typically have improved solubility in comparison with high-charge density polyampholyte copolymers. Acrylamide is much cheaper than the ionic monomers used in synthetic polyampholytes, thus, the incorporation of AM into synthetic polyampholytes is desirable for cost-effective polyampholyte systems.

Most of the literature reports on polyacrylamide polyampholytes are composed of AM, a sulfonated anionic monomer, for example, sodium 2-acrylamido-2-methylpropanesulfonate (NaAMPS), or sodium styrenesulfonate, and a quaternary ammonium cationic monomer, for example, (3-methacrylamidopropyl)trimethylammonium chloride, (2-methacryloyloxyethyl)trimethyl ammonium chloride, or (2-acrylamido-2-methylpropyl)trimethylammonium chloride (AMPTAC).[58] In these systems, the sulfonate and quaternary ammonium functionalities are not pH-responsive; thus; the charge balance of these terpolymers is determined solely the relative molar amounts of cationic and anionic monomers in the polymer. Many of these systems suffer from the effects of compositional drift during synthesis because of the differences in the reactivities of the (meth)acrylamido, methacrylic and/or styrenic

monomers, and the polymer products tend to have a heterogeneous composition of macromolecules.[57]

The free radical copolymerization of acrylamide (AM) with 3-(2-acrylamido-2-methylpropane-dimethylammonio)-1-propanesulfonate (AMPDAPS) was investigated.[59] In this study, copolymers of AM and AMPDAPS were synthesized in the range from 99 % to 25 % AM in the feed. The copolymer compositions were determined from ^{13}C NMR and elemental analysis data. The reactivity ratio values were determined from monomer feed ratios and resultant copolymer compositions obtained at low conversions. The microstructural features of these copolymers were elucidated using the equations of Igarashi and Pyun.[59] The fractions of AM-AM, AMPDAPS-AMPDAPS, and AM-AMPDAPS units (the mol % blockiness, the mol % alternation, and the mean sequence length) in these copolymers were calculated from the reactivity ratios and the copolymer compositions. The mean sequence lengths of AM and AMPDAPS reverse in value when the amount of AMPDAPS in the copolymers increases from 25 mol % and 40 mol % to 60 mol % and 75 mol %. This behavior is indicative of a random microstructure.

However, McCormick and co-workers have shown that the effects of compositional drift are negligible, when PAM based polyampholytes are synthesized with only acrylamido monomers.[60] Braun and co-workers further validated this method of eliminating compositional drift by synthesizing polyampholyte terpolymers from *N*-isopropylacrylamide (NIPAM), NaAMPS, and (3-acrylamidopropyl)trimethylammonium chloride (APTAC).[61] These terpolymers exhibited compositions close to that of the monomer feed compositions at all degrees of conversion, thus indicating the formation of homogeneous polymer products. The PAM-based polyampholyte systems, synthesized by

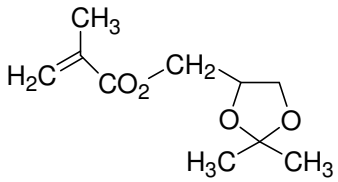
McCormick and co-workers demonstrate pH-responsive polyampholyte behavior with (2-acrylamido-2-methylpropyl)dimethylammonium chloride (AMPDAC) or sodium 3-acrylamido-3-methylbutanoate (NaAMB), as pH-responsive monomers, with NaAMPS or AMPTAC, respectively.[57] However, attempts at synthesizing polyampholytes containing pH-responsive cationic and anionic units, for example, APMDAC and NaAMB, resulted in highly swollen gels cross-linked by hydrogen bonds between the carboxylate and tertiary ammonium groups that could not be solubilized by the addition of electrolytes or changes on pH.[62]

The main research objective of this dissertation was to synthesize model random polyampholytes, with high molecular weights and narrow molecular weight distributions, from uncharged neutral monomers by a controlled radical polymerization method. The need for model random polyampholytes arises from the fact that theoretical models as well as computer simulations of a polyampholyte chain provide a qualitative understanding of the conformations in dilute solutions, but overestimate the strength of the attractive interactions.[21] As a result, the properties of the whole ensemble of chains are often represented by the properties of the most probable member, which may not always be valid. The purpose of employing a controlled radical polymerization method was to afford copolymers with a controlled molecular weight (M_n) and a narrow molecular weight distribution ($1 < (M_w/M_n) < 1.5$).

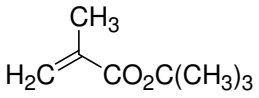
ABC triblock copolymers of methyl methacrylate (MMA), 2-(*N,N*-dimethylamino)ethyl methacrylate (DMAEMA), and tetrahydropyranyl methacrylate (THPMA) were successfully synthesized by group transfer polymerization (GTP).[63] The THPMA units in the triblocks were chemically modified by conversion to

methacrylic acid. Atom transfer radical polymerization (ATRP)[35] and reversible addition-fragmentation chain transfer (RAFT) polymerization[18] are the two most versatile methods of controlled radical polymerization (CRP) for acrylate and methacrylate monomers. The RAFT method, however, has the distinction of being the most widely compatible in terms of monomer choice. For example, species such as acrylamide and tertiary amine containing monomers are readily polymerized.[64,65] Previously, we synthesized binary copolymers of *tert*-butyl methacrylate (tBMA) and 2-(*N,N*-dimethylamino)ethyl methacrylate (DMAEMA) with glyceryl monomethacrylate (GMA) by conventional free radical polymerization. However, GMA was consumed at a much faster rate than the other two monomers. The faster consumption of GMA would not be appropriate to synthesize random copolymers or copolymers of constant composition over the course of the polymerization. It was thus decided to switch to the protected form of GMA, namely solketal methacrylate (2,2-dimethyl-1,3-dioxolan-4-yl)methyl methacrylate (SMA) to synthesize the ternary copolymers, which could later be converted to the diol after deprotection.

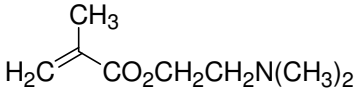
The uncharged monomers used in this study were solketal methacrylate (SMA, **10**), *tert*-butyl methacrylate (tBMA, **11**), and 2-(*N,N*-dimethylamino)ethyl methacrylate (DMAEMA, **12**) as shown in Figure 6. Cumyl dithiobenzoate (CDB, **13**) was the RAFT CTA employed for these polymerizations.



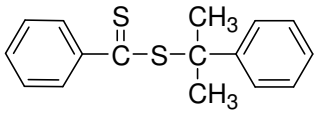
Solketal methacrylate
[SMA, **10**]



***tert*-butyl methacrylate**
[tBMA, **11**]



2-(N,N-dimethylamino)ethyl methacrylate
[DMAEMA, **12**]



Cumyl dithiobenzoate
[CDB, **13**]

Figure 6. Structures of monomers and RAFT CTA

We have also determined binary copolymer reactivity ratios for all combinations of SMA, DMAEMA and tBMA by conventional radical polymerization.[66] The results are shown in Table 1.

Table 1. Binary Copolymer Reactivity Ratios of Polyampholyte Precursors[a]

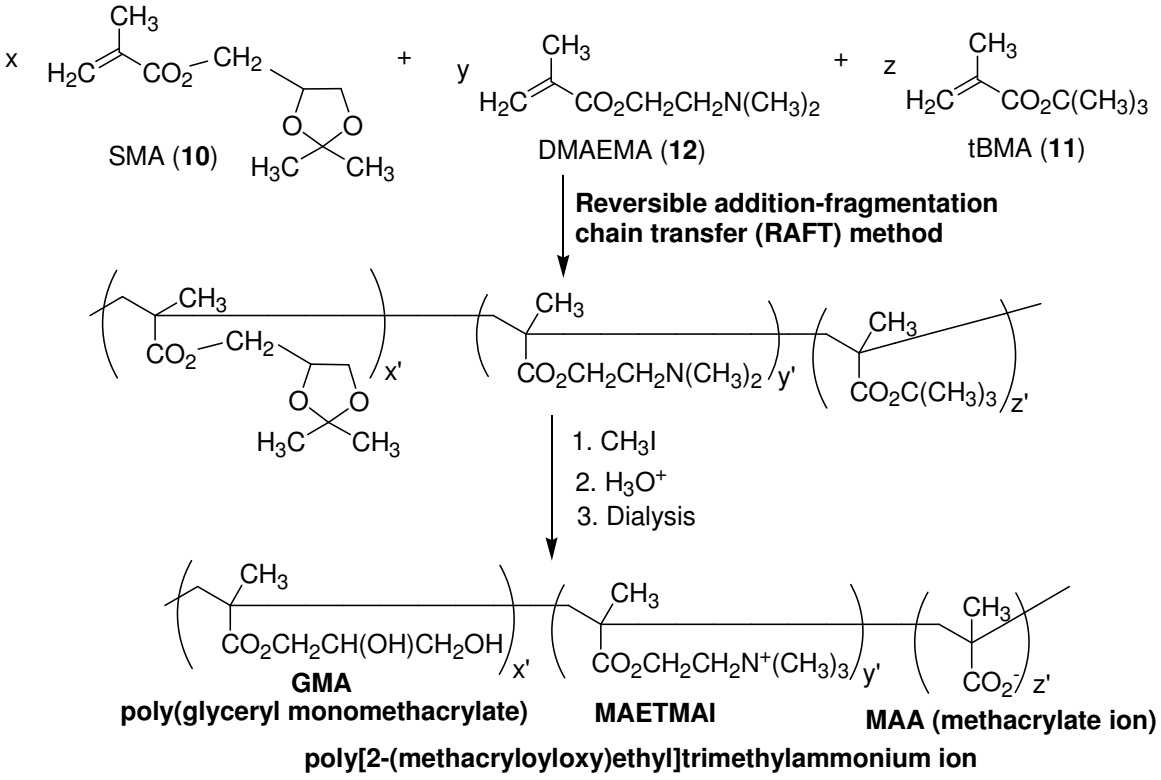
M_1, M_2	r_1	r_2	$r_1 r_2$
tBMA, SMA	1.40	0.79	1.10
tBMA, DMAEMA	1.26	0.97	1.22
DMAEMA, SMA	1.40	0.65	0.91

[a]Results were calculated from compositions of residual monomers in solution by ^{1}H NMR spectroscopy, based on the terminal model and the Tidwell-Mortimer (TM) non-linear least squares method, using Procop, a commercial software.[67,68]

Although the RAFT method has been extensively used to synthesize various methacrylate esters,[32] currently there are no reports on RAFT polymerization of SMA. SMA has however been polymerized by ATRP.[69-71] *tert*-Butyl methacrylate (tBMA), the precursor of the negatively charged units, has been polymerized by the RAFT method.[72,73] 2-(*N,N*-dimethylamino)ethyl methacrylate (DMAEMA), the precursor of the positively charged units is known to polymerize conveniently by the RAFT method.[74,75]

There are two possible synthetic approaches to polyampholytes; synthesis in an aqueous medium, and synthesis in an organic solvent. Since previous literature reports indicate a tendency to form alternating polymers in aqueous media,[76,77] we chose the organic route as shown in Scheme 7.

Scheme 7. Synthesis of polyampholytes – organic solvent route



As shown in Scheme 7, the target polyampholytes contain glyceryl monomethacrylate (GMA) as the hydrophilic uncharged component, 2-(trimethylammonio)ethyl methacrylate ions (TMAEMA) and methacrylate ions (MAA) respectively for the positively and negatively charged components. The compositions for our model random polyampholytes were targeted at a mole ratio of approximately 80:10:10 of SMA, DMAEMA and tBMA respectively. As mentioned earlier, both tBMA, the precursor of the acidic units and DMAEMA, the precursor of the basic groups, have been polymerized by the RAFT method. SMA was chosen to be the major component, to ensure the final polyampholytes would be water-soluble at room temperature and at all pH ranges. Solketal methacrylate is not a commercially available monomer. However, since it is the major component in the polyampholyte, it had to be synthesized on a large scale.

The work in this study can be divided into two main sections. The first section concerns the syntheses of SMA and RAFT chain transfer agent, cumyl dithiobenzoate (CDB).[78,79] This section details the synthesis of homopolymers and terpolymers of SMA, DMAEMA and tBMA by the RAFT method in an organic solvent, and the results from the functional group conversions of RAFT terpolymers in attempts to synthesize water-soluble polyampholytes.[48,71,74,78-80] The second section concerns the synthesis of a water-soluble RAFT CTA, namely, 4-Cyano-4-dithiobenzoylthiyl pentanoic acid and the synthesis of binary and ternary copolymers of glyceryl monomethacrylate (GMA), DMAEMA and methacrylic acid (MAA) by conventional free radical polymerization.[65]

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CHAPTER II

SYNTHESIS OF POLYAMPHOLYTES

Introduction

The main research objective was to synthesize the precursor terpolymers and hence water-soluble polyampholytes with an 80:10:10 composition of solketal methacrylate (SMA), *tert*-butyl methacrylate (tBMA) and 2(*N,N*-dimethylamino)ethyl methacrylate (DMAEMA) respectively. Solketal methacrylate (**10**), a cyclic ketal monomer, is the protected form of the diol, glyceryl monomethacrylate (GMA). SMA is not a commercially available monomer. Moreover, since it was necessary to have 80 % of SMA incorporated in the terpolymers, and SMA is the slowest propagating of the three monomers, we had to start with a much higher concentration of SMA than tBMA or DMAEMA in the feed mixture. Thus SMA had to be synthesized on a large scale.[1]

Among the various RAFT chain transfer agents (CTA), cumyl dithiobenzoate, (**13**) and 2-cyanoprop-2-yl dithiobenzoate (**14)** are effective in the polymerization of methacrylate monomers.[2] This chapter outlines the synthesis and characterization of solketal methacrylate (SMA) on a scale greater than a 100 g and the RAFT CTA cumyl dithiobenzoate (CDB).[3] The synthesis of homopolymers of SMA, tBMA, and (2-bromoethyl methacrylate) (BEMA) using 2-cyanoprop-2-yl dithiobenzoate (CPDB, **14**)

as the RAFT CTA[4], and homopolymers of SMA, tBMA and DMAEMA using cumyl dithiobenzoate (CDB) as the RAFT CTA respectively are also discussed.

The homopolymers were synthesized to determine if the RAFT CTAs, CDB and CPDB behaved in a controlled manner, namely, afforded a linear increase in molecular weights (M_n) with percent conversion and narrow polydispersities (M_w/M_n). Moreover, the ^{1}H NMR spectra of the isolated homopolymers would help to assign the peaks in the NMR spectra of ternary copolymers.

RAFT polymerizations of *tert*-butyl methacrylate (tBMA) and 2-(*N,N*-dimethylamino)ethyl methacrylate (DMAEMA) have already been reported.[5-7] However, there have been no reports on RAFT polymerization of SMA to date. Moreover, polymerization of ternary mixtures of solketal methacrylate (SMA), 2-(*N,N*-dimethylamino)ethyl methacrylate (DMAEMA) and *tert*-butyl methacrylate (tBMA) via the RAFT method have not been reported thus far. This chapter details the syntheses of terpolymers of SMA, tBMA and DMAEMA using cumyl dithiobenzoate as the RAFT CTA (Scheme 7, Chapter I).[4]

The proposed compositions of polyampholytes to be synthesized are listed in Table 2. This table of six polyampholytes is proposed to test the solution properties of polyampholytes as a function of net charge, sequence distribution, and degree of polymerization. Entry 2 with degree of polymerization 300 and an 8:1:1 mol ratio of SMA:tBMA:DMAEMA respectively was set as the target composition for our first large scale model polyampholyte. However, in order to test the synthesis of terpolymers on a small scale, and optimize the conditions necessary to carry out the functional group conversions to polyampholytes, we decided to start with entry 4 in Table 8, namely,

degree of polymerization 100 and an 8:1:1 mol ratio of SMA:tBMA:DMAEMA respectively.

Table 2. Proposed Compositions of Polyampholytes

DP[a]	N_+[b]	N_-[c]	N_n[d]	% ($N_+ + N_-$)	balanced
300	60	60	180	40	yes
300	30	30	240	20	yes
300	15	15	270	10	yes
100	10	10	80	20	yes
1000	100	100	800	20	yes
300	30	60	210	30	no

[a]DP = degree of polymerization [b]N_+ = number of (+) units. [c]N_- = number of (-) units. [d]N_n = number of uncharged units.

The transformation of ternary copolymers of SMA, tBMA, and DMAEMA to water-soluble polyampholytes (Scheme 7, Chapter I) is also discussed. This transformation from uncharged terpolymers to polyampholytes involves three functional group conversions, the alkylation of tertiary amino groups in DMAEMA to quaternary ammonium ions, the removal of *tert*-butyl groups in tBMA, and the hydrolysis of the ketal ring in SMA, to yield the final product. Previous literature reports successful quaternization of *N*-methyl groups in DMAEMA using methyl iodide in THF as well as the acid-catalyzed removal of *tert*-butyl ester and deprotection of the cyclic ketal SMA.[8,9]

Amphiphilic block copolymers of polystyrene and poly(acrylic acid) were prepared via controlled radical polymerization techniques such as atom transfer radical polymerization (ATRP) and nitroxide-mediated polymerization (NMP), using *tert*-butyl acrylate as the precursor monomer to acrylic acid.[9] Copolymers of 2-(trimethylsilyloxy)ethyl methacrylate (HEMA-TMS) and *tert*-butyl methacrylate (tBMA) have been synthesized via atom transfer radical polymerization.[10] The complete hydrolysis of the *tert*-butyl groups in tBMA units was achieved using trifluoroacetic acid (TFA) and dichloromethane (DCM).[10] Acetals are stable to basic and nucleophilic reagents, but are readily cleaved under mild acidic conditions.[1] In a similar manner, the two hydroxyl groups of DHPMA may be suitably protected with a dioxolane linkage in the form of solketal methacrylate (SMA), which could later be cleaved to yield the diol functionality. In our target polyampholyte structures, the positively charged units were provided by quaternizing the $N(CH_3)_2$ groups in DMAEMA with methyl iodide, while the acid-catalyzed conversion of the *tert*-butyl ester to carboxylic acid provided the negatively charged carboxylate end units.[1,8,9] The cyclic ketal ring in SMA was also simultaneously opened in acid, leading to the diol, poly(GMA), which afforded the polymers solubility in water at room temperature. These preliminary experiments for the functional group conversions of the small scale uncharged terpolymers to polyampholytes were carried out to test and optimize the conditions for future large scale experiments.

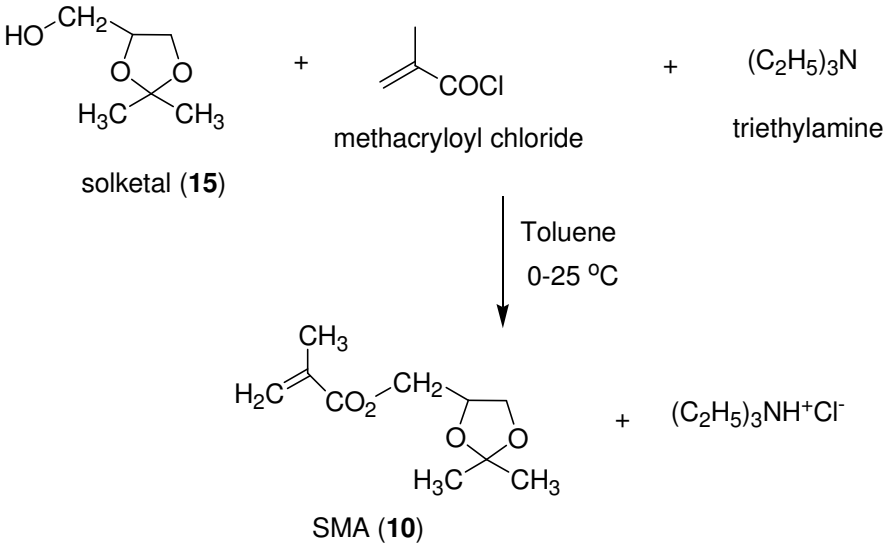
Based on the results of the small scale terpolymer syntheses utilizing the RAFT technique, large scale (> 1 g) terpolymer preparations using cumyl dithiobenzoate as RAFT CTA in 1,4-dioxane at 75 ^{o}C were carried out. Our goal was to achieve a degree of polymerization 300 with an 8:1:1 mol ratio of SMA:tBMA:DMAEMA respectively.

RAFT polymerizations have been carried out to degree of polymerization (DP = 300) with low molecular weight distributions, however, polymerizations with DP >> 300 have not yet been reported.[2,4,11] The results of functional group conversions of the large scale ternary copolymers of SMA, tBMA, and DMAEMA are also discussed in this chapter.[1,8,9,12]

Results and Discussion

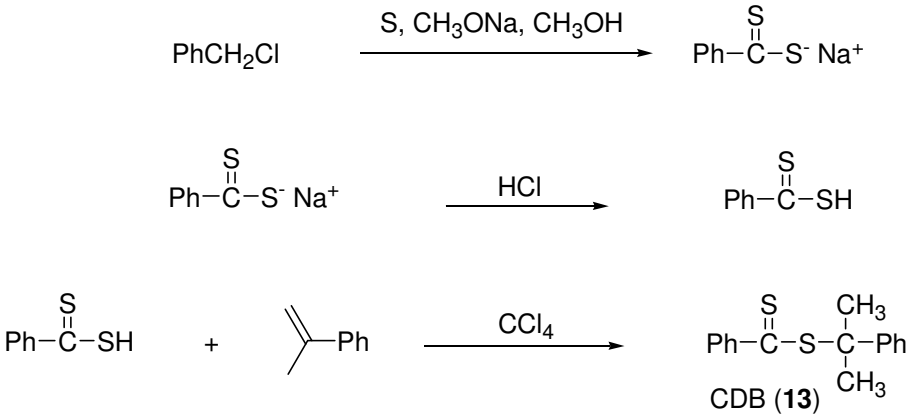
Synthesis of Solketal Methacrylate (SMA, **10**).[1] The synthesis of solketal methacrylate is outlined in Scheme 8. The structure of **10** was confirmed by ^{1}H and ^{13}C NMR spectroscopy (Figures 1, 2 and 3 in appendices).

Scheme 8. Synthesis of Solketal Methacrylate



Synthesis of Cumyl Dithiobenzoate (CDB, **13**).[3] The synthesis of cumyl dithiobenzoate **(13)** was carried out following a literature procedure and can be divided into two steps, as represented in Scheme 9.[3]

Scheme 9. Synthesis of Cumyl Dithiobenzoate



The structure of (**13**) was confirmed by ^{1}H and ^{13}C NMR spectroscopy, infra red and UV-visible spectroscopy (Figures 4-7 in appendices), elemental analysis, infrared and UV-visible spectroscopy. From the elemental analysis data, hydrogen is in excess by 0.07 % and sulfur is in excess by 2.70 %. However, carbon is deficient by 2.58 %. The results of elemental analysis suggest that the synthesized CDB sample could contain some elemental sulfur. The percent purity of cumyl dithiobenzoate from the integrated ^{1}H NMR spectrum on a mole basis was calculated to be 92 % cumyl dithiobenzoate and 8 % of impurities based on the relative areas of the large singlet at 1.9 ppm and the small peaks close to 1.9 ppm in the ^{1}H NMR spectrum.

Synthesis of Homopolymers Using CDB as RAFT CTA. The ^{1}H NMR spectra of poly(SMA), poly(tBMA) and poly(DMAEMA) synthesized using cumyl dithiobenzoate in toluene-d_8 are shown in Figures 8-10 respectively of appendices. The percent conversions for the three homopolymers in solution were calculated from the integrations of the ^{1}H NMR spectra before polymerization, and after heating at 60 $\pm$ 1 ^{o}C for 20 h (Table 3). The GPC measurements of the molecular weights and molecular weight distributions for homopolymers of SMA, tBMA and DMAEMA isolated after 20 h are listed in Table 4.

Table 3. Conversion Data for RAFT Homopolymerizations at 60 ^{o}C Using Cumyl Dithiobenzoate

time (h)	% conv. SMA[a]	% conv. tBMA[a]	% conv. DMAEMA[a]
0	0	0	0
4	39	6	5
6	55	13	12
8	66	23	20
12	81	40	36
16	88	54	50
20	93	64	62

[a]% Conversions of SMA, tBMA, and DMAEMA determined from integrated ^{1}H NMR spectra of samples before polymerization and after partial conversion.

As seen in Table 3, the homopolymerizations of tBMA and DMAEMA exhibit an initial inhibition period lasting for < 4 h. This could be due to traces of oxygen in the reaction mixtures.

Table 4. GPC Data for RAFT Homopolymers Using Cumyl Dithiobenzoate

polymer	% conv.[a,b]	$M_{n,th}$[c]	$M_{n,GPC}$[d]	M_w/M_n[d]
Poly(SMA)	93	70000	28000	1.38
Poly(tBMA)	64	38000	19000	1.45
Poly(DMAEMA)	62	37000	47000	1.61

[a]From integrated ^{1}H NMR spectra collected initially at room temperature and after partial conversion.

[b]Polymerizations carried out for 20 h at 60 $\pm$ 1 ^{o}C.

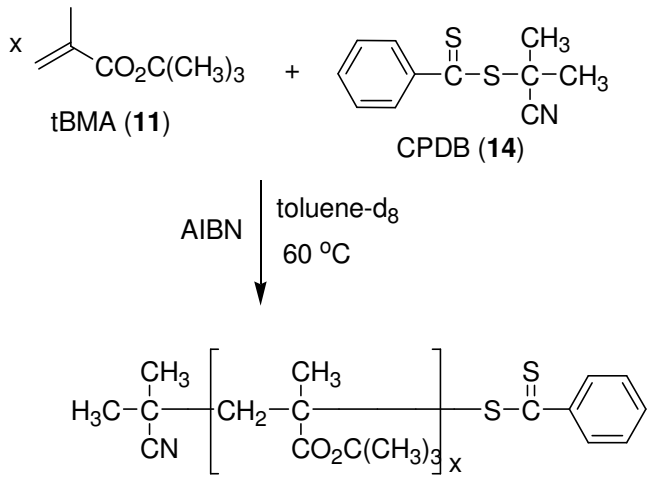
[c]$(M_{n,th}) = \{([M]_o M_M C)/ [CTA]\} + M_{CTA}$

where $[M]_o$, [CTA], M_M, M_{CTA} and C are the initial monomer concentration, the initial CTA concentration, the molecular weight of the monomer, the molecular weight of the RAFT CTA and the mol fraction conversion respectively.[4]

[d]Calibration using linear polystyrene standards.

Synthesis of Homopolymers Using 2-Cyanoprop-2-yl Dithiobenzoate (CPDB, **14**) **as RAFT CTA.** The homopolymerization of tBMA is represented in Scheme 10. These experiments were carried out to determine the percent conversions of the monomers with respect to time and to determine the molecular weights and molecular weight distributions by gel permeation chromatography.

Scheme 10. Homopolymerization of tBMA with CPDB as RAFT CTA



The molecular weights (M_n) and polydispersities (M_w/M_n) for homopolymers of SMA and tBMA, as measured by gel permeation chromatography are listed in Tables 5 and 6 respectively. The plots of the number average molecular weights (M_n) and the polydispersities (M_w/M_n) as a function of percent conversion for poly(SMA) and poly(tBMA) are shown in Figures 7 and 8 respectively.

Table 5. GPC Data for Poly(tBMA) at 60 °C Using 2-Cyanoprop-2-yl Dithiobenzoate

time (h)	$M_{n,th}$[a]	$M_{n,GPC}$[b]	M_w/M_n[b]	% conv.[c]
2	12000	5100	1.15	21
4	28000	8300	1.11	47
8	39000	18300	1.18	66
12	43000	23800	1.17	76

[a]$(M_{n,th}) = \{([M]_o M_M C)/ [CTA]\} + M_{CTA}$

where $[M]_o$, [CTA], M_M, M_{CTA} and C are the initial monomer concentration, the initial CTA concentration, the molecular weight of the monomer, the molecular weight of the RAFT CTA and the mol fraction conversion respectively.[4]

[b]Calibration using poly(styrene) standards.

[c]From integrated ^{1}H NMR spectra collected initially at room temperature and after partial conversion.

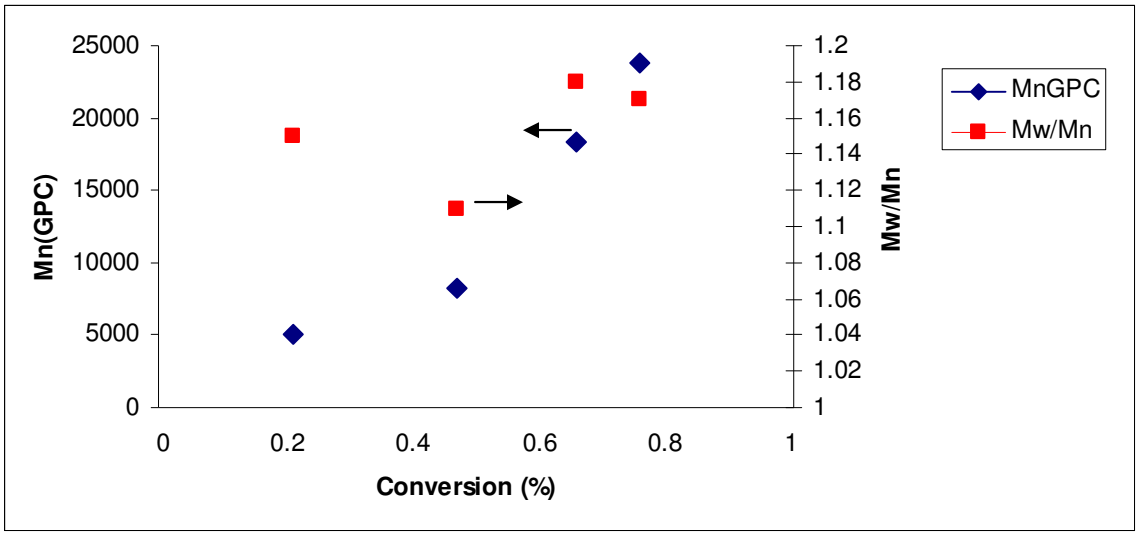


Figure 7. Evolution of M_n and M_w/M_n for RAFT polymerization of tBMA at 60 °C.

Table 6. GPC Data for Poly(SMA) at 60 °C Using 2-Cyanoprop-2-yl Dithiobenzoate

time (h)	$M_{n,th}$ [a]	$M_{n,GPC}$ [b]	M_w/M_n [b]	% conv. [c]
2	14000	12100	1.18	19
4	38000	28700	1.15	51
8	55000	33300	1.24	76
12	69000	38100	1.24	92

[a,b,c]Refer to Table 5.

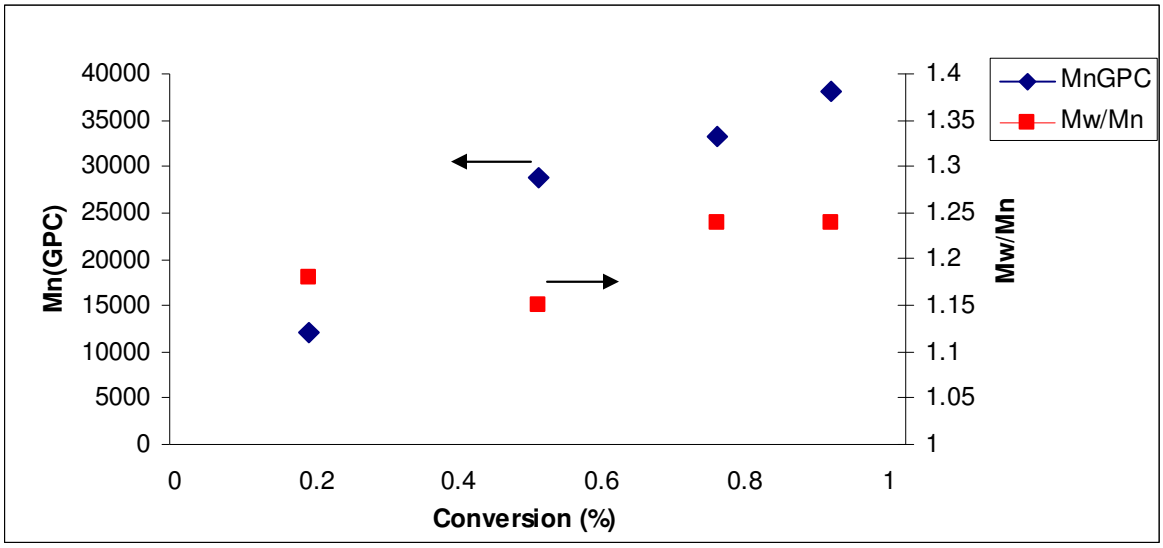


Figure 8. Evolution of M_n and M_w/M_n for RAFT polymerization of SMA at 60 °C.

Previous studies indicate that differences in the calculated and observed molecular weights may arise due to incomplete consumption of the RAFT chain transfer agent.[4] 2-Cyanoprop-2-yl dithiobenzoate (C_{tr}=13) has been reported to have a higher chain transfer constant than cumyl dithiobenzoate (C_{tr} =10) in the polymerization of methyl

methacrylate (MMA) at 60 ^{o}C.[13] The fact that cumyl dithiobenzoate failed to give narrow polydispersities could be attributed to marked retardation in the early stages of polymerization. Although the cumyl and 2-cyanoprop-2-yl groups are examples of good leaving groups, the cumyl radical may be less effective in re-initiating polymerization. Literature data suggests no significant differences in the rates of initiation (k_i) in the polymerization of methyl methacrylate (MMA) with either $^{\cdot}C(CH_3)_2CN$ or $^{\cdot}C(CH_3)_2Ph$ as the initiating species. The similarity in the k_i values suggests that the difference in behavior of 2-cyanprop-2-yl and cumyl dithiobenzoate may be due to k-β, the rate constant of addition of R$^{\cdot}$ to macro-CTA (**4**) (Scheme 3, Chapter I), for $^{\cdot}C(CH_3)_2CN$ being lower than that for $^{\cdot}C(CH_3)_2Ph$.[4]

Moreover, DMAEMA containing polymers are known to be difficult to characterize by size exclusion chromatography because of the adsorption of poly(DMAEMA) to the column.[14,15] This usually results in broader peaks (larger polydispersities) with longer retention times (lower molecular weights).

Small Scale Synthesis of RAFT Ternary Copolymers.[4] The synthesis of homopolymers was done in toluene-d_8. However, in a ternary mixture of SMA, tBMA and DMAEMA, the vinyl protons of SMA and DMAEMA were not well resolved to do accurate NMR integrations. Since 1,4-dioxane-d_8 gave a good separation of the multiplets for the vinyl protons of SMA and DMAEMA, the rest of the small scale terpolymer syntheses were carried out in 1,4-dioxane-d_8.

Three small scale ternary copolymers of **10**, **11** and **12** were synthesized in an NMR tube using the RAFT CTA **13**. These terpolymers have been characterized by ^{1}H

and ^{13}C NMR spectroscopy. The gel permeation chromatograms indicate fairly narrow molecular weight distributions ($M_w/M_n < 1.5$), a characteristic of controlled free radical polymerizations. Figure 11 in appendices, is the ^{1}H NMR spectrum of DP 98 terpolymer in $CDCl_3$. The term *degree of polymerization* refers to the number average of repeating units in the polymer molecule.[16]

The monomer conversions were determined from ^{1}H NMR spectra by integrating the vinyl resonances between 5 ppm and 6 ppm relative to the singlet for the aromatic protons of the internal standard *p*-xylene at 6.98 ppm. The theoretical degree of polymerization was calculated using the total moles of monomers employed, moles of RAFT CTA (CDB) and the weighted average percent conversion of the three monomers after partial conversion. The experimental degree of polymerization was calculated as the product of the weighted average percent conversion of the three monomers, calculated from ^{1}H NMR integrated peak areas of vinyl protons of monomers and *p*-xylene, and the theoretical degree of polymerization.

Calculation of Percent Conversions and Compositions of Monomers in Solution by ^{1}H NMR Spectroscopy

From the room temperature ^{1}H NMR spectrum of the ternary monomer mixture (Figure 12, appendices), the values of the areas under the integrals for the vinyl hydrogens of SMA, tBMA and DMAEMA were assigned as a and b for SMA, c and d for DMAEMA, and e and f for tBMA respectively. The area under the singlet for the protons of the aromatic ring in *p*-xylene was denoted as z. Ratios were then calculated by dividing the sum of the areas for the three vinyl hydrogens, belonging to SMA (denoted

as A), DMAEMA (denoted as B), and tBMA (denoted as C) respectively, by the area of *p*-xylene (z).

$$\text{SMA ratio} \quad (A) = \frac{(a+b)}{z} \tag{3}$$

$$\text{DMAEMA ratio} \quad (B) = \frac{(c+d)}{z} \tag{4}$$

$$\text{tBMA ratio} \quad (C) = \frac{(e+f)}{z} \tag{5}$$

The mol fraction feed compositions, f_1 of SMA, f_2 for DMAEMA and f_3 for tBMA, were calculated as follows:

$$f_1 = \frac{A}{(A+B+C)} \tag{6}$$

$$f_2 = \frac{B}{(A+B+C)} \tag{7}$$

$$\text{and} \quad f_3 = 1-(f_1+f_2) \tag{8}$$

In a similar manner, from the integrated ^{1}H NMR spectrum of the ternary mixture of SMA, tBMA and DMAEMA obtained after partial conversion, ratios for the three monomers were calculated, denoted by D for SMA, E for DMAEMA and F for SMA respectively. The percent conversion for each monomer was determined as follows:

$$\%\ \text{SMA left} \quad (P) = \left(\frac{D}{A}\right) x100 \tag{9}$$

$$\%\ \text{SMA consumed} \quad (Q) = 100 - P \tag{10}$$

$$\%\ \text{DMAEMA left}\ (R) = \left(\frac{E}{B}\right)100 \tag{11}$$

$$\%\ \text{DMAEMA consumed}\ (S) = 100 - R \tag{12}$$

$$\%\ \text{tBMA left}\ (T) = \left(\frac{F}{C}\right)100 \tag{13}$$

$$\%\ \text{tBMA consumed}\ (U) = 100 - T \tag{14}$$

The composition of the co-monomers incorporated into the copolymer is then calculated as follows:

$$\text{Amount of SMA consumed}\ (X) = f_1\left(\frac{Q}{100}\right) \tag{15}$$

$$\text{Amount of DMAEMA consumed}\ (Y) = f_2\left(\frac{S}{100}\right) \tag{16}$$

$$\text{Amount of tBMA consumed}\,(Z) = f_3\left(\frac{U}{100}\right) \tag{17}$$

$$F_1 = \frac{X}{(X + Y + Z)} \tag{18}$$

$$F_2 = \frac{Y}{(X + Y + Z)} \tag{19}$$

$$F_3 = 1 - (F_1 + F_2) \tag{20}$$

The isolation of terpolymers by precipitation from *n*-hexane was not quantitative (34 %-47 %). Moreover, it was a problem to get rid of residual SMA monomer and *p*-xylene in the terpolymers, even though the precipitations from *n*-hexane were repeated twice. The supernatant solution after precipitating the terpolymer in *n*-hexane did not

have a pink color, thus indicating that the polymer is not partially soluble in *n*-hexane. The experimental data including feed compositions for the small scale terpolymer syntheses are shown in Tables 7 and 8 respectively.

Table 7. Feed Compositions of Monomers in Small Scale RAFT Terpolymer Syntheses

sample	DP	mol fractions (^{1}H NMR)			mol fraction (based on weight)		
		SMA	tBMA	DMAEMA	SMA	tBMA	DMAEMA
6571	90	0.767	0.117	0.116	0.789	0.111	0.100
6652	98	0.792	0.103	0.105	0.796	0.101	0.102
6633	186	0.767	0.106	0.127	0.806	0.097	0.097

Table 8. Experimental Data for Small Scale Terpolymer Syntheses

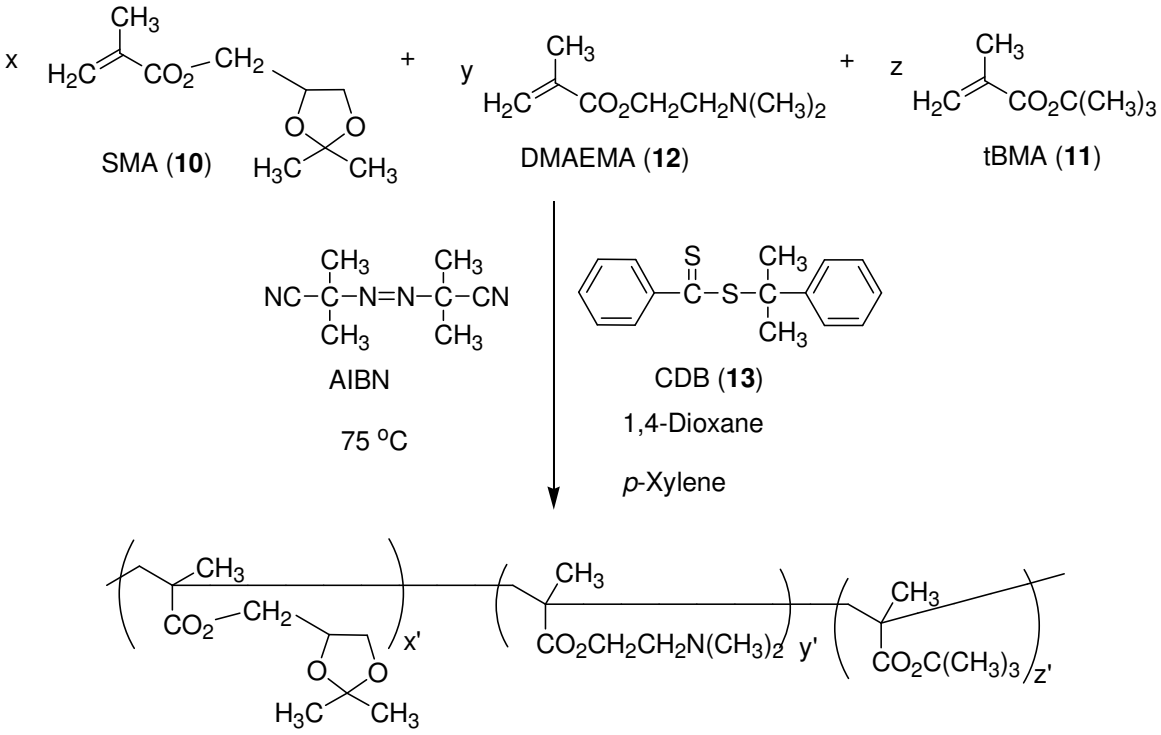
DP[a]	monomers	CDB	AIBN	*p*-xylene	1,4-dioxane-d_8	conv.
	mmol	μmol	μmol	mmol	mL	(%)
90	1.27	10.9	3.65	0.480	0.41	78
98	2.50	9.70	3.31	0.169	0.30	38
186	2.47	9.41	3.31	0.198	0.30	71

[a] DP = ([monomer]/ [CDB]) x (fractional conversion).

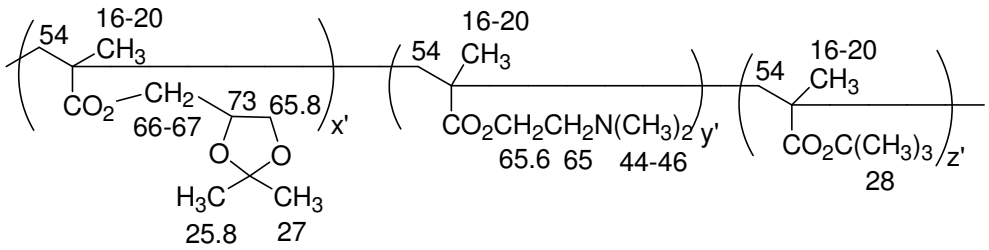
Large Scale Synthesis of RAFT Ternary Copolymers. Terpolymers of **10**, **11** and **12** with degrees of polymerization 135, 278, 360 and 532 were synthesized on a scale

greater than one gram, by employing cumyl dithiobenzoate as the RAFT CTA (Scheme 11). Figures 13 and 14 are the ^{1}H and ^{13}C NMR spectra respectively of RAFT terpolymer with degree of polymerization 135 in $CDCl_3$. The assignments for the quaternary carbons in SMA, tBMA, and DMAEMA, backbone CH_2's, and backbone CH_3's were made in comparison with a ^{13}C NMR spectrum of poly(methyl methacrylate).[17]

Scheme 11. Synthesis of ternary copolymers by RAFT method



DEPT NMR Spectrum of Terpolymer. The DEPT (distortionless enhancement of polarization transfer) experiment has helped in identifying peaks in the ^{13}C NMR spectrum of the terpolymer as CH_3's, CH_2's and CH's. From the DEPT spectrum of the terpolymer (sample 6571), the following assignments were made (δ, ppm):



A partial conversion ^{1}H NMR spectrum for DP 135 terpolymer is shown in Figure 12 (appendices). Monomer conversions were determined from ^{1}H NMR spectra as described for the small scale terpolymers. The feed compositions of the three monomers in the ternary mixture prior to polymerization, as well as the composition of the monomers incorporated in the terpolymer after partial conversion were also calculated from ^{1}H NMR spectra. The experimental data and percent yields for the large scale RAFT terpolymers are presented in Tables 9 and 10 respectively.

Table 9. Experimental Data for Large Scale RAFT Terpolymer Syntheses

sample	DP[a]	monomers	CDB	AIBN	*p*-xylene	1,4-dioxane	time
		mmol	μmol	μmol	mmol	mL	(min)
7341	135	1.31	52.7	17.6	0.914	1.11	150
7794	278	5.28	70.3	23.1	3.81	4.40	65
7703	360	2.63	35.1	11.6	1.92	2.20	90
7622	532	1.32	17.6	5.48	0.942	1.10	50

[a] DP = ([monomer]/ [CDB]) x (fractional conversion).

Table 10. Summary of Final Conversions of Large Scale RAFT Terpolymers

sample	% conv.[a]	% isolated	weight (g)
7341	54	48	1.20
7794	37	21	2.11
7703	48	31	1.52
7622	71	46	1.14

[a] Weighted average percent conversion.

Calculations of Copolymer Compositions from Binary Copolymer Reactivity Ratios.[18,19] The calculations of copolymer compositions in the terpolymers were carried out using Procop.[19] The Procop program calculates the compositions of ternary copolymers by inputting the reactivity ratio values for binary monomer mixtures (Table 1, Chapter I), the feed compositions and the weighted average percent conversion of the monomers. The program considers the random errors in the copolymer composition to be normally distributed and statistically independent from run to run. The independent variable, the co-monomer feed composition is assumed to be errorless.

The instantaneous copolymer composition refers to the composition of the copolymer at a given instant in time, while the global copolymer composition refers to the overall composition of the copolymer. The overall copolymer composition is the sum of the instantaneous copolymer compositions which in turn are obtained using the instantaneous monomer compositions.[19] As a function of the conversion, any copolymerization process is a succession of instant copolymerizations; a single experiment (a unique monomer feed composition) includes several reinitiated instant

copolymerizations. The copolymerization of a ternary mixture of monomers occurs with the consumption to different degrees of each monomer. Thus a shift in the composition of the monomer mixture will be found from one extent of conversion to another. In other words, the instantaneous copolymer composition will be continuously changing. The summing of the instantaneous copolymer compositions results in the overall copolymer composition. Instantaneous copolymer compositions are functions of reactivity ratios and monomer feed compositions, and differ from the compositions of the starting monomers. The reactivity ratios determined for binary monomer mixtures of SMA, tBMA and DMAEMA via conventional radical polymerization (Table 1, Chapter I), were used to predict the compositions of the ternary copolymers.[20] The global copolymer represents the overall composition of the copolymer mixture. At 100 % conversion the polymer composition is the same as the composition of the original co-monomer mixture.[19]

The reactivity ratios for binary monomer mixtures of SMA, tBMA and DMAEMA (Table 1, Chapter I) predict that in a ternary copolymerization, DMAEMA and tBMA will be consumed faster than SMA.[20] The overall comparison of copolymer compositions in the small scale terpolymers calculated from ^{1}H NMR and the reactivity ratios are presented in Table 11. These copolymer compositions are the output results after the reactivity ratios of the three monomer pairs,[20] the mole fractions of the monomers in the feed, and the average percent conversion are put into the Procop program.

Table 11. Comparison of Copolymer Compositions from NMR and Reactivity Ratios

DP[a]	conv.	copolymer comp. after partial conv.[b] (NMR)			instantaneous copolymer comp. after partial conv.[c] (Procop)			global copolymer after partial conv.[c] (Procop)		
	(%)	SMA	tBMA	DMAEMA	SMA	tBMA	DMAEMA	SMA	tBMA	DMAEMA
90	78	0.767	0.109	0.123	0.804	0.103	0.093	0.744	0.126	0.130
98	38	0.803	0.098	0.099	0.765	0.113	0.121	0.748	0.119	0.132
186	71	0.774	0.097	0.129	0.788	0.099	0.112	0.738	0.116	0.146

[a]Refer to Table 7 for sample identification.

[b]From integrated ^{1}H NMR spectra collected initially at room temperature and after partial conversion.

[c]From Procop, based on reactivity ratios of binary mixtures of SMA, tBMA and DMAEMA, feed compositions and the weighted average % conversion of monomers in column 2.

The data for the copolymer compositions after partial conversion calculated from ^{1}H NMR and the global copolymer compositions calculated using reactivity ratios are listed in Tables 12 and 13. The calculated and experimental drifts in overall composition for RAFT polymerizations an initial 79/10/11 mixture of SMA/tBMA/DMAEMA (DP 98) and an initial 76/10/12 mixture of SMA/tBMA/DMAEMA (DP 186) are shown in Figures 9 and 10 respectively. The data plotted in Figures 9 and 10 are listed in Tables 12 and 13 respectively.

Table 12. Data for Copolymer Compositions in RAFT Terpolymer with DP 98[a]

copolymer comp. after partial conv.[b]			% conv.[b]	time	global copolymer comp. after partial conv.[c]		
SMA	tBMA	DMAEMA		(min)	SMA	tBMA	DMAEMA
			0.01	-	0.733	0.125	0.142
0.794	0.103	0.104	0.04	60	0.734	0.124	0.141
0.798	0.101	0.100	0.21	120	0.741	0.122	0.137
0.803	0.097	0.099	0.38	180	0.748	0.119	0.132

[a]See Tables 7 and 8.

[b]Calculated from integrations of ^{1}H NMR spectra collected initially at room temperature and after partial conversion.

[c]Calculated using reactivity ratios.

Table 13. Data for Copolymer Compositions in RAFT Terpolymer with DP 186[a]

copolymer comp.[b] after partial conv. (NMR)			% conv.[b]	time (min)	global copolymer comp. after partial conv.[c] (Procop)		
SMA	tBMA	DMAEMA			SMA	tBMA	DMAEMA
			0.01	-	0.703	0.127	0.169
0.778	0.103	0.119	0.14	60	0.709	0.125	0.165
0.776	0.099	0.125	0.38	120	0.719	0.122	0.158
0.775	0.099	0.126	0.54	180	0.727	0.119	0.152
0.776	0.098	0.126	0.64	240	0.734	0.117	0.148
0.774	0.097	0.129	0.71	300	0.739	0.116	0.146

[a]See Tables 7 and 8.

[b]Calculated from integrations of ^{1}H NMR spectra collected initially at room temperature and after partial conversion.

[c]Calculated using reactivity ratios.

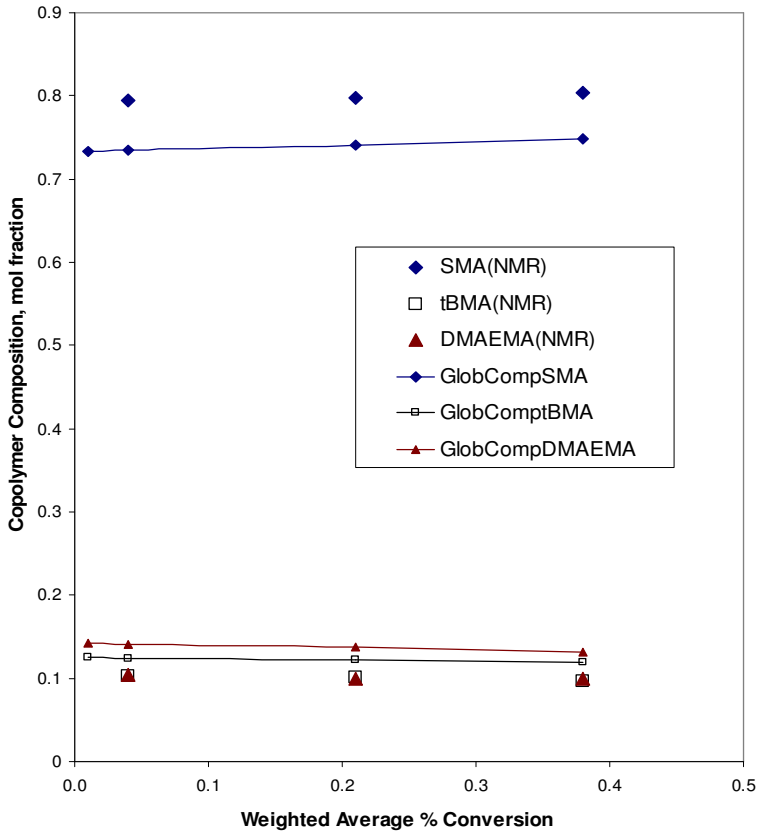


Figure 9. Calculated and experimental polymer compositions from terpolymerization of a 79/10/11 molar mixture of SMA, DMAEMA, and tBMA. (DP 98)

Tables 14 and 15 present a comparison of feed compositions and copolymer compositions for the large scale terpolymers calculated from ^{1}H NMR spectroscopy and that determined using the reactivity ratios of all combinations of binary monomer mixtures.

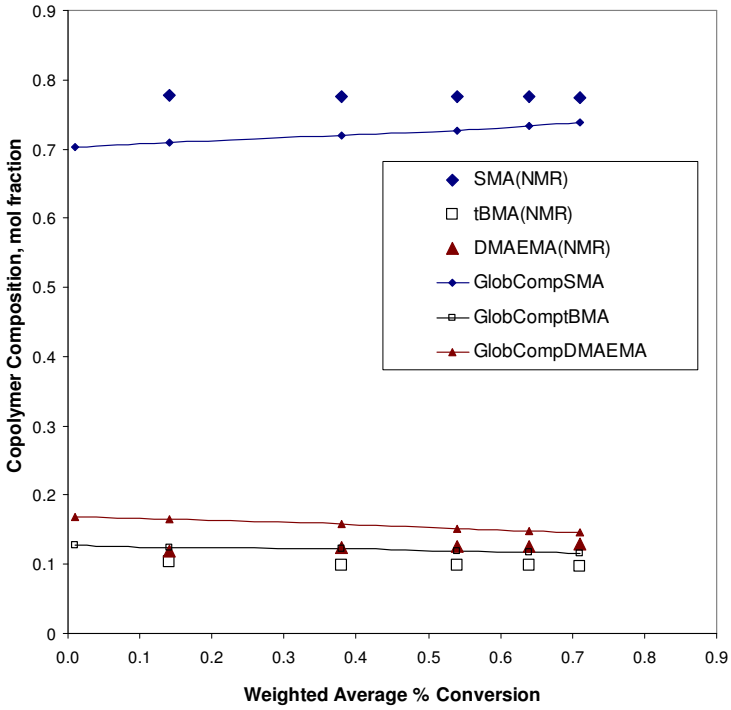


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Figure 10. Calculated and experimental polymer compositions from terpolymerization of a 76/10/12 molar mixture of SMA, DMAEMA, and tBMA. (DP 186)

The reactivity ratios for binary monomer mixtures of SMA, tBMA and DMAEMA predict for an initial feed mixture of 77/11/12 (DP 135) of SMA:tBMA:DMAEMA (experimental NMR), an instantaneous composition of 77/11/12 after 54 % conversion, for an initial feed composition of 79/11/11 of SMA:tBMA:DMAEMA (DP 278), an instantaneous composition of 76/12/12, for an initial 80/10/10 mixture of monomers (DP 360), an instantaneous composition of 78/10/11, and for an initial 77/11/12 mixture of monomers (DP 532), an instantaneous composition of 79/11/10 respectively.

Table 14. Data for Compositions in Large Scale RAFT Terpolymer Syntheses

sample	DP	feed comp.[a] (NMR)			comp. after partial conv.[a]			% conv.[b]
		SMA	tBMA	DMAEMA	SMA	tBMA	DMAEMA	
7341	135	0.777	0.105	0.118	0.779	0.101	0.119	54
7794	278	0.786	0.107	0.107	0.794	0.102	0.103	37
7703	360	0.798	0.098	0.104	0.799	0.098	0.104	48
7622	532	0.772	0.113	0.115	0.774	0.109	0.117	71

[a]From integrated ^{1}H NMR spectra at room temperature spectra and after partial conversion.

[b]Weighted average percent conversion.

Table 15. Copolymer Compositions in Large Scale Terpolymer Syntheses from Reactivity Ratios

sample	% conv.[a]	instantaneous copolymer comp. after partial conv.[b]			global copolymer comp. after partial conv.[b]		
		SMA	tBMA	DMAEMA	SMA	tBMA	DMAEMA
7341	54	0.769	0.108	0.123	0.739	0.119	0.143
7794	37	0.758	0.118	0.124	0.741	0.124	0.135
7703	48	0.783	0.104	0.113	0.759	0.112	0.128
7622	71	0.792	0.106	0.102	0.744	0.124	0.132

[a]From integrated ^{1}H NMR spectra of samples before polymerization and after partial conversion (weighted average percent conversion).

[b]Calculated using reactivity ratios.

The experimental compositions of the starting monomer mixtures (based on weights of monomers) for the above terpolymers was 79/11/10. These data agree well with cumulative polymer compositions calculated from residual monomer contents in solution The feed compositions of the three monomers have been calculated from ^{1}H NMR spectroscopy, while the instantaneous copolymer compositions have been determined using Procop.

The feed and copolymer compositions of the large scale ternary reaction mixtures containing SMA, tBMA, and DMAEMA in solution were determined in a similar manner as the small scale terpolymer mixtures. From the data given in Tables 15 and 16, it is evident that the feed compositions of the starting reaction mixtures and that after partial polymerization do not differ much from our target copolymer compositions of 80:10:10 respectively of SMA, tBMA and DMAEMA. This means there was very little drift in the copolymer compositions over the course of the polymerizations.

The compositions of the ternary reaction mixtures in solution were also estimated using the reactivity ratio values for binary monomer mixtures, calculated by Procop.[18] The input data in Procop involved the reactivity ratios of the three monomer pairs (Table 1, Chapter I), the mole fractions of the monomers in the feed mixture, and the weighted average percent conversion of the three monomers determined from ^{1}H NMR spectroscopy.[18] Moreover, the instantaneous copolymer compositions determined by using Procop and the compositions calculated from NMR differ by 0.012–0.034 mol fraction for SMA, 0.003-0.015 mol fraction for tBMA and 0.005-0.020 for DMAEMA in all large scale terpolymers.

We have not been able to confirm the cumulative polymer compositions by NMR analysis of the polymers isolated. We have however determined the compositions of SMA and DMAEMA repeat units in the isolated terpolymers from the integrated ^{1}H NMR spectra. The signal corresponding to the five protons of SMA (CH_2-CH-CH_2) overlaps with the signal due to the O-CH_2 peak in DMAEMA from 3.70-4.40 ppm. However, the peaks due to the $N(CH_3)_2$ in DMAEMA are well resolved at 2.25 ppm, and were used to calculate the area under that peak for one proton. The deduction for two protons of DMAEMA was then made from the collective area under the peaks at 3.70-4.40 ppm and the relative amounts of SMA and DMAEMA in the terpolymer were determined.

Although we have been able to determine the compositions of SMA and DMAEMA, determination of tBMA composition in the terpolymers still remains a challenge. This is because the only characteristic peak of tBMA that can be used for this purpose is the *tert*-butyl peak at 1.40 ppm. The problem arises because this peak overlaps with the two CH_3 peaks from the ketal ring in SMA and possibly small components of the backbone CH_3 signals, as a result of which there is very poor baseline resolution to do accurate NMR integrations. It may be possible, however, to determine the composition of tBMA from the ^{13}C NMR spectrum of the terpolymer by doing a quantitative ^{13}C NMR experiment and integrating the peaks arising from the *tert*-butyl methyl's at 28 ppm that are well resolved from the two CH_3's of SMA at 18- 20 ppm.

Longitudinal Spin Relaxation Times (T_1) of DP 90 Terpolymer. The longitudinal relaxation time T_1 helps to determine how often we can scan or what the

length of the relaxation delay (d_1) should be for quantitative ^{1}H NMR analysis. Since relaxation is an exponential decay process, it is considered that a delay of five times T_1 allows enough time for complete relaxation of the spin system to thermal equilibrium, before the beginning of the next pulse. The maximum signal is obtained by using a 90^o pulse. The measured relaxation times (T_1s) for the terpolymer (DP 90) are listed in Table 16.

Table 16. Proton Relaxation Times of DP 90 Terpolymer

type of proton	chemical shift (ppm)	T_1 (sec)
backbone CH_3	0.862	0.28-0.29
backbone CH_2	1.79	0.46
tert-butyl	1.39	0.61
SMA (CH_3's)	1.33	0.65
SMA (CH_2-**CH**)	4.30	0.92
SMA (CH-**CH_2**)	4.05	0.69
SMA (O-**CH_2**)	3.94	0.62
	3.76	0.77
DMAEMA(2H)	3.72	0.68
residual monomer CH_3	1.92	0.94

The T_1 values for the monomer CH_3 signals at 1.92 ppm (0.94 sec) and SMA (CH_2-C**H**) between 3.72-4.30 ppm (0.92 sec) have the longest relaxation times. Since the relaxation delay time (d_1) needs to set to at least 5 times T_1 (in this case 4.7 sec), the

delay time used in spectra of the polymers (5.0 sec), is long enough for a 90^{o} flip angle to allow for sufficient relaxation of all protons.

GPC Analysis of RAFT Terpolymers. The results from the GPC analyses of the RAFT terpolymers are presented in Table 17.

Table 17. GPC Data for RAFT Ternary Copolymers

sample	DP	% conv.[a]	$M_{n,th}$[b]	$M_{n,GPC}$[c]	M_w/M_n[c]	$M_{n,GPC}$[d]	M_w/M_n[d]
6571	90	78	15000	-	-	6800	1.30
6652	98	38	16000	8800	1.39	7900	1.36
6633	186	71	32000	12300	1.44	11000	1.38
7341	135	54	22000	11000	1.33		
7794	278	37	48000	13000	1.46		
7703	360	48	60000	11000	1.42		
7622	532	71	90000	15000	1.42		

[a]From integrated ^{1}H NMR spectra of samples before polymerization and after partial conversion (weighted average percent conversion).

[b]$M_{n,th} = \{([M]_o M_M C)/ [CTA]\} + M_{CTA}$

where $[M]_o$, $[CTA]$, M_M, M_{CTA} and C are the initial monomer concentration, the initial CTA concentration, the molecular weight of the monomer, the molecular weight of the RAFT CTA and the weighted average percent conversion respectively.[4]

[c]Calibration done using poly(methyl methacrylate) standards.

[d]Calibration done using polystyrene standards.

As seen in Table 17, the theoretical and measured molecular weights are not in agreement with each other, with the theoretical molecular weights being more than twice that of the observed molecular weights. The molecular weights (M_n) of samples 6652 and 6633 using linear poly(styrene) and poly(methyl methacrylate) standards do not differ much from each other.

The huge difference between $M_{n,th}$ and $M_{n,GPC}$ could be due to the smaller coil expansion of the terpolymer, resulting in smaller hydrodynamic volumes (longer retention times), and consequently lower relative molecular weights. The narrow molecular weight distributions or polydispersities ($M_w/M_n < 1.5$) however, provide evidence for the controlled nature of these RAFT terpolymerizations.

We have measured only relative molecular weights. Although the use of standards with low polydispersities allows the corelation of retention time with molecular weight, the actual correlation is with the hydrodynamic volume. The absolute values of molecular weights of terpolymers will need to be measured using aqueous size exclusion chromatography by combining refractive index and differential viscometer detectors and the application of the Mark-Houwink equation or by light scattering detection.

Functional Group Conversions

Quaternization of DMAEMA in RAFT Terpolymers.[8] The experimental data for quaternization of RAFT terpolymers are presented in Table 18. The quaternization procedure is shown in Scheme 7, Chapter I.

Table 18. Experimental Data for Quaternization of RAFT Terpolymers

terpolymer sample	DP	terpolymer (mg)	THF (mL)	CH_3I (mL)	DMAEMA[a] mmol	%[b] recovery
6571	90	43	3.5	0.80	0.0993	92
6652	98	44	3.5	0.87	0.0106	86
6633	186	53	3.5	1.37	0.0171	88
7341	135	350	15	5.62	0.695	98
7794	278	750	15	16.2	2.01	90
7703	360	500	15	9.71	1.20	97
7622	532	550	15	7.22	0.889	94

[a]Calculated from % conversion of DMAEMA in terpolymer after partial conversion and moles of DMAEMA in feed mixture.

[b]Isolated quaternized terpolymer (includes the weight gain due to CH_3I).

The ^1H NMR spectrum of quaternized DP 532 terpolymer is shown in Figure 15 (appendices). The disappearance of the characteristic strong peak at 2.35 ppm corresponding to the $N(CH_3)_2$ group of DMAEMA in the terpolymer, and the presence of a new peak at 3.60 ppm corresponding to the $-N^+(CH_3)_3$ groups demonstrates complete quaternization.

The small scale experiments were carried out with the aim of synthesizing terpolymers with a degree of polymerization 100 (entry 4, Table 2), with an 80:10:10 mol ratio of SMA:tBMA:DMAEMA respectively. These experiments were done to develop the methods necessary to carry out the functional group transformations of terpolymers to

water-soluble polyampholytes, determine the compositions of the terpolymers from ^{1}H NMR spectroscopy and analyze the compositions of terpolymers by comparing the results from NMR and Procop (based on reactivity ratios of binary monomer mixtures). The amounts of polyampholytes isolated from the small scale experiments were insufficient to carry out further analyses. In order to isolate large quantities of terpolymers, large scale experiments (> 1 g) with the aim of achieving a degree of polymerization 300 (entry 2, Table 2) at 40 % conversion, with an 80:10:10 mol ratio of SMA, tBMA and DMAEMA respectively were carried out. Since we wanted to carry out the polymerizations to only about 40-50 % and not 100 % conversion to avoid a drift in the copolymer compositions, we had to start with a much higher ratio of [M]/[CTA]. For example in order to reach our target of DP 300 at 40 % conversion, [M]/[CTA] = 750 is required at the start of RAFT polymerization.

Acid-catalyzed Deprotection of Quaternized Terpolymers.[1,9] The results of the acid-catalyzed deprotection procedures are summarized in Table 19.

Table 19. Acid-catalyzed Deprotection of Small Scale RAFT Terpolymers

deprotected sample	amount (mg)	sample treated with	days at 25 °C	h at 65 °C	observations
6571-1	39	CF_3CO_2H/CH_2Cl_2[a]	4		*t*-butyl ester left
		HCl/ dioxane-d_8[a]	4		Water-insoluble gel
6652-1	12	HCl/dioxane-d_8[b]	26	16	Water-soluble
6652-2	21	HCl/dioxane-d_8[b]	14		Water-soluble
6652-3	14	$CF_3CO_2H/CDCl_3$[c]	14		*t*-butyl ester left
6633-1	12	HCl/dioxane-d_8[b]	20	16	Water-soluble
6633-2	28	HCl/dioxane-d_8[b]	26		Water-soluble

[a]CF_3CO_2H (0.21 mL) in CH_2Cl_2 (3.0 mL) and aq. 1M HCl (1.0 mL) in 1,4-dioxane (3.0 mL). [b]Aq. 1M HCl (0.17 mL) in 1,4-dioxane-d_8 (0.50 mL). [c]CF_3CO_2H (0.05 mL) in $CDCl_3$ (0.60 ml).

Sample 6652-1 (original terpolymer sample with DP 98) was treated with aqueous 1M HCl and 1,4-dioxane-d_8 and was monitored by ^{1}H NMR spectroscopy on a daily basis for 26 days. The ^{1}H NMR spectrum of this sample immediately shows new peaks at 2.10 ppm corresponding to the methyl protons in acetone and 1.28 ppm corresponding to the *tert*-butyl peak of *tert*-butyl alcohol. These peaks are indicative of the hydrolysis of the ketal ring in SMA, as well as the conversion of *tert*-butyl groups in tBMA. During this time period at room temperature, it could be clearly seen from the ^{1}H NMR spectra, that the area of the peaks belonging to $C(CH_3)_3$ groups in tBMA at 1.40 ppm and the two CH_3's of SMA at 1.34 ppm and 1.38 ppm had greatly reduced in intensity, but were not completely absent. This sample was then heated in the NMR tube at 65 °C. The ^{1}H NMR

spectrum at 65 ^{o}C was arrayed to monitor the disappearance of the methyl signals. After 16 h, the *tert*-butyl peak at 1.40 ppm and the two CH_3 peaks of SMA were absent. This sample was lyophilized and a ^{1}H NMR spectrum of the deprotected terpolymer in D_2O was acquired. Figure 16 in appendices, represents the ^{1}H NMR spectrum of sample 6652-1 in D_2O. The overall results for the isolated polyampholytes on a small scale are shown in Table 20. Qualitatively, from the ^{1}H NMR spectra of the isolated polyampholytes, after treatment with aqueous 1M HCl and 1,4-dioxane-d_8, the *tert*-butyl peak at 1.40 ppm and the peaks due to the two CH_3's of the ketal ring of SMA at 1.34 ppm – 1.38 ppm are completely absent.

Table 20. Summary of Isolated Water-soluble Polyampholytes

original terpolymer sample	quat. terpolymer (mg)	polyampholyte (mg)	overall recovery[a] polyampholyte (%)
6652-1	12	8.5	41
6652-2	21	17	51
6633-1	12	9.1	40
6633-2	28	22	43

[a]Calculated using the product of % recovery of quaternized terpolymer (column 7, Table 18) and % recovery of polyampholyte.

Deprotection of Quaternized Large Scale RAFT Terpolymers. The results of deprotection of large scale terpolymers are summarized in Table 21.

Table 21. Acid-Catalyzed Deprotection of Large Scale RAFT Terpolymers

original terpolymer sample	amount (mg)	deprotected sample	treated with	conditions	observations
7341-1	100	7541	HCl/1,4-dioxane[a]	7 days at 25 ^{o}C	gel formed
7622-1	97	7681	HCl/1,4-dioxane-d_8[b]	54 h at 25 ^{o}C	*t*-butyl peak left
7622-2	185	7872	Amberlyst 15/ methanol[c]	26 ^{o}C – 50 ^{o}C	SMA and *t*-butyl CH_3's left
7622-3	100	7763	HCl/1,4-dioxane-d_8[d]	34 h at 45 ^{o}C 10 h at 65 ^{o}C	*t*-butyl peak left gel formed
7703	103	7761	CF_3CO_2H/ CD_2Cl_2[e]	3.5 h at 28 ^{o}C 5 h at 28 ^{o}C	*t*-butyl peak left phase separation

[a]Aq. 1M HCl (4.0 mL) in 1,4-dioxane (12.0 mL). [b]Aq. 1M HCl (0.16 mL) in 1,4-dioxane-d_8 (0.45 mL). [c]Amberlyst 15 (0.500 g) in CH_3OH (5.0 mL). [d]Aq. 1M HCl (0.2 mL) in 1,4-dioxane-d_8 (0.6 mL). [e]CF_3CO_2H (0.18 mL) in CD_2Cl_2 (0.71 mL).

Sample 7622-3, 100 mg of terpolymer (DP 532) was treated with 1,4-dioxane-d_8 (0.60 mL) and aqueous 1M HCl (0.20 mL). The sample was transferred to an NMR tube and a ^{1}H NMR spectrum at room temperature was acquired daily for 8 days to monitor disappearance of *tert*-butyl and SMA methyl signals. This sample was then heated at 65 ^{o}C for 10 hours. The sample had turned viscous and some of it formed a film on the inner walls of the NMR tube and thus, not all of the sample could be poured out. The ^{1}H NMR spectrum of the freeze dried sample indicates the formation of glycerol. This is evident from the presence of several sharp peaks between 3.20 ppm to 4.40 ppm. Heating the

terpolymer sample at 65 ^{o}C may have been too harsh, and thus resulted in the hydrolysis of the ester units in SMA.

Samples 7341-1 and 7622-3 formed gels. One reason for gel formation could be a cross-linked polymer. The deprotection reactions are acid-catalyzed, and could lead to trans-esterification between the alcohol groups of the partially deprotected SMA (GMA) and other ester units in tBMA. One way to avoid the formation of gels would be to carry out the deprotection step under milder conditions, without heating at high temperatures to avoid cross-linking. Another possibility would be to first dialyze the sample to remove HCl and lyophilize the sample. This step could prevent cross-linking arising from the presence of traces of HCl trapped in the terpolymer matrix.

To achieve the goal of synthesizing polyampholytes with compositions listed in Table 2, we need to find a suitable deprotection method that results in the quantitative conversion of *tert*-butyl ester units into methacrylic acid (MAA) units, and subsequently hydrolyzes SMA to GMA. We have been able to determine the compositions of the terpolymers from residual monomers left in solution by ^{1}H NMR spectroscopy. But, we need to be able to determine the composition of the isolated polyampholyt**e** and compare it with the precursor terpolymer composition by doing quantitative ^{13}C NMR spectroscopy. In this case, the peak areas of the well resolved backbone CH_3 peaks could be integrated and used to determine the copolymer compositions. The absolute values of molecular weights and polydispersities of the polyampholytes will need to be measured using aqueous size exclusion chromatography by combining refractive index and differential viscometer detectors and the application of the Mark-Houwink equation or by light scattering detection.

Conclusions

The monomer solketal methacrylate (SMA, **10**) has been synthesized on a scale greater than 100 g, in 63 % yield and characterized by ^{1}H and ^{13}C NMR spectroscopy. The RAFT chain transfer agent, cumyl dithiobenzoate (CDB, **13**) was synthesized in 42 % yield and characterized by elemental analysis and ^{1}H NMR, ^{13}C NMR, infrared and UV-visible spectroscopy.

The GPC analyses of RAFT homopolymers mediated by 2-cyanoprop-2-yl dithiobenzoate (CPDB) indicate that M_n increases linearly with percent conversion, and the polydispersities were $M_w/M_n < 1.3$. This is a characteristic feature of controlled radical polymerizations.

Ternary copolymers of SMA, tBMA, and DMAEMA with narrow molecular weight distributions have been synthesized on a small scale by the RAFT technique in 1,4-dioxane-d_8 using CDB as the chain transfer agent. The data on copolymer compositions calculated from ^{1}H NMR spectroscopy, and the instantaneous and global copolymer compositions, calculated from binary copolymer reactivity ratios indicate that the terpolymers do not drift in composition at higher conversions. These results are encouraging, since our goal is to synthesize random polyampholytes with homogeneous compositions. Based on the results of small scale terpolymer syntheses, terpolymers of SMA, tBMA and DMAEMA were synthesized on a scale > 1 g. All of the terpolymers were characterized by ^{1}H and ^{13}C NMR spectroscopy and gel permeation chromatography. Complete functional group conversions of the small scale RAFT terpolymers to water-soluble polyampholytes have been accomplished within the limits

of NMR detection. The small scale water-soluble polyampholytes have been isolated in average overall recoveries of 60 % - 79 %. Moreover, the solutions of all isolated polyampholytes in D_2O have been stable for 1 year, and no phase separation has been observed. However, we have not been able to determine the compositions of these polyampholytes from the existing ^1H NMR spectra, due to the broad NMR lines and poor baseline resolution.

Currently, methods for complete deprotection are being tested. A 50/50 mixture of 1,4-dioxane and concentrated HCl at room temperature for 4-8 h now results in complete deprotection without any gel formation.[21]

Experimental Section

Materials. Solketal (Aldrich, 98%) and methacryloyl chloride (Aldrich, 97%) were used without further purification. Anhydrous sodium carbonate (Aldrich), copper chloride dihydrate (EM Science), benzyl chloride (Alfa Aesar, 99+%), sulfur (Alfa Aesar, 99.5 %), sodium methoxide (Alfa Aesar, 25 % solution in methanol w/w), aluminum oxide (EM Science, neutral activity I), and silica gel (60 A^o, 70-230 mesh size, Aldrich) were used as received. Reagent grade toluene, triethylamine, *n*-hexane, methanol, dichloromethane and diethyl ether were used as received. 2-Cyanoprop-2-yl dithiobenzoate was provided by Dr. Craig Hawker (IBM Almaden Laboratories). *tert*-Butyl methacrylate (Aldrich) and 2-(*N,N*-dimethylamino)ethyl methacrylate (Polysciences, Inc.) were purified by passing through a short column of basic alumina to remove any phenolic inhibitors. 2,2'-Azobisisobutyronitrile (AIBN) (Aldrich) was recrystallized from ethanol. Tetrahydrofuran (Aldrich, HPLC grade), 1,4-dioxane

(Aldrich, anhydrous, 99.8 %) and trifluoroacetic acid (Aldrich) were used as received. Methyl iodide and hydrochloric acid (Fisher Scientific), and *p*-xylene (Eastman Chemicals) were used as received. Toluene-d_8 (Aldrich, 99.9 %D), $CDCl_3$ (Aldrich, 99.8 atom %D), CD_2Cl_2 (Aldrich, 99.5 atom % D), 1,4-dioxane-d_8 (99 atom % D) and D_2O (99.9 atom % D), (Cambridge Isotope Laboratories, Inc.) were used as received. Amberlyst 15 (wet) ion exchange resin (Aldrich) was washed with 10 bed volumes of CH_3OH and 10 bed volumes of deionized water prior to use. Spectra/Por dialysis tubing (MWCO 3500, Spectrum) was washed under a stream of deionized water and left to soak in a 1L beaker with deionized water to get rid of sodium azide.

Characterization

The 400 MHz ^1H NMR spectra of the homopolymers were recorded using the quad probe and toluene-d_8 as the NMR lock solvent at 60 $\pm$ 1 ^oC. The ^1H and ^{13}C NMR spectra of the ternary copolymer mixtures were recorded using the quad probe and 1,4-dioxane-d_8 as the NMR lock solvent at 75 $\pm$ 1 ^oC. The following conditions were used to acquire the ^1H NMR spectra of the terpolymers: 44 K data points, flip angle of 20 ^{o} and a relaxation delay of 5 s. Thirty two scans were accumulated for each spectrum.

The number average molecular weights (M_n) and molecular weight distributions (M_w/M_n) of the homopolymers and ternary copolymers were determined using an Agilent 1100 series instrument equipped with two PLGEL 10 µm MIXED-B, 300 x 7.5 mm columns and a refractive index detector. In polymerizations employing 2-cyanoprop-2-yl dithiobenzoate as RAFT CTA, no polymer was precipitated. Instead, 1 mL of tetrahydrofuran (THF) was added via a 1 mL disposable syringe to 5 mg of each of the

homopolymer solutions of SMA, tBMA and BEMA, collected after partial polymerization at 60 $\pm$ 1 ^{o}C. Measurements were performed in tetrahydrofuran (THF) as the mobile phase at 40 ^{o}C with a flow rate of 1.0 mL/min.

The molecular weights of the homopolymers were calibrated against linear polystyrene standards in the range of 1,800,000-500 g/mol. The molecular weights of the small scale terpolymers were calibrated against polystyrene and poly(methyl methacrylate) standards obtained from Polymer Labs, Inc. (now a division of Varian, Inc.) in the range of 1,800,000-500 g/mol and 625,500-1430 g/ mol respectively. The molecular weights of the large scale terpolymers were calibrated against linear poly(methyl methacrylate) standards. All GPC samples were filtered through a Whatman polypropylene (0.2 μm) filter prior to injection. The samples used for GPC analyses were prepared at a known concentration (5 mg/ mL) and an injection volume of 10 μL was used.

The elemental analysis data was provided by Desert Analytics.

Longitudinal Spin Relaxation Times (T_1) of DP 90 Terpolymer. The ^{1}H 90^{o} pulse was determined to be half of the 180^{o} pulse where peaks are equally positive and negative and was found to be 22.5 μs (transmitter power setting of 53). The delay time was first arrayed from 1 s to 6 s, to find the appropriate delay time to be set to measure the 90^{o} pulse width. After a delay of 5 s, the intensity of the peaks did not increase further. To determine the 90^{o} pulse width, a one dimension ^{1}H NMR spectrum was acquired and the spectral width was set to cover the peaks of interest. The pulse width was arrayed from 3 to 60 seconds to estimate the range in which the 180^{o} pulse width

appeared with peaks that were equally positive and negative, after which the array for pw was fine tuned to a much narrow range to accurately determine the 180^{o} pulse width and thus the 90^{o} pulse width. Next, a measurement for the longitudinal relaxation time was made, by setting the 90^{o} and 180^{o} pulses, and the appropriate delay time.

Synthesis of Solketal Methacrylate (SMA, **10**)[1]**.** Toluene (1000 mL) was added to a four neck 3 L round bottom flask and the flask was evacuated. Solketal (**15**) (2.54 mol, 315 mL) was added next, and finally triethylamine (2.54 mol, 357 mL) was added. The round bottom flask was chilled in an ice bath to 6 - 8 ^{o}C. Methacryloyl chloride (1.91 mol, 187 mL) was added dropwise, through a pressure equalizing addition funnel over a period of 3.5 h with stirring. After the completion of methacryloyl chloride addition, the flask was left to warm to room temperature and the contents were stirred for 16 h. The triethylammonium chloride formed was filtered using Whatman filter paper number 4. The extractions were carried out in two 1L separatory funnels, wherein 250 mL of the filtrate was washed thrice with deionized water (100 mL). The lower aqueous phase washings were discarded. The upper organic phases wee drained into another Erlenmeyer flask. All of the organic phases were combined and dried over anhydrous sodium carbonate until the Na_2CO_3 stopped clumping together and filtered using a 600 mL fritted glass filter (pore size = 10-20 μm). $CuCl_2.2H_2O$ (150 mg) was added as an inhibitor prior to rotary-evaporating toluene under vacuum. The crude solketal methacrylate was purified by vacuum distillation in three batches. The three batches distilled at reduced pressures ranging 0.50–0.75 mmHg, as recorded on a McLeod gauge. The temperature of the solution in the round bottom flask ranged from 78 ^{o}C - 82 ^{o}C,

when the liquid started to distill, and stayed constant at 79 ^{o}C. The rate of distillation in all the batches was about 1 drop per second, with no bumping. The distillate (a colorless liquid) was stored in the freezer. Pure solketal methacrylate (**10**) was obtained as a colorless liquid (126 g, 63 % yield). ^{1}H NMR (Figures 8 and 9 in appendices) (400 MHz, $CDCl_3$) δ: 6.10 and 5.59 (s, =C**H$_2$**), 4.31 (m, CH_2-C**H**), 4.16 (s, CO_2-C**H**-H), 4.15 (m, CO_2-CH-**H**), 4.04 (m, -CH-C**H**-H), 3.74 (-CH-CH-**H**), 1.96 (s, -C**H$_3$**), 1.38 and 1.34 (s, 2 -C**H$_3$**). ^{13}C NMR (Figure 10 in appendices) (100 MHz, $CDCl_3$) δ: 166.9 (-**C**O_2), 135.7 (CH_2=**C**-CH_3-CO_2-), 125.9 (-**C**$(CH_3)_2$), 109.6 (=**C**H_2), 73.5 (-CO_2-**C**H_2-CH-), 66.2 (-CO_2-CH_2-**C**H-), 64.5 (-O-CH-**C**H_2-O), 26.5 and 25.2 (2 **C**H_3's of ring), 18.2 (-**C**H_3).

Synthesis of Cumyl Dithiobenzoate (CDB, **13**)**.**[2] Benzyl chloride (0.100 mol, 12.6 g) was added to a stirring mixture of methanol (50 mL), sulfur (0.20 mol, 6.4 g) and sodium methoxide solution (0.200 mol, 45.7 mL) over a period of one h. The reaction mixture was heated at 70 °C under a nitrogen atmosphere for 5 h. The mixture was allowed to cool to room temperature. The sodium chloride salt was filtered and washed with methanol (20 mL). The combined filtrate was concentrated on a rotary evaporator until methanol was removed. The brown colored mixture was re-dissolved by adding water (100 mL). The brownish aqueous solution was extracted three times with diethyl ether (3 x 50 mL). The aqueous layer was retained. The purpose of this step was to remove any unreacted starting material and other organic soluble by-products. Another portion of diethyl ether (50 mL) was added and the aqueous layer was acidified with concentrated hydrochloric acid (about 10 mL). The diethyl ether layer was separated and the aqueous layer was extracted twice with ether (2 x 50 mL). The organic layers were

combined and dried over anhydrous calcium chloride. The ether was evaporated to give 8.0 g dithiobenzoic acid (52 % yield). The product was a dark purple oil, and because of its low stability, it was used immediately in the next step.

A mixture of dithiobenzoic acid (0.0519 mol, 7.99 g), α-methylstyrene (0.0638 mol, 7.54 g) and carbon tetrachloride (40 mL) was heated at 70 ^{o}C for 4 h under a nitrogen atmosphere. The solvent and excess α-methylstyrene were removed on a rotary evaporator. A ^{1}H NMR spectrum of the purple oil in $CDCl_3$ showed the presence of vinyl protons, thus indicating that it was a mixture of cumyl dithiobenzoate and α-methylstyrene. The mixture was separated by chromatography using 200 g of alumina (activity III) deactivated with 8.2 g of water. The mixture of alumina and water was mixed thoroughly for 3 hours by tumbling it on the rotary evaporator in order to let it equilibrate before loading it onto the column. On eluting with *n*-hexane, the purple compound separated into different colored bands on the column, with colors ranging from pale yellowish orange at the top of the column to purplish pink at the bottom. The fractions that were purple in color were combined and rotary-evaporated under vacuum to give cumyl dithiobenzoate (6.1 g, 32.6 % yield) as a dark purple oil. ^{1}H NMR (Figure 11, appendices) (400 MHz, $CDCl_3$) δ: 2.03 (s, 6H), 7.15-7.50 (m, 8H) and 7.78 (m, 2H). ^{13}C NMR (Figure 12, appendices) (100 MHz, $CDCl_3$) δ: 146.25 (s, quaternary C adjacent to C=S), 144.16 (s, quaternary C adjacent to $–C(CH_3)_2$, 126.58 – 131.76 (aromatic ring C's), 56.47 (s, $-C(CH_3)_2$), 28.27 (s, 2 CH_3). IR (Figure 13, appendices) (cm^{-1}): 3053 and 3026 (sp^2 C-H stretch), 2966 and 2920 (sp^3 C-H stretch), 1596 and 1590 and 1496 and 1443 (C=C ring stretch), 1043 (C=S stretch). UV-Visible (Figure 14): Absorption maximum at

522 nm due to the thiocarbonylthio (S-C=S) chromophore. Anal. Calcd for $C_{16}H_{16}S_2$: C, 70.54; H, 5.93; S, 23.54. Found: C, 67.96; H, 5.99; S, 26.24.

General Procedure for Synthesis of Homopolymers. A) Cumyl Dithiobenzoate as RAFT CTA.[4] The monomers, SMA, tBMA, and DMAEMA, cumyl dithiobenzoate, *p*-xylene and toluene-d_8 were degassed by bubbling nitrogen gas through them. Stock solutions of cumyl dithiobenzoate (0.012 g in 1.0 mL in toluene-d_8) and AIBN (0.0040 g in 1.0 mL of toluene-d_8) were prepared. SMA (0.300 mL, 1.65 x 10^{-3} mol), AIBN (0.100 mL of stock solution, 2.43 x 10^{-6} mol), CDB (0.100 mL of stock solution, 4.39 x 10^{-6} mol), an internal standard, *p*-xylene (0.5 mmol, 0.06 mL) and toluene-d_8 (0.15 mL) were measured into a scintillation vial. The homogenous solution was transferred to an NMR tube and nitrogen gas was blown in a gentle stream, through a syringe needle into the tube. The NMR tube was firmly capped with a plastic cap and the contents in the tube were mixed by gently tilting the tube several times. The tube was placed in the ^{1}H NMR Quad probe, and a room temperature spectrum was acquired. The temperature of the probe was equilibrated to 60 $\pm$ 1 ^{o}C and the probe was shimmed and locked at the temperature setting of the probe. The homopolymerizations were conducted at 60 $\pm$ 1 ^{o}C for a period of 20 h. The ^{1}H NMR spectra were arrayed to collect data every 2 h. The polymerization was quenched by immersing the NMR tube in a beaker of ice-cold water. The percent conversions of monomers with respect to time were determined by integrating the peaks corresponding to the vinyl protons in the monomers relative to *p*-xylene. The homopolymers were precipitated by adding the solution of the homopolymer to 5.0 mL of vigorously stirring *n*-hexane. The homopolymers were isolated by vacuum

filtration and dried under vacuum at room temperature for 24 h. The homopolymers isolated were pink in color. Poly(SMA): (48.6 % yield); pink powder; ^{1}H NMR (Figure 15, appendices) (400 MHz, $CDCl_3$) δ: 6.10 and 5.60 (s, residual =C**H$_2$**, monomer), 4.31 (m, CH_2-C**H**), 4.16 (s, CO_2-C**H**-H), 4.15 (m, CO_2-CH-**H**), 4.04 (m, -CH-C**H**-H), 3.74 (-CH-CH-**H**), 1.70-2.10 (backbone -C**H$_2$'s**), 1.50 (peak due to H_2O in $CDCl_3$), 1.38 and 1.42 (2 -C**H$_3$'s**, SMA), 0.70-1.30 (backbone -C**H$_3$'s**). IR (NaCl plate, $CDCl_3$, cm^{-1}): 2887 and 2935 (sp^3 C-H stretch), 1731 (C=O stretch) and 1153 (C-S stretch). Poly(tBMA): (52.0 % yield); pink lustrous solid; ^{1}H NMR (Figure 16, appendices) (400 MHz, $CDCl_3$) δ: 6.0 and 5.50 (s, residual =C**H$_2$**, monomer), 2.28 (s, -C**H$_3$**, *p*-xylene), 1.70-2.10 (backbone -C**H$_2$'s**), 1.50 (peak due to H_2O in $CDCl_3$), 1.40-1.42 (-C(C**H$_3$)$_3$**, tBMA), 0.90-1.30 (backbone -C**H$_3$'s**). IR (NaCl plate, $CDCl_3$, cm^{-1}): 2976 and 2935 (sp^3 C-H stretch), 1140 (C-S stretch), and 1721 (C=O stretch). Poly(DMAEMA): (48.8 %); pink fluffy powder; ^{1}H NMR (Figure 17, appendices) (400 MHz, DMSO-d_6) δ: 4.20 (br, -OC**H$_2$**), 2.90 (br, -NC**H$_2$**), 2.50 (-N(**CH$_3$)$_2$**), 1.60-2.05 (backbone -C**H$_2$'s**), 0.70-1.10 (backbone -C**H$_3$'s**).

B) 2-Cyanoprop-2-yl Dithiobenzoate as RAFT CTA.[4] Stock solutions of 4.0 mg AIBN in 0.50 mL of toluene-d_8 and 12.0 mg CPDB in 0.50 mL of toluene-d_8 were prepared. tBMA (0.263 g, 1.85 x 10^{-3} mol), AIBN (0.400 mg, 2.43 x 10^{-6} mol), CPDB (1.20 mg, 4.39 x 10^{-6} mol), and solvent (toluene-d_8) (0.25 mL) were measured into a scintillation vial. Nitrogen gas was bubbled in a gentle stream, into the solution contained in the vial**,** and the homogenous solution was transferred through a syringe needle into an NMR tube. A stream of nitrogen gas was bubbled through a syringe needle into the NMR tube, and the tube was firmly capped with a plastic cap. The contents in the tube were

mixed by gently tilting the tube several times. The NMR tube was placed in the ^{1}H NMR Quad probe and a room temperature spectrum with thirty two transients was acquired. The temperature of the probe was equilibrated to 60 $\pm$ 0.1 ^{o}C and the probe was shimmed and locked at this temperature. The polymerizations were conducted at 60 $\pm$ 1 ^{o}C, and the ^{1}H NMR spectra were recorded at time intervals of 2 h, 4 h, 8 h, and 12 h respectively for each of the three monomers.

General Procedure for Small Scale RAFT Terpolymer Syntheses.[4] Ternary copolymers of SMA (**10**), tBMA (**11**) and DMAEMA (**12**) in the mole ratio of 8:1:1 were initially synthesized on a small scale, using AIBN as the radical initiator and cumyl dithiobenzoate (**13**) as the RAFT chain transfer agent. In an example preparation for the terpolymer with a degree of polymerization 186, SMA (399 mg, 1.99 x 10^{-3} mol), tBMA (36.0 mg, 2.53 x 10^{-4} mol) and DMAEMA (40.0 mg, 2.54 x 10^{-4} mol) were weighed and transferred to a scintillation vial. Stock solutions of AIBN (6.0 mg AIBN in 1.0 mL of 1, 4-dioxane-d_8) and cumyl dithiobenzoate (30.0 mg CDB in 1.0 mL of 1,4-dioxane-d_8) were prepared. AIBN (0.10 mL) and cumyl dithiobenzoate (0.10 mL) from prepared stock solutions were measured and transferred to the vial. *p*-Xylene (21.0 mg, 1.98 x 10^{-4} mol) was added next followed by 1,4-dioxane-d_8 (0.115 g, 1.19 x 10^{-3} mol). These polymerizations were carried out at 75 $\pm$ 1 ^{o}C, and the ^{1}H NMR spectra were acquired at time intervals of 3 h, 5 h and 6 h respectively, using *p*-xylene as the internal reference. The quad probe was tuned, locked and shimmed prior to acquiring a room temperature spectrum. The temperature was set to 75 ^{o}C and left to equilibrate for 10 min. Thereafter,

the probe was locked and shimmed at 75 $\pm$ 1 ^{o}C. The spectra were arrayed to collect data every hour.

The terpolymers were isolated as bright pink solids by adding each of the ternary copolymer solutions to a vigorously stirring solution of *n*-hexane (12.0 mL). The terpolymers was filtered off and dried under vacuum at room temperature for 48 h. The amounts of terpolymers recovered after drying under vacuum were as follows: DP90 terpolymer (87.9 mg, 46.7 % recovery), DP 98 terpolymer (73 mg, 38.0 % recovery), and DP186 terpolymer (115 mg, 34.0 % recovery). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 176.9 (-**C**=O, SMA, tBMA, DMAEMA), 126.6 (residual SMA monomer), 109.7 (-**C**-, ketal ring), 72.9 (-CH_2-**C**H-CH_2, SMA), 66.4 (-CO_2-**C**H_2-CH-, SMA), 65.4 (-CH_2-CH-**C**H_2-, SMA), 64.7 (-CH_2-**C**H_2-N-, DMAEMA), 54-56 (backbone -**C**H_2's), 44.5-46 (quat-**C**-, tBMA, SMA and DMAEMA), 44.1 (-N(**C**H_3)$_2$, DMAEMA), 28.0 (-**C**(**C**H_3)$_3$, tBMA), 25.3 and 26.6 (2 -**C**H_3's, SMA), 16.8-18.7 (backbone -**C**H_3's).

General Procedure for Large Scale RAFT Terpolymer Syntheses. Stock solutions of AIBN (0.038 g AIBN in 10 mL of 1,4-dioxane) and cumyl dithiobenzoate (0.192 g CDB in 10.0 mL of 1,4-dioxane) were prepared. *p*-Xylene was used as the internal reference to facilitate determination of monomer conversions from ^{1}H NMR integrations of polymerization mixtures prior to, and at the end of the polymerization. These reactions were performed in heavy walled glass tubes that were heated by immersing the tube completely in an 8 L glass beaker filled with ethylene glycol for the required time period. (The monomers were weighed into a scintillation vial and later transferred to an amber-colored bottle. The scintillation vial was rinsed with 1,4-dioxane

(2.0 mL) and the washings were transferred to the amber colored bottle. In an example preparation, SMA (4.20 x 10^{-2} mol, 8.40 g), tBMA (5.68 x 10^{-3} mol, 0.807 g) and DMAEMA (5.09 x 10^{-3} mol, 0.801 g) were weighed and transferred to an amber colored wide neck glass bottle. AIBN (2.31 x 10^{-5} mol, 0.0038 g) and CDB (7.03 x 10^{-5} mol, 0.0192 g) were weighed out from the prepared stock solutions and transferred to the amber colored bottle. A small amount of *p*-xylene (3.81 x 10^{-3} mol, 0.405 g) was added to serve the purpose of an internal reference, followed by 1,4-dioxane (2.40 mL). Using a syringe with a long needle, the mixture was carefully transferred to the heavy walled glass tube, so as not to wet the walls around the constriction in the tube. Prior to polymerizing the sample, 0.25 mL of the ternary mixture was kept aside. To this sample, 0.50 mL of 1,4-dioxane-d_8 was added and a ^{1}H NMR spectrum was acquired at room temperature. The contents in the tube were degassed using four freeze-pump-thaw cycles and flame-sealed under vacuum. The tube was allowed to warm up to room temperature, enclosed in an aluminum wire-mesh to prevent the contents from splattering in the event of an implosion, and subsequently immersed in a pre-heated bath at 75 $\pm$ 2 ^{o}C. The polymerization was quenched by immersing the tube in liquid nitrogen, and the seal was broken using an oxygen flame. A sample of the partially polymerized reaction mixture (0.5 mL) was transferred to a scintillation vial and a ^{1}H NMR spectrum in 1,4-dioxane-d_8 (0.5 mL) was acquired.

The terpolymer was precipitated by dripping the mixture into vigorously stirring *n*-hexane (800 mL). A pink colored polymer precipitated out of solution, was filtered off, and dried under vacuum at room temperature for 24 h. (sample 7341, Figure 22, appendices): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.10 and 5.60 (s, residual =C**H$_2$** of SMA

monomer), 4.20 and 3.65 (residual SMA monomer), 4.31 (m, CH_2-C**H**), 4.16 (s, CO_2-C**H**-H), 4.15 (m, CO_2-CH-**H**), 4.04 (m, -CH-C**H**-H), 3.74 (-CH-CH-**H**), 3.60 (O-C**H$_2$**, DMAEMA), 2.55–2.70 (-N-C**H$_2$**, DMAEMA), 2.35 (-N(**CH$_3$)$_2$**, DMAEMA), 1.93 (-CH_3's residual SMA monomer), 1.70-2.10 (backbone -C**H$_2$'s**), 1.50 (peak due to H_2O in $CDCl_3$), 1.30-1.42 (-$C(CH_3)_3$, tBMA and 2 -CH_3's, SMA), 0.70-1.15 (backbone -C**H$_3$'s**). ^{13}C NMR (Figure 23, appendices) (100 MHz, $CDCl_3$) δ: 176.9 (-**C**=O, SMA, tBMA, DMAEMA), 126.6 (residual SMA monomer), 109.7 (-**C**-, ketal ring), 72.9 (-**C**H_2-CH-CH_2, SMA), 66.4 (-CO_2-CH_2-C**H**-, SMA), 65.4 (-CH_2-CH-**C**H_2-, SMA), 64.7 (-**C**H_2-CH_2-N-, DMAEMA), 54-56 (backbone -**C**H_2's,), 44.5-46 (quat-**C**-, tBMA, SMA and DMAEMA), 44.1 (-N(**C**H_3)$_2$, DMAEMA), (28.0 (-$C(CH_3)_3$, tBMA), 25.3 and 26.6 (2 -CH_3's, SMA), 16.8-18.7 (backbone -**C**H_3's). The amount of residual SMA monomer calculated from the integrated ^{1}H NMR spectrum was 11 mg with respect to the weight of the terpolymer isolated.

Quaternization of DMAEMA in RAFT Terpolymers.[8] In an example preparation for quaternization of DMAEMA on a small scale, to a solution of 0.053 g of DP 186 terpolymer ($1.71x10^{-4}$ mol DMAEMA) in 3.5 mL of THF, was added a large excess (0.022 mol, 1.37 mL) of methyl iodide. This solution was magnetically stirred at room temperature for 48 h. The quaternized terpolymer was obtained by rotary evaporating THF and excess methyl iodide, and drying under vacuum at room temperature for 48 h. The quaternized products from sample 6571 (0.039 g, 90 %), sample 6652 (0.037 g, 84 %), and sample 6633 (0.046 g, 87 %) were characterized by ^{1}H NMR spectroscopy. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.10 and 5.60 (s, residual =C**H$_2$** of

SMA monomer), 3.65–4.40 (m, -C**H**$_2$C**H**C**H**$_2$, 5 H from SMA, 2H from-O-C**H**$_2$, 2H from -N-C**H**$_2$, DMAEMA), 3.60 (m, br, -N$^+$(C**H**$_3$)$_3$ DMAEMA), 2.25 (-C**H**$_3$, *p*-xylene), 1.90 (-C**H**$_3$**'s** from monomer), 1.70-2.05 (backbone -C**H**$_2$**'s**), 1.34-1.42 (-C(C**H**$_3$)$_3$, tBMA and 2 -C**H**$_3$**'s** SMA), 0.70-1.25 (backbone -C**H**$_3$**'s**). Neither isolation of terpolymer by precipitation from *n*-hexane nor alkylation with CH_3I/THF and isolation of the quaternized terpolymer removed the residual SMA monomer.

In an example preparation for quaternization of DMAEMA on a large scale, to 350 mg of DP 135 terpolymer (sample 7341) (6.95 x 10^{-4} mol DMAEMA) contained in a 14/20 50 mL round bottom flask was added 15 mL of THF. The solution was magnetically stirred and methyl iodide (5.62 mL, 9.03 x 10^{-2} mol) was added dropwise. The solution was stirred at room temperature for 4 days. Rotary evaporation of THF and excess CH_3I, and drying in vacuum at room temperature for 24 h gave 336 mg of a pale yellowish brown solid (96 % yield). (sample 7341, Figure 24 in appendices): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.10 and 5.60 (s, residual =C**H**$_2$ of SMA monomer), 3.65–4.40 (m, -C**H**$_2$C**H**C**H**$_2$, 5 H from SMA, 2H from -O-C**H**$_2$, and 2H from -N-C**H**$_2$, DMAEMA), 3.60 (m, br, -N$^+$(C**H**$_3$)$_3$, DMAEMA), 3.30 (residual CH_3, CH_3I), 2.25 (-C**H**$_3$, *p*-xylene), 1.90 (-C**H**$_3$**'s** from monomer), 1.70-2.05 (backbone -C**H**$_2$**'s**), 1.50 (H_2O from $CDCl_3$), 1.34-1.42 (-C(C**H**$_3$)$_3$, tBMA and 2 -C**H**$_3$**'s** SMA), 0.70-1.25 (backbone -C**H**$_3$**'s**).

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CHAPTER III

AQUEOUS ROUTE TO POLYAMPHOLYTES

Introduction

4-Cyano-4-dithiobenzoylthiyl pentanoic acid (CPADB, **16**) has been extensively used in reversible addition-fragmentation chain transfer (RAFT) polymerizations in aqueous media.[1,2] The key to RAFT polymerizations is a highly efficient dithioester chain transfer agent (CTA).[2] The CTA can react with either the primary radicals, derived from a free radical initiator such as azobis-isobutyronitrile (AIBN) (Scheme 3, step III, Chapter I), or a propagating polymer chain, eliminating a free radical R$^{\bullet}$ and forming a new CTA (Scheme 3, step V, Chapter I). In CPADB, the phenyl group imparts a significant stabilization of the intermediate radical, and also promotes addition to C=S bond.[2] Furthermore, CPADB is particularly well suited for aqueous polymerizations because of the presence of the carboxylate moiety on the R-group that imparts water solubility at pH > 5.

4-Cyano-4-dithiobenzoylthiyl pentanoic acid CPADB) has been used in the aqueous RAFT polymerizations of styrenic AB-diblock copolymers.[3] Homopolymers of 2-(*N,N*-dimethylamino)ethyl methacrylate (DMAEMA) with controlled molecular

weights and molecular weight distributions (M_w/M_n < 1.3) have been synthesized in aqueous media by RAFT polymerization using 4,4'-azobis(4-cyanopentanoic acid) (ACPA) as the water-soluble free radical azo-initiator and CPADB as the RAFT CTA.[4] CPADB has also proved to be an effective RAFT CTA for polymerizing methacrylamide monomers.[5]

In this research, CPADB (**16**) was synthesized to study terpolymerizations of ionic monomers, 2-(*N,N*-dimethylamino)ethyl methacrylate (DMAEMA, **12**), methacrylic acid (MAA, **17**), and glyceryl monomethacrylate (GMA, **18**) using the water-soluble azo-initiator 4,4'-azobis(4-cyanopentanoic acid) (ACPA, **19**) in aqueous media. The structures of the above monomers, (CPADB, **16**), azo-initiator ACPA (**19**), 2-[(methacryloyloxy)ethyl]trimethylammonium iodide (MAETMAI, **20**) and 2-[(methacryloyloxy)ethyl]trimethylammonium chloride (MAETMAC, **21**) are shown in Figure 11.

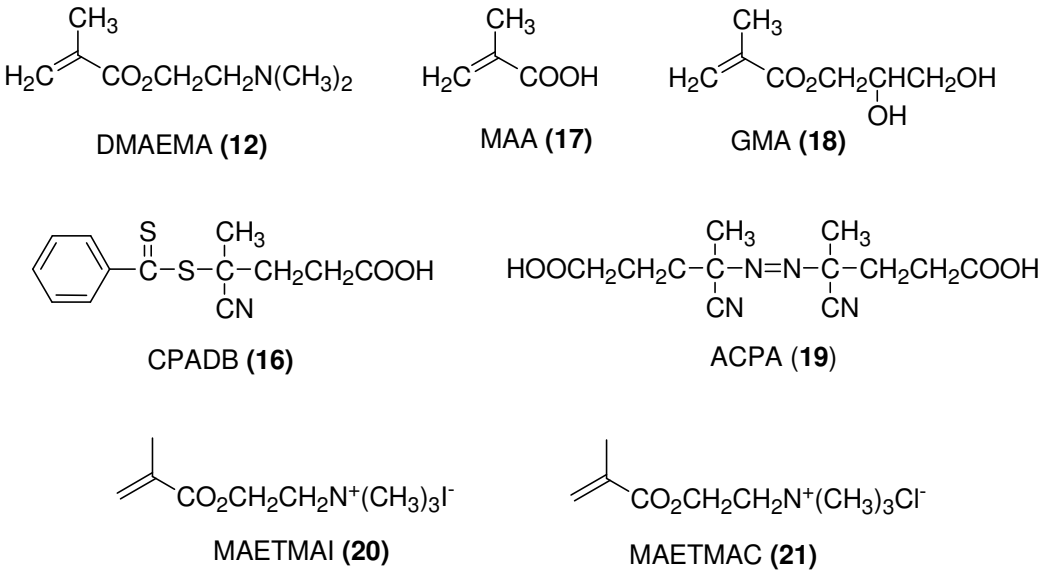


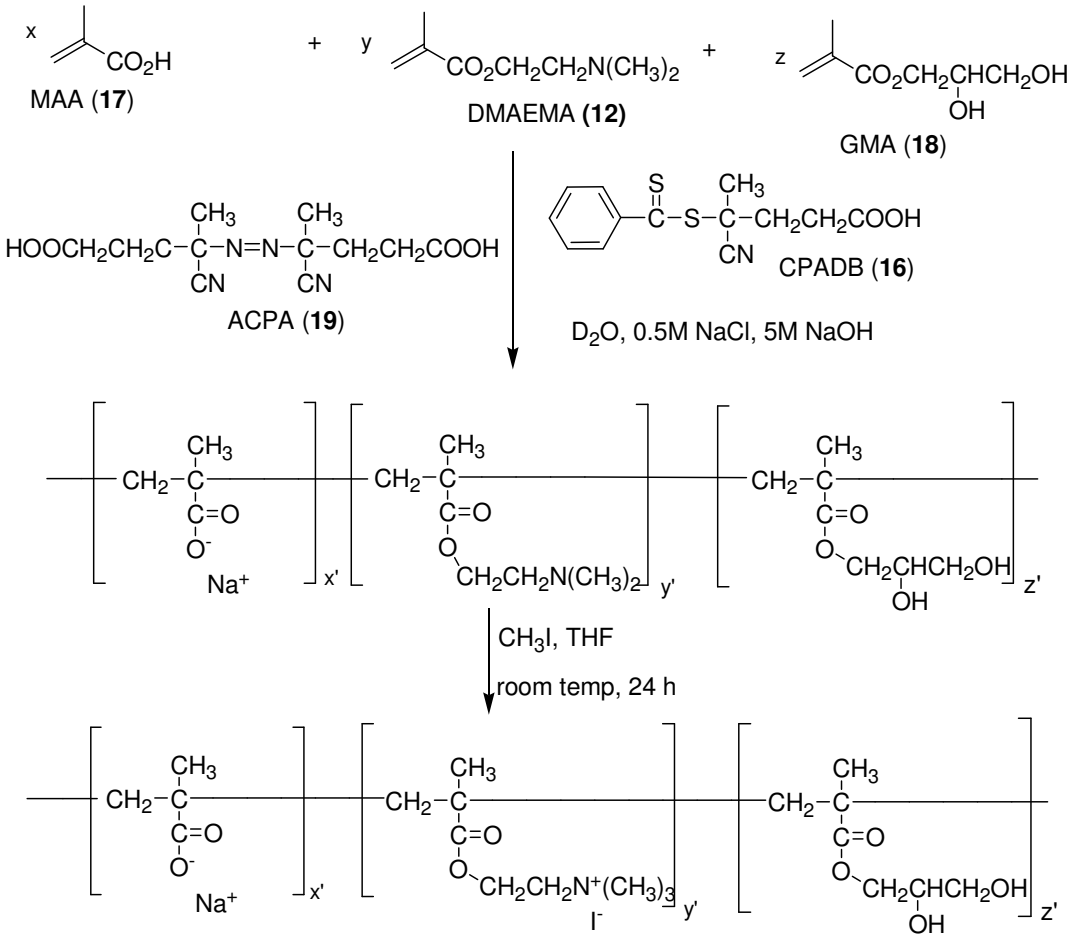
Figure 11. Structures of monomers and water-soluble RAFT CTA

Previously, ternary copolymers were synthesized using non-polar uncharged monomers solketal methacrylate (SMA, **10**), *tert*-butyl methacrylate (tBMA, **11**), and 2-(*N,N*-dimethylamino)ethyl methacrylate (DMAEMA, **12**) by the reversible addition-fragmentation chain transfer (RAFT) technique using cumyl dithiobenzoate (CDB, **13**) as the chain transfer agent. This section discusses the results of binary copolymerizations of mixtures of (MAA, **17**), (DMAEMA, **12**) and (GMA, **18**) using the water-soluble azo-initiator ACPA (**19**) at varying pH in aqueous solution. These polymerizations were done in an NMR tube. The binary copolymerizations were carried out to determine the reactivities of these monomers in binary mixtures, before proceeding to terpolymer synthesis using the water-soluble RAFT agent CPADB (**16**).

The aqueous route was explored for two main reasons. Utilizing glyceryl monomethacrylate (GMA, **18**) would be economical because it is commercially available, as opposed to solketal methacrylate (SMA, **10**), which has to be synthesized on a large scale. SMA is the major component in the synthesis of model polyampholytes via the organic route. Secondly, the synthetic route to polyampholytes in aqueous media using charged monomers DMAEMA (**12**), MAA (**17**) and GMA (**18**) could be less time consuming, because the quaternization of $-N(CH_3)_2$ groups in DMAEMA is the only polymer functional group transformation needed. Using the non-polar monomers, SMA, tBMA and DMAEMA in an organic solvent, requires the quaternization of $-N(CH_3)_2$ groups in DMAEMA, the deprotection of *tert*-butyl ester units in tBMA to methacrylic acid units, and hydrolysis of the ketal ring in SMA to glyceryl monomethacrylate (GMA). The one possible drawback is that polyampholytes synthesized in aqueous media may not have a random structure because of a tendency to form alternating copolymer

pairs between the cationic and anionic monomers.[6-8] The proposed route for the synthesis of polyampholytes in an aqueous medium is shown in Scheme 12.

Scheme 12. Proposed synthesis of polyampholytes- aqueous solution route



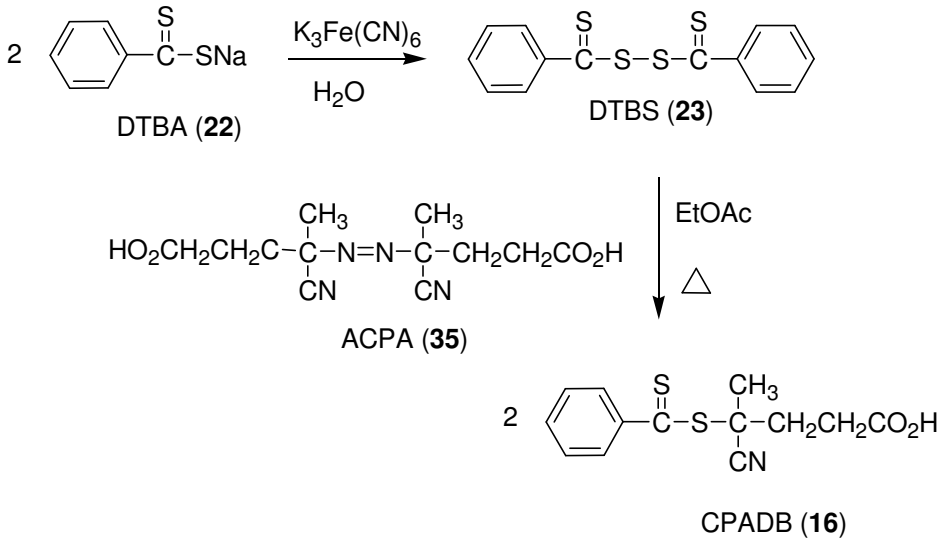
The binary copolymer experiments in D_2O indicate that DMAEMA was more reactive than GMA and MAA, because of which we concluded that DMAEMA could not be used in the synthesis of ternary copolymers. It was thus decided to quaternize

DMAEMA using methyl iodide and THF at room temperature,[9] and employ 2-[(methacryloyloxy)ethyl]trimethylammonium chloride MAETMAC (**21**) in the terpolymer synthesis. In this chapter the synthesis of MAETMAC (**21**) and experiments to synthesize terpolymers using MAA (**17**), DMAEMA (12), GMA (**18**) and MAETMAI (**20**) are discussed.

Results and Discussion

Synthesis of 4-Cyano-4-dithiobenzoylthiyl Pentanoic Acid (CPADB, **16**).[1] The synthesis of CPADB is shown in Scheme 13.

Scheme 13. Synthesis of 4-Cyano-4-dithiobenzoylthiyl pentanoic acid

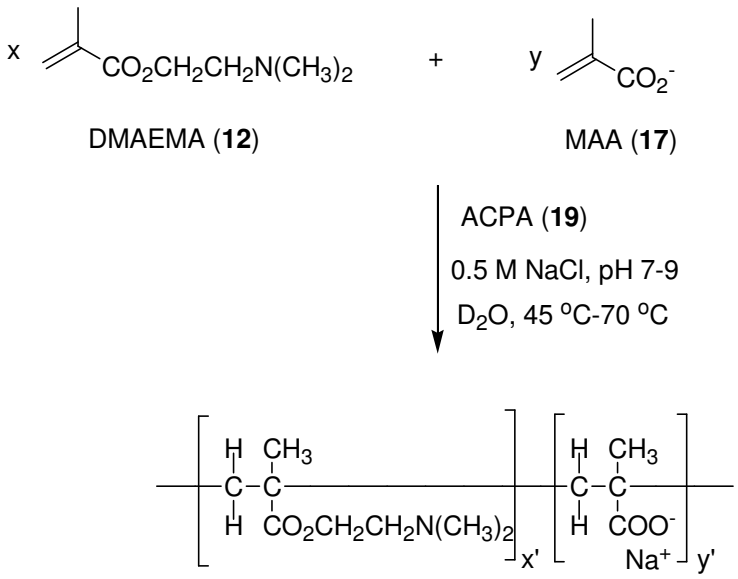


RAFT polymerizations are carried out using dithioester compounds as chain transfer agents. Many of these chain transfer agents are not commercially available. 4-

Cyano-4-dithiobenzoylthiyl pentanoic acid, the CTA most commonly used for RAFT polymerizations in aqueous media is prepared via a multi-step procedure involving the synthesis of DTBA, which is subsequently oxidized to di(thiobenzoyl) disulfide, before reacting with 4,4'-azobis(4-cyanopentanoic acid) to yield CPADB (**16**) (Scheme 14).[1,2] DTBA (**22**) can be synthesized by a variety of routes, for example, (1) reaction of phenylmagnesium bromide with carbon disulfide, followed by acidification;[10] (2) reaction of trichlorophenyl methane, potassium hydrogen sulfide, and potassium hydroxide;[11] and (3) reaction of benzyl chloride, elemental sulfur, and sodium methoxide. Previous literature reports that route (3) gave the best yields and purity of DTBA.[2] DTBA is susceptible to oxidation, and in route (3) it is converted to the sodium salt and used immediately in the synthesis of DTBDS. Figures 17 and 18 (appendices) represent the ^{1}H and ^{13}C NMR spectra of CPADB (**16**) in $CDCl_3$.

Binary Copolymerizations. Binary monomer mixtures of DMAEMA **(12)**, MAA (**17**) and GMA **(18)** in equimolar ratios were polymerized using ACPA (**19**) as the initiator at temperatures ranging from 45 ^{o}C to 70 ^{o}C. D_2O was used as the solvent and 3-(trimethylsilyl)propionic acid-d_4 sodium salt was used as a chemical shift reference. A 0.5 M sodium chloride solution was added to screen the interactions between oppositely charged ion pairs and decrease formation of ion aggregates,[12] while sodium hydroxide was added to dissolve the initiator ACPA, since ACPA is soluble only at pH > 5. The pH of the binary monomer mixtures prior to polymerizing them ranged from 7.2 to 9.0. The polymerization of a binary mixture of DMAEMA and MAA is shown in Scheme 14.

Scheme 14. Copolymerization of a binary mixture of DMAEMA and MAA



Figures 19 (a and b, appendices) are ^{1}H NMR spectra of a binary mixture of DMAEMA and MAA at basic pH: (a) at room temperature and (b) after 1 hour at 50 ^{o}C. The results from polymerizations of binary monomer mixtures of DMAEMA, MAA and GMA are shown in Table 22.

Table 22. Polymerizations of Binary Monomer Mixtures in Aqueous Media

sample	monomers	initiator, wt %	temp	observations
691	DMAEMA/ MAA	5	70 ^{o}C	solid polymer in tube
694	DMAEMA/ MAA	5	60 ^{o}C	highly viscous
696	DMAEMA/ MAA	5	50 ^{o}C	solid polymer in tube
698	DMAEMA/ MAA	2.1	50 ^{o}C	highly viscous
697	DMAEMA/ MAA	0.5	50 ^{o}C	solid polymer in tube
701	DMAEMA/ MAA	2.9	50 ^{o}C	highly viscous
706	DMAEMA/ MAA	5	50 ^{o}C	phase separation
695	GMA/ MAA	5	60 ^{o}C	solid polymer in tube
699	GMA/ MAA	2.5	50 ^{o}C	solid polymer in tube
700	DMAEMA/ GMA	2.8	50^{o}C	solid polymer in tube

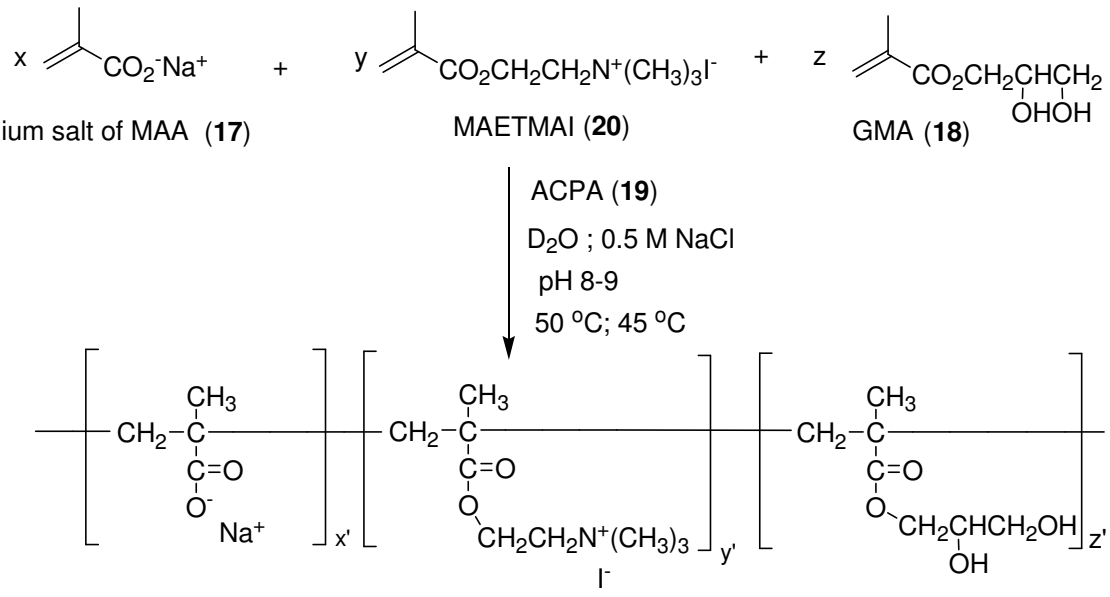
The polymer solutions turned highly viscous in all of the samples listed above, after polymerizing for only 1 h, which indicates the formation of high molecular weight polymer. In sample 696, after heating the mixture at 50 ^{o}C for 1 h, the amount of DMAEMA consumed was 84.6 %, and the amount of MAA consumed was 42.6 %. After 1 h 20 min of heating at 50 ^{o}C, the amount of DMAEMA consumed was 94.8 %, and the amount of MAA consumed was 51.5 %.

Binary monomer mixtures of GMA (**18**) and MAA (**17**) (sample 695) were polymerized using 5 weight percent of initiator and 2.5 weight percent of initiator respectively. The ^{1}H NMR spectra of the partially polymerized mixtures indicate that GMA was consumed much faster than MAA after only 20 minutes of reaction time. In

the polymerization of a binary mixture of DMAEMA and GMA (sample 700), DMAEMA was observed to be much more reactive than GMA with solid polymer formed in the NMR tube.

Ternary Copolymerizations. Attempts were made to synthesize ternary copolymers of MAETMAI (**20**) relative to MAA (**17**) and GMA (**18**) in D_2O between pH 8 and 9 (Scheme 15) to understand the reactivities of these monomers.

Scheme 15. Ternary copolymerization of MAETMAI, GMA and MAA



2-[(Methacryloyloxy)ethyl]trimethylammonium Iodide (MAETMAI, **20**). The polymerization of binary monomer mixtures of DMAEMA (**12**), MAA (**17**) and GMA (**18**) predicted DMAEMA to be the most reactive of the three monomers. We thus

decided to polymerize 2-[(methacryloyloxy)ethyl]trimethylammonium chloride (MAETMAC, **21**) directly instead of DMAEMA.

The next strategy was to carry out the alkylation of DMAEMA with an excess of CH_3I and THF at room temperature, exchange the iodide ion for the chloride ion, and utilize MAETMAC (**21**) in terpolymer synthesis. Alkylation of DMAEMA with CH_3I/ THF has always been successful.[9] Each time, within the limits of NMR detection, complete quaternization was always observed qualitatively. The quaternary ammonium iodide monomers were isolated as pale-yellow solids in yields ranging from 98 % to 100 %. The ^1H NMR spectrum of MAETMAI (**20**) shows both the complete absence of the peak due to $N(CH_3)_2$ group at 2.35 ppm, and a new peak due to $N^+(CH_3)_3$ group at 3.45 ppm.

The iodide ion of MAETMAI was exchanged for chloride ion, as the iodide form of the monomer may be unstable and susceptible to further oxidation. Getting rid of all the water collected from the ion exchange process was a very time consuming task. The water was removed either under vacuum, or by using a water aspirator, and the samples were later dried under vacuum at room temperature. One of these samples was also lyophilized. The monomer MAETMAC (**21**) was isolated as a white solid in 85.9 % yield. After two days of storage in the freezer, however, the monomer had polymerized significantly. This was evident from the ^1H NMR spectrum of the monomer. Efforts to separate the monomer from polymer failed. The quaternization procedure was repeated again as described earlier. The removal of water collected from the ion exchange experiment was a time consuming process. These samples were rotary evaporated to remove water and dried under vacuum at room temperature for 24 h. However, they

formed gels. One of these samples was lyophilized, but the lyophilized sample also formed a gel.

Since the isolation of MAETMAC (**21**) was a problem, it was decided to employ the quaternary ammonium iodide monomer (MAETMAI) (**20**) in ternary copolymerizations with MAA (**17**) and GMA (**18**). It is worth pointing out that stripping water out from samples of (MAETMAC, **21**) has always resulted in gelation. This suggests that MAETMAC monomer polymerizes rapidly. This could be one reason why no procedure exists in literature for the synthesis of 2-[(methacryloyloxy)ethyl]trimethylammonium chloride. The commercially available MAETMAC monomer (75 wt % solution in water) was however, purified and characterized by ^{1}H NMR spectroscopy.

Purification of 2-[(Methacryloyloxy)ethyl]trimethylammonium Chloride.[13] The monomer, (MAETMAC, **21**) was isolated from a commercially available sample by precipitation into acetone.

Ternary Copolymerizations. The ternary copolymerizations using MAA (**17**), DMAEMA (**12**) and GMA (**18**) at a pH range of 11-12, and MAA, MAETMAI (**20**) and GMA (**18**) at pH range of 8-9 resulted in phase separations. MAA, DMAEMA and GMA were polymerized at a pH of 11–12 to keep DMAEMA in the amine form.

In the above terpolymerizations, the samples phase separated immediately after ejecting the NMR tubes out from the NMR probe. MAA, MAETMAI and GMA, however, were polymerized at a pH of 8–9 to keep MAA in the ionized form. The sample

that was polymerized at 50 ^{o}C phase separated, but the one heated at 45 ^{o}C stayed in solution. The integration of the spectra collected in the terpolymer experiments after partial conversion were difficult due to severe line broadening, which may be indicative of high viscosity or gelation. The samples that phase separated could have actually formed high molecular weight polymer. The gel phases from the above ternary copolymerizations were isolated by breaking the bottom of the NMR tubes and diluting them ten-fold times with water (5.0 mL). However, these polymers did not go into solution.

Conclusions

Our goal is to synthesize random polyampholytes with homogeneous compositions. For this purpose, ideally we would need monomers with reactivities that do not greatly differ from one another. However, the results of polymerizations of binary monomer mixtures of DMAEMA, MAA and GMA in aqueous media clearly indicate that DMAEMA was the most reactive of the three monomers, and MAA is the least reactive. These results suggest that 2-(*N,N*-dimethylamino)ethyl methacrylate is not a suitable monomer for the synthesis of ternary polyampholytes in aqueous media.

Because of lack of success with the binary and ternary copolymer experiments carried out in aqueous solution, it was decided to switch back to the organic route to synthesize polyampholytes from solketal methacrylate (SMA, **10**), *tert*-butyl methacrylate (tBMA, **11**), and 2-(*N,N*-dimethylamino)ethyl methacrylate (DMAEMA, **12**). This would be a lengthy route because of two functional group conversions.

However, since the organic route worked on a small scale, we have now resorted to using the organic route to synthesize model random polyampholytes.

Experimental Section

Materials. Benzyl chloride (99+%, Alfa Aesar), sodium methoxide (25 % w/w solution in methanol), sulfur powder (99.5 %, Alfa Aesar), potassium ferricyanide (III) (99+%, Aldrich), anhydrous sodium sulfate (Spectrum) and silver nitrate (EM Sciences) were used as received. 4,4'-Azobis(4-cyanopentanoic acid) (Fluka), silica gel (60 A^o, 70-230 mesh size) (Aldrich) and HCl (Fisher-Scientific) were used as received. Reagent grade anhydrous methanol, ethyl alcohol, diethyl ether, *n*-hexane and ethyl acetate were used as received.

Glyceryl monomethacrylate (Monomer-Polymer and Dajac Laboratories) and 2-(*N,N*-dimethylamino)ethyl methacrylate (Polysciences, Inc.) were purified by passing through a short column of basic alumina to remove phenolic inhibitors, prior to use. Methacrylic acid (Aldrich), sodium hydroxide (Aldrich), D_2O (99.9 atom % D, Aldrich), 3-(trimethylsilyl)propionic acid-d_4 sodium salt (98 atom % D, Aldrich) and concentrated hydrochloric acid (Fisher Scientific) were used as received. Deionized water was obtained from a Barnstead water purification system. Amberlite-IRA-402 (strongly basic anion exchanger, chloride form) (Aldrich) (358 mL) was washed with methanol (1400 mL), 2 M HCl (200 mL), and deionized water (11 L), until the pH of the eluate and the eluent were the same. The elemental analysis was performed by Desert Analytics Laboratories, Tucson, Arizona.

NMR Spectroscopy. The ^{1}H NMR spectra of the binary polymerization mixtures were recorded using the quad probe and D_2O as the NMR lock solvent. 3-(Trimethylsilyl)propionic acid-d_4 sodium salt was used as a chemical shift reference. The following conditions were used to acquire the spectra: 44 K data points, flip angle of 20 ^{o} and a relaxation delay of 5 s. Thirty two scans were accumulated for each spectrum. The binary monomer mixtures were polymerized at temperatures ranging from 45 ^{o}C to 70 ^{o}C. The ternary copolymerizations were carried out at 45 ^{o}C and 50 ^{o}C.

Sodium Dithiobenzoate (DTBA, **22**)**.** Dithiobenzoic acid (DTBA) was synthesized by a modification of the method of Becke and Hagen.[2] To a dry 250 mL three-necked round-bottom flask equipped with a magnetic stirring bar, a 25 mL addition funnel and thermometer, was added sodium methoxide (25% w/w solution in methanol, 0.200 mol, 44.0 g), anhydrous methanol (1.56 mol, 49.9 g) and elemental sulfur (0.200 mol, 6.40 g). Benzyl chloride (0.099 mol, 12.6 g) was added dropwise via an addition funnel over a period of 1 h, at room temperature under a nitrogen atmosphere. The reaction mixture was heated in an oil bath at 65 ^{o}C for 10 h. After this time, the reaction mixture was cooled to 5 ^{o}C using an ice bath. The precipitated salt was removed by filtration, and the solvent was removed under vacuum at room temperature. Deionized water (100 mL) was added to the residue and the solution was filtered a second time. The filtrate was transferred to a 1 L separatory funnel and washed with diethyl ether (3 x 40 mL). Diethyl ether (40 mL) and 1 M HCl (100 mL) were added, and the dithiobenzoic acid was extracted into the ether layer. Deionized water (60 mL) and 1 M NaOH (120 mL) were added to the ether solution, and sodium dithiobenzoate was extracted to the

aqueous layer. This washing process was repeated two more times to yield an orange-red solution of sodium dithiobenzoate.

Di(thiobenzoyl) Disulfide (DTBDS, **23**)**.** Potassium ferricyanide (III) (0.100 mol, 32.9 g) was dissolved in deionized water (500 mL). The sodium dithiobenzoate solution (DTBA, **22**) (350 mL) was transferred to a 1 L conical flask, equipped with a magnetic stirring bar. Potassium ferricyanide solution was added dropwise to the sodium dithiobenzoate solution via a 250 mL addition funnel over a period of 1 h with vigorous stirring. The orange-red precipitate was filtered and washed with deionized water (250 mL) until the washings became colorless. The red solid was dried for 36 h under vacuum at room temperature. The product (red solid) was recrystallized from ethanol.

4-Cyano-4-dithiobenzoylthiyl Pentanoic Acid (CPADB, **16**)**.** The target compound was prepared by the method of Thang and co-workers.[14] To a 100 mL round bottom flask was added 25 mL of ethyl acetate. 4,4'-Azobis(4-cyanopentanoic acid) (ACPA) (2.85×10^{-3} mol, 0.798 g) and di(thiobenzoyl) disulfide (DTBDS, **23**) (1.90×10^{-3} mol, 0.583 g) were added to the flask in a mole ratio of 1.5:1.0 of ACPA to DTBDS. The reaction mixture was magnetically stirred and refluxed for 18 h. The ethyl acetate was removed under vacuum at room temperature. The crude product was isolated by column chromatography (silica gel 60 A^{o}, 70-230 mesh) using ethyl acetate:*n*-hexane (2:3) as eluent. The fractions that were red in color were combined and dried over anhydrous sodium sulfate overnight. The ethyl acetate:*n*-hexane solvent mixture was removed under vacuum at room temperature, and the red oily residue was dried under

vacuum for 12 h while warming the flask in a water bath at 40 ^{o}C - 50 ^{o}C. Later the flask was further dried under vacuum at room temperature for 6 h and placed in the freezer, wherein CPADB crystallized.

CPADB (**16**) was recrystallized using a mixture of benzene and *n*-hexane. To the crude product in a test tube, was added 1.53 mL of benzene and the test tube was warmed in a 56 ^{o}C water bath until the solution was homogeneous. *n*-Hexane (0.74 mL) was added dropwise, and the test tube was left to cool at room temperature and later placed in an ice-bath. A red solid crystallized out from solution, and was filtered and dried under vacuum at room temperature for 2 days to yield of 4-Cyano-4-dithiobenzoylthiyl pentanoic acid (CPADB, **16**) (0.429 g, 1.53 x 10^{-3} mol, 80.5 % yield). The recrystallized product showed only one spot on a TLC (thin layer chromatography) plate. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.38-7.90 (m, 5H, Ar-**H**), 2.40-2.80 (m, 4H, -C**H$_2$**-C**H$_2$**), 1.96 (s, 3H, -C**H$_3$**), 1.65-1.80 (impurities from $CDCl_3$), 1.50 (H_2O from $CDCl_3$), 1.20-1.40 (impurities from $CDCl_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 225.0 (-**C**=S), 178.0 (-**C**OOH), 143-118 (Ar-**C** and -**C**N), 45.0 (-**C**-CH_3), 38.0-25.0 (impurities from $CDCl_3$), 33.0 (-**C**H_2-CO_2H), 30.0 (-**C**$H_2CH_2CO_2H$) and 24.0 (-**C**H_3). IR (NaCl plate, $CDCl_3$, cm^{-1}): 2850-3100 (-COOH), 2250 (-CN), 1740 (-C=O), and 1062 (-C=S).

Binary Copolymerization. In an example preparation for sample 698, DMAEMA (5.15 x 10^{-4} mol, 0.081 g) and MAA (5.11 x 10^{-4} mol, 0.044 g) were weighed into a scintillation vial followed by 0.5 M NaCl (0.03-0.05 mL) and ACPA (5.71 x 10^{-5} mol, 0.016 g). Lastly, 5 M NaOH was added dropwise to dissolve ACPA followed by the addition of 0.5 mL of D_2O. The sample was transferred to an NMR tube and the pH of

the solution was measured. The NMR tube was placed in the ^{1}H NMR quad probe and a room temperature spectrum was acquired. The temperature of the probe was left to equilibrate to the desired temperature for 10 min. Thereafter, the probe was locked and shimmed at the desired temperature setting. The spectra were arrayed to collect data every 20 minutes.

2-[(Methacryloyloxy)ethyl]trimethylammonium Iodide (MAETMAI, **20**)**.** To a solution of DMAEMA (0.0502 mol, 8.46 mL) and THF (100 mL) in a 500 mL round bottom flask, methyl iodide (2.51 mol, 156 mL) was added dropwise with vigorous stirring via an addition funnel over a period of 1 h. The solution was stirred at room temperature for five days. The excess methyl iodide and THF were rotary evaporated and dried under vacuum at room temperature for 48 h. The isolated pale yellow solid (15.0 g, 100 % yield) was stored in an amber colored bottle. ^{1}H NMR (400 MHz, D_2O) δ: 6.05 and 5.65 (=C**H$_2$**), 4.50 (-OC**H$_2$**), 3.68 (-NC**H$_2$**), 3.10 (-N$^+$(C**H$_3$**)$_3$), 1.80 (-C**H$_3$**).

2-[(Methacryloyloxy)ethyl]trimethylammonium Chloride (MAETMAC, **21**)**.** An aqueous solution of 14.925 g of MAETMAI (**20**) was loaded on the top of the column (358 mL Cl^- resin) and drained down to about 1-2 cm into the column. Deionized H_2O was used as the eluent and fractions containing about 15-16 mL of eluate were collected. The collected fractions were tested for chloride through the formation of a white precipitate by adding 1-2 drops of a 0.1 M $AgNO_3$ solution. The fractions that gave a white precipitate were rotary evaporated for several hours using a water aspirator and later under vacuum. It was further dried under vacuum at room temperature for 36 h.

MAETMAC (**21**) was isolated as a white powder (85.9 % yield). ^{1}H NMR (400 MHz, D_2O) δ: 6.05 and 5.65 (=C**H$_2$**), 4.50 (-OC**H$_2$**), 3.68 (-NC**H$_2$**), 3.10 (-N$^+$(C**H$_3$**)$_3$), 1.80 (-C**H$_3$**). Anal. Calcd for $C_9H_{18}NClO_2$: C, 52.03; H, 8.75; N, 6.75; Cl, 17.07. Found: C, 50.18; H, 9.07; N, 6.53; Cl, 16.90; I, <0.1.

Ternary Copolymerization. In the terpolymerization of MAA (**17**), GMA (**18**) and MAETMAI (**20**), GMA (1.04 x 10^{-3} mol, 0.167 g), MAETMAI (1.2 x 10^{-4} mol, 0.036 g) and MAA (1.5 x 10^{-4} mol, 0.013 g) were weighed into a scintillation vial. 3-(Trimethylsilyl)propionic acid-d_4 sodium salt (9-10 mg) was added followed by 0.5 M NaCl (0.03–0.05 mL). D_2O (0.5 mL) was added followed by (ACPA, **19**) (2.5 x 10^{-5} mol, 0.007 g). A 4 M NaOH solution was added dropwise to make the solution basic and dissolve the azo-initiator ACPA. The pH of the resultant starting solution was adjusted using an aqueous solution of 2 M HCl to maintain the pH between 8 and 9, to keep MAA in the ionized form. The sample was transferred to an NMR tube, and the pH of the solution was measured. A room temperature ^{1}H NMR spectrum was acquired, and later the probe was equilibrated to 50 ^{o}C.

In the terpolymerizations employing DMAEMA (**12**), MAA (**17**) and GMA (**18**), GMA (1.03 x 10^{-3} mol, 0.167 g), DMAEMA (1.2 x 10^{-4} mol, 0.036 g) and MAA (1.5 x 10^{-4} mol, 0.013 g) were weighed and transferred to a scintillation vial. 3-(Trimethylsilyl)propionic acid-d_4 sodium salt (9-10 mg) was added followed by 0.5 M NaCl (0.03-0.05 mL). D_2O (0.5 mL) was added followed by ACPA (2.5 x 10^{-5} mol, 0.007 g). A 4 M NaOH solution (0.08 mL) was added to dissolve the initiator ACPA. The pH of the resulting solution was 11.3-11.7.

Purification of 2-[(Methacryloyloxy)ethyl]trimethylammonium Chloride.[13] The commercially available (MAETMAC) monomer (0.3 mL) was added dropwise to a vigorously stirred solution of acetone (8.0 mL) chilled in an ice-bath. The solution starts getting cloudy initially and a white solid falls out of solution. The supernatant solution was decanted using a Pasteur pipette and the solid was washed with acetone. The washings were decanted and the solid was dried under vacuum for 24 h. The product (white fluffy solid) was isolated in 79.8 % yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.05 and 5.65 (=C**H$_2$**), 4.50 (-OC**H$_2$**), 3.68 (-NC**H$_2$**), 3.10 (-N$^+$(C**H$_3$**)$_3$), 1.80 (-C**H$_3$**).

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APPENDICES

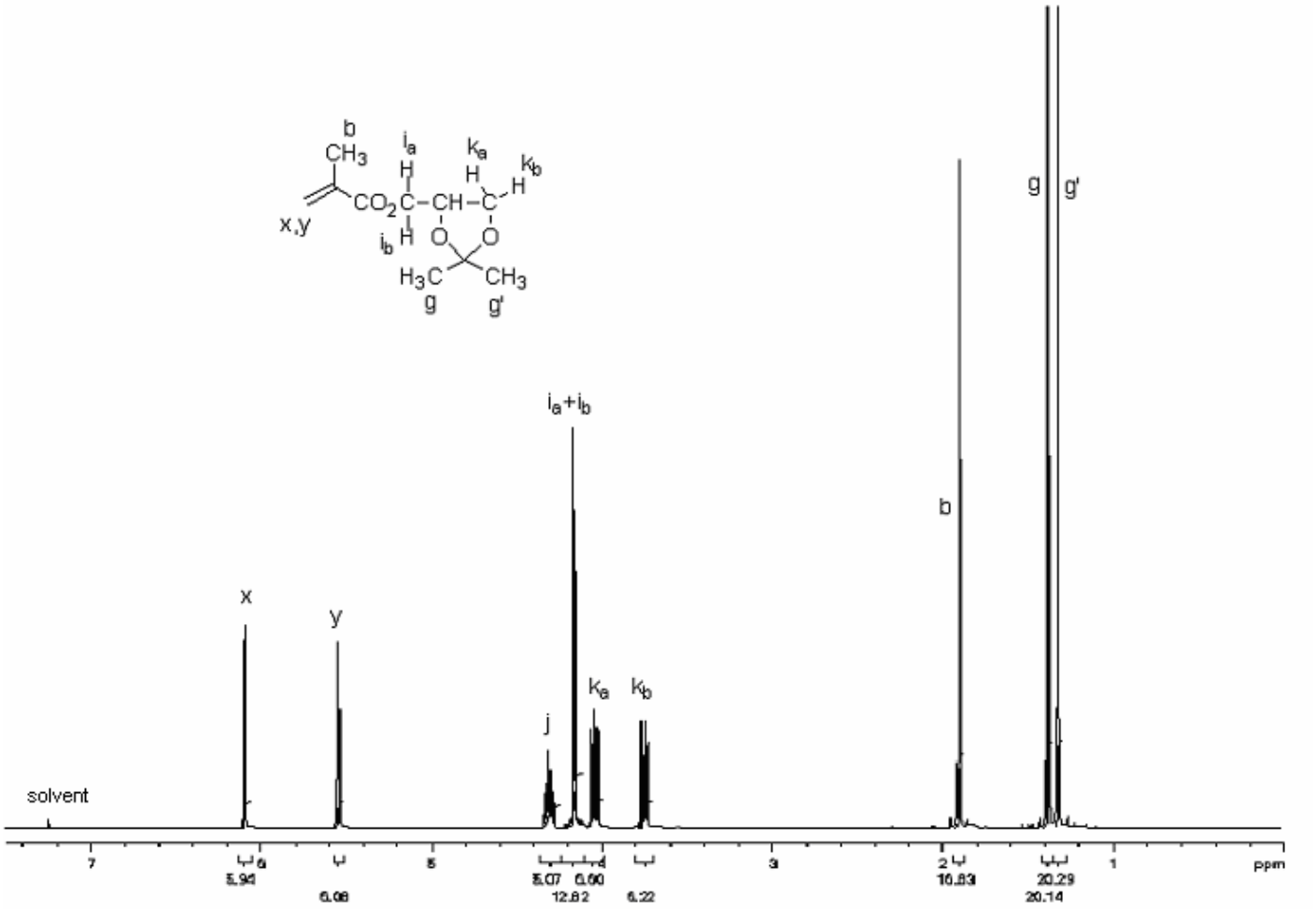

Figure 1. ^{1}H NMR spectrum of solketal methacrylate in $CDCl_3$.

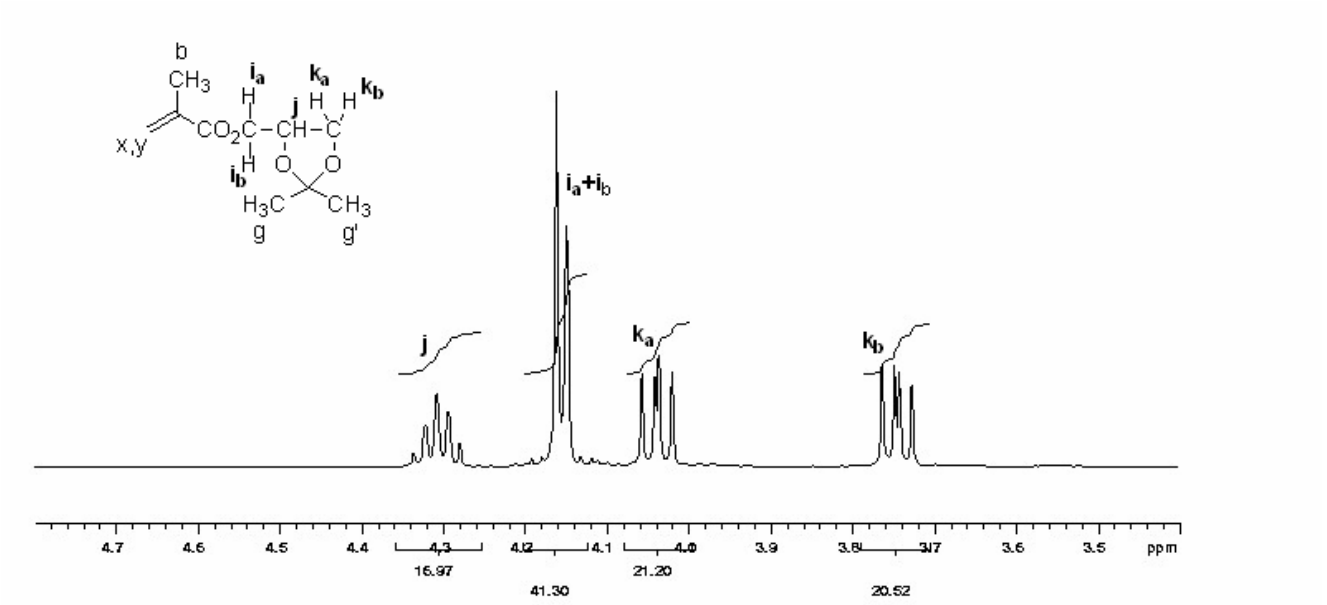

Figure 2. ^{1}H NMR spectrum showing the coupling patterns in solketal methacrylate.

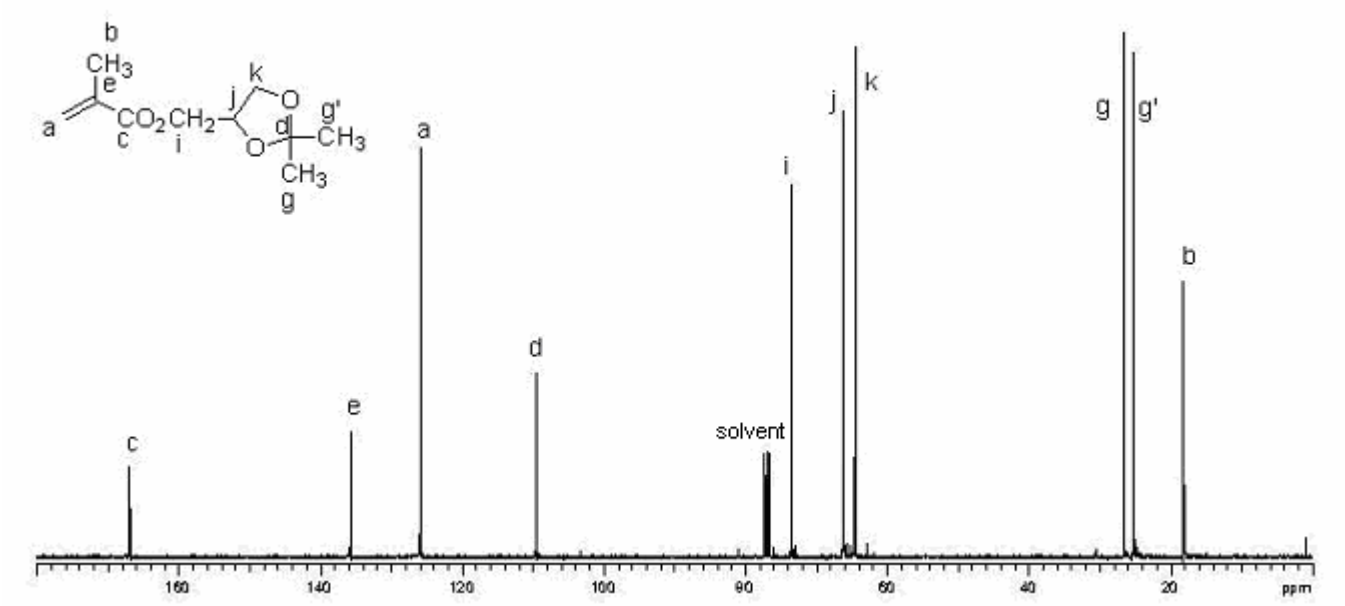

Figure 3. ^{13}C NMR spectrum of solketal methacrylate in $CDCl_3$.

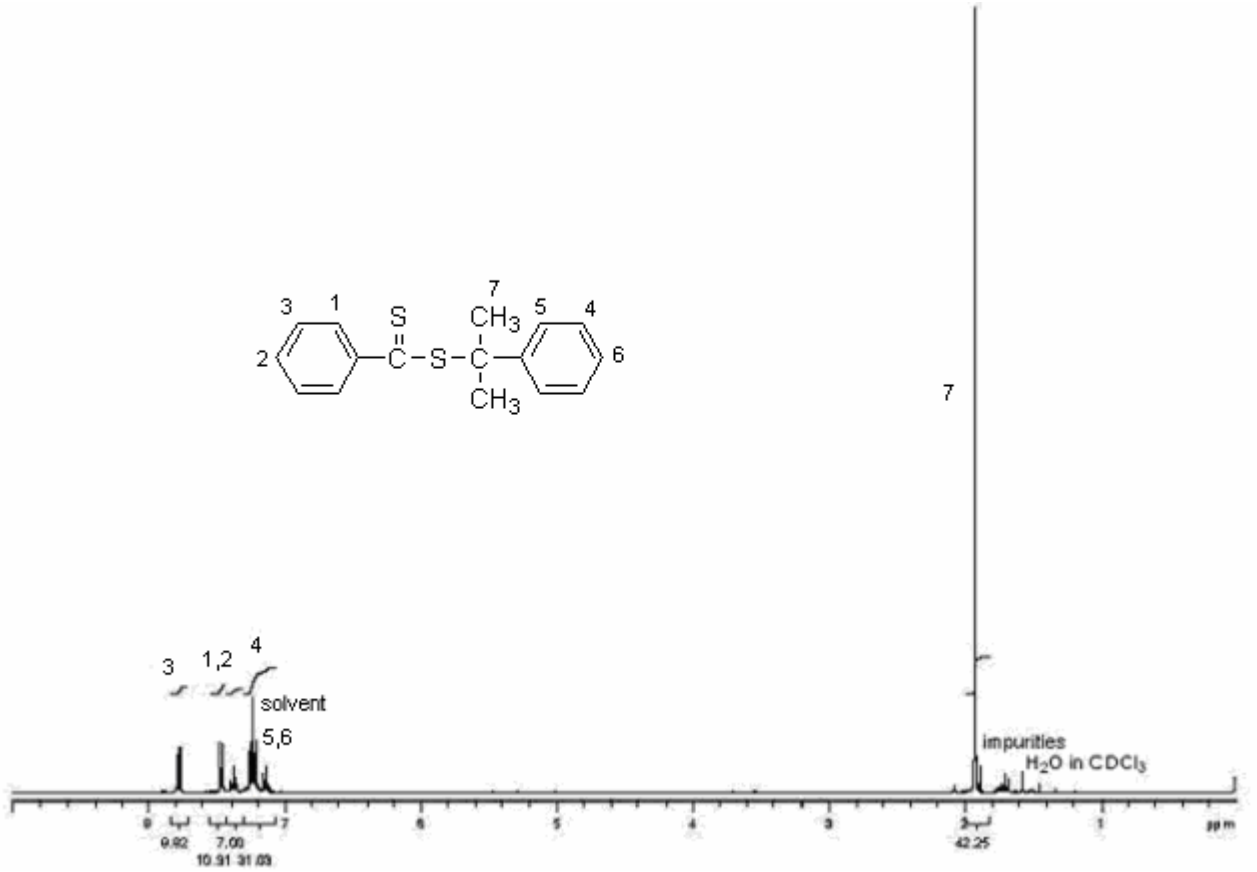

Figure 4. ^{1}H NMR spectrum of cumyl dithiobenzoate in $CDCl_3$.

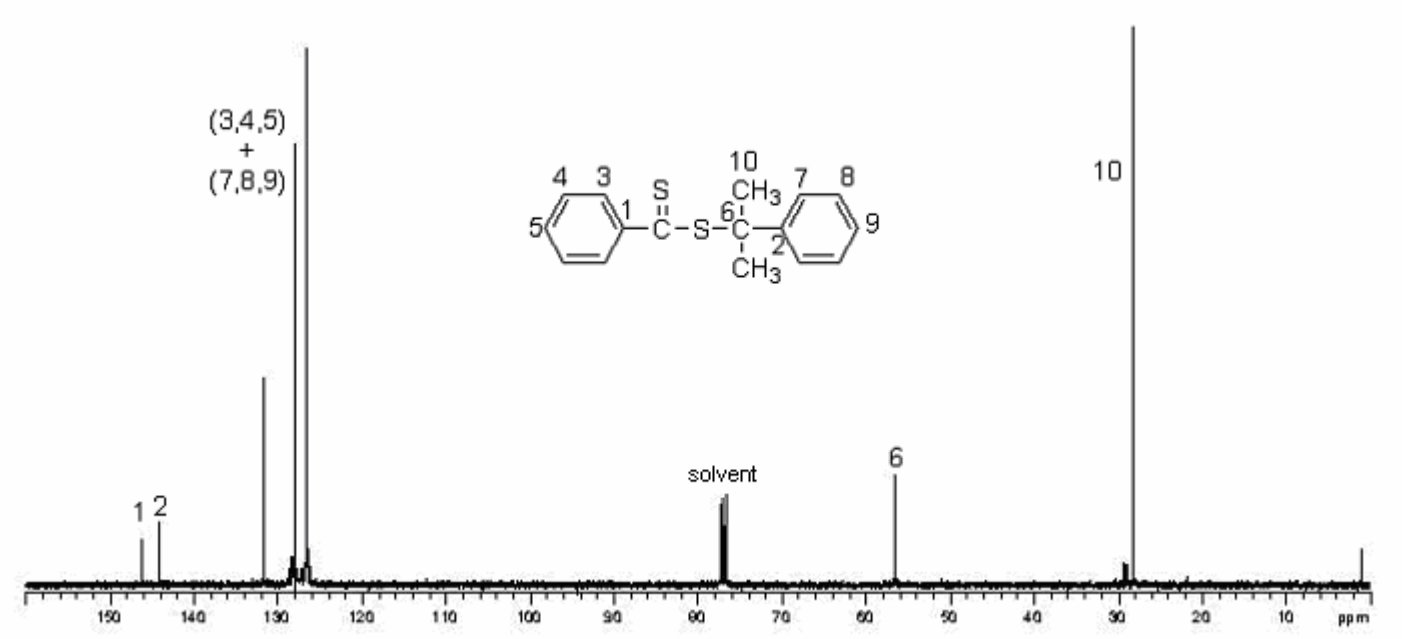

Figure 5. ^{13}C NMR spectrum of cumyl dithiobenzoate in $CDCl_3$.

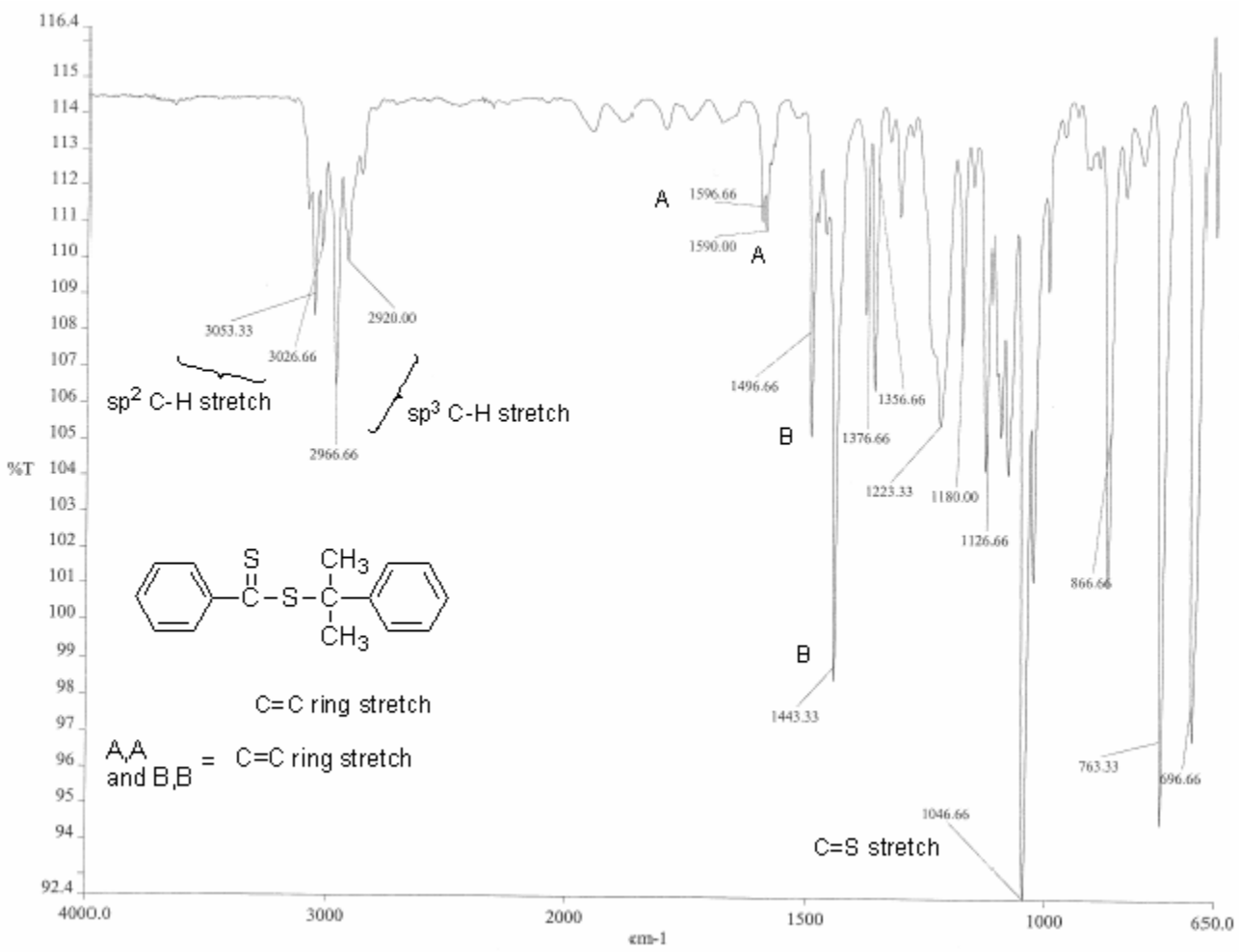

Figure 6. Infrared spectrum of cumyl dithiobenzoate.

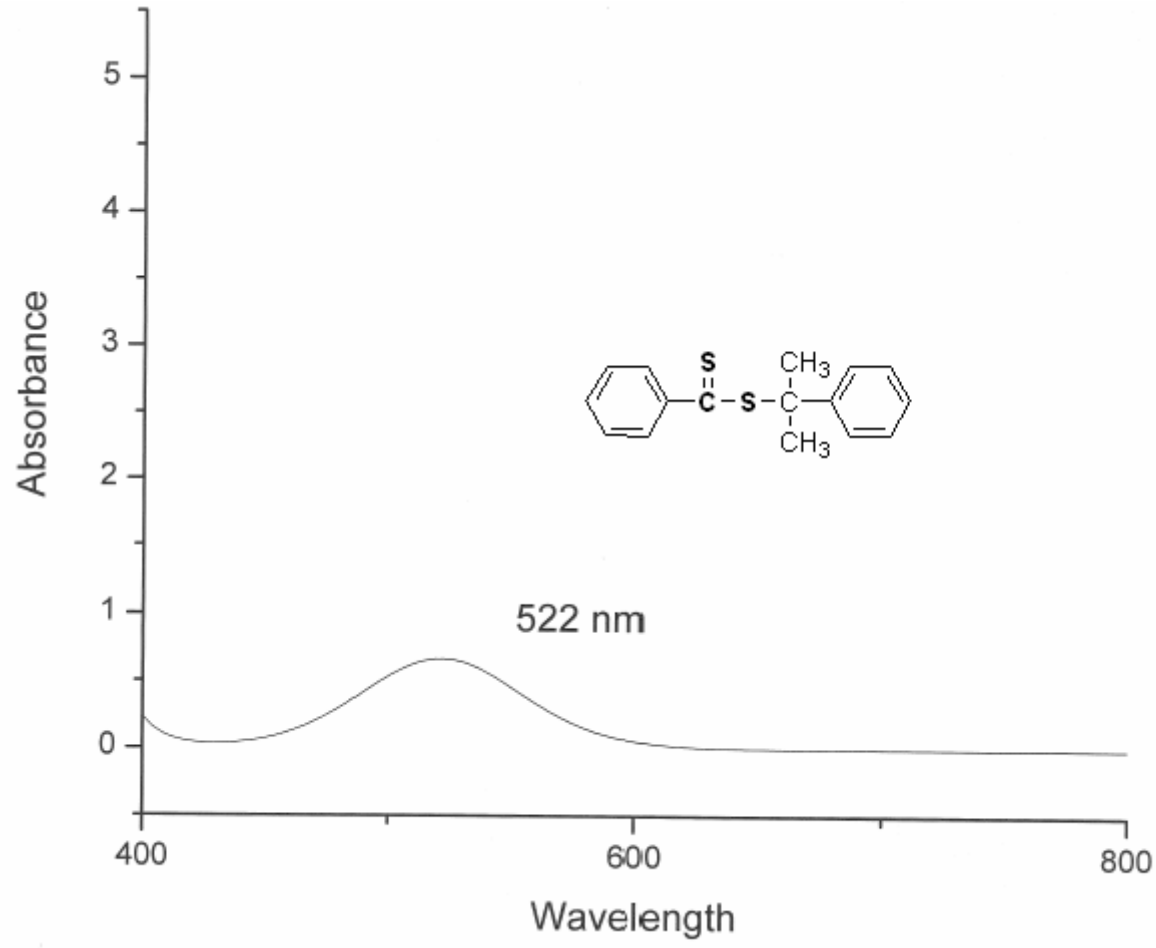

Figure 7. UV-visible spectrum of cumyl dithiobenzoate.

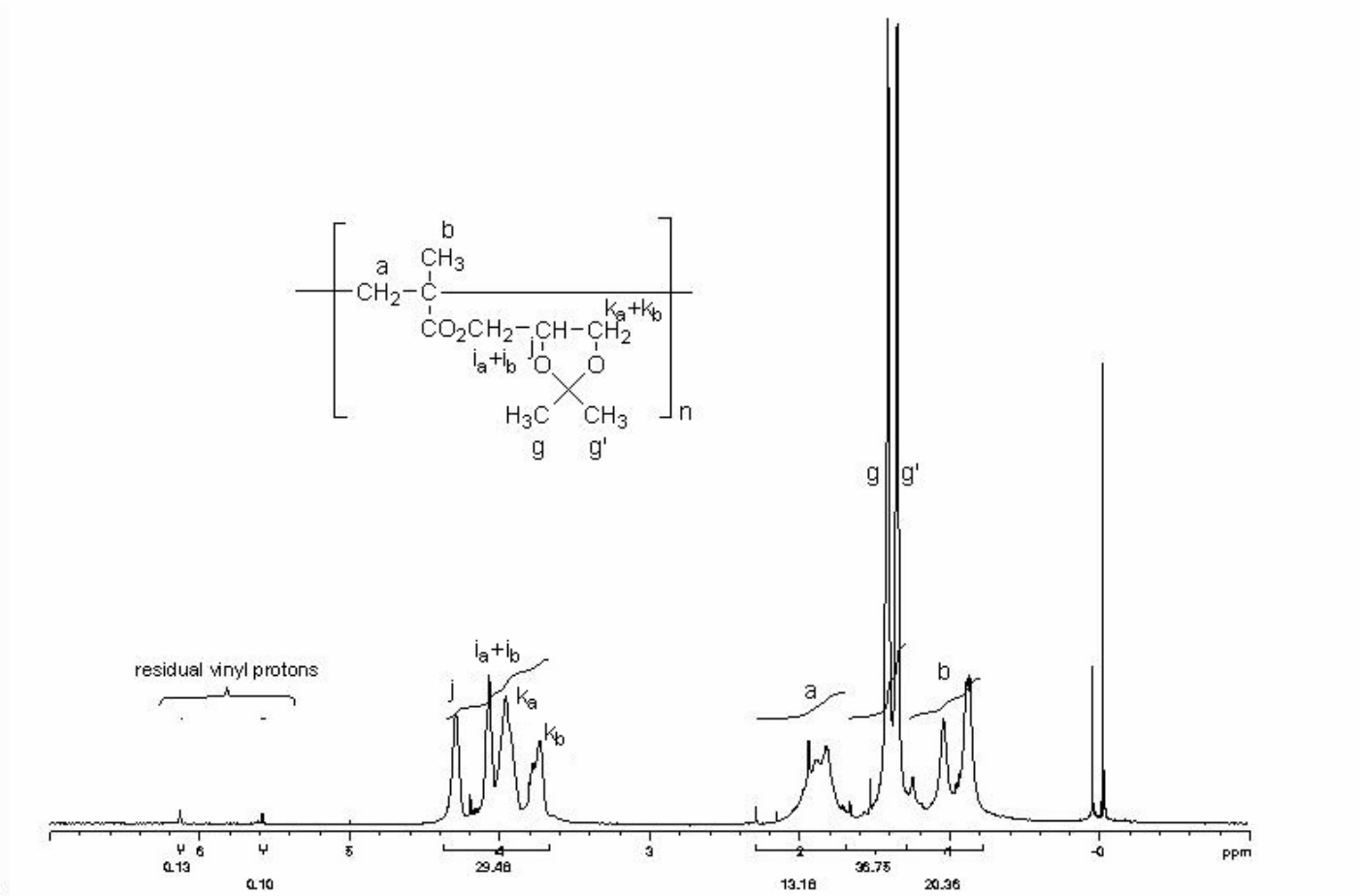

Figure 8. ^{1}H NMR spectrum of poly(solketal methacrylate) in $CDCl_3$.

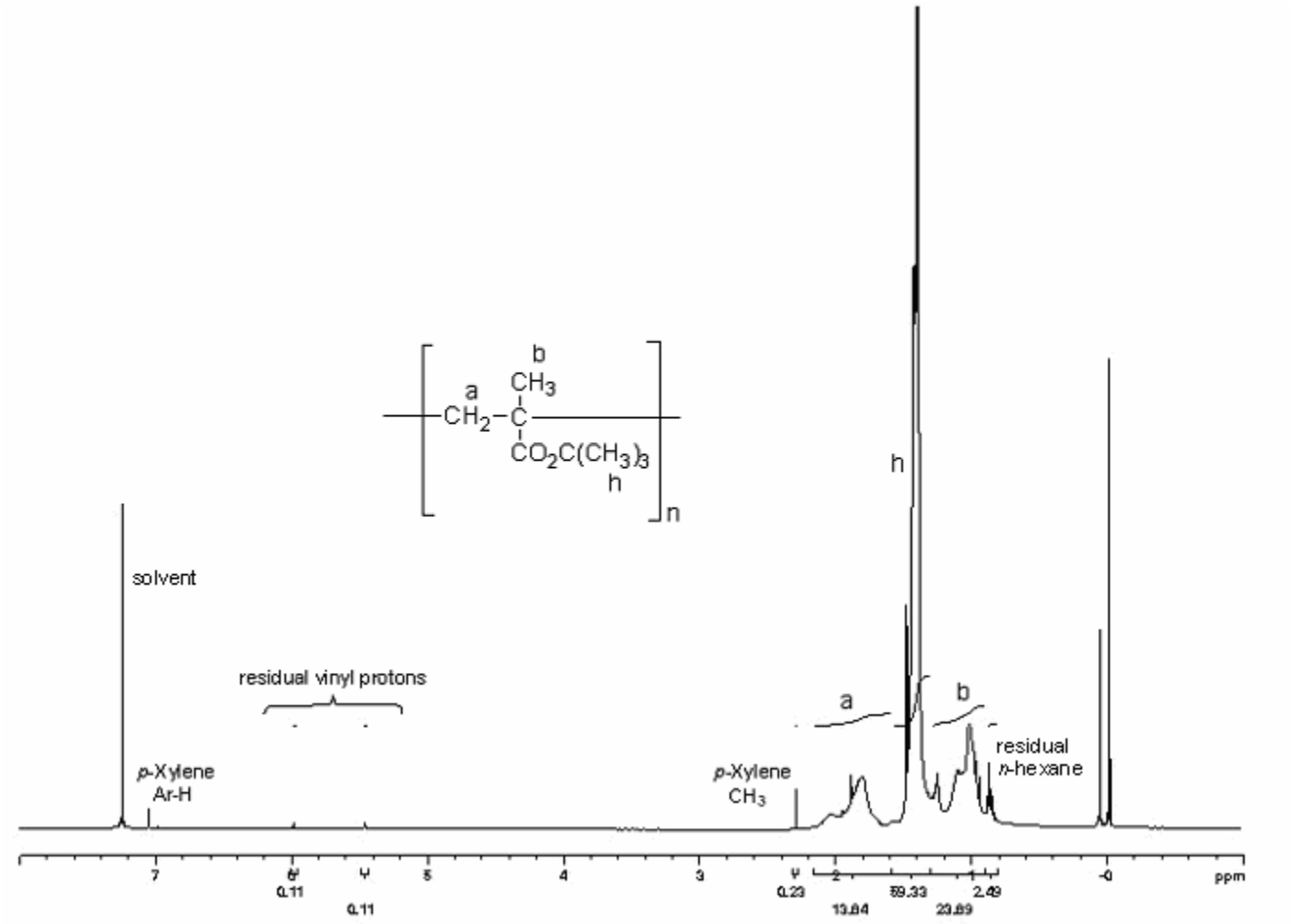

Figure 9. ^{1}H NMR spectrum of poly(*tert*-butyl) methacrylate in $CDCl_3$.

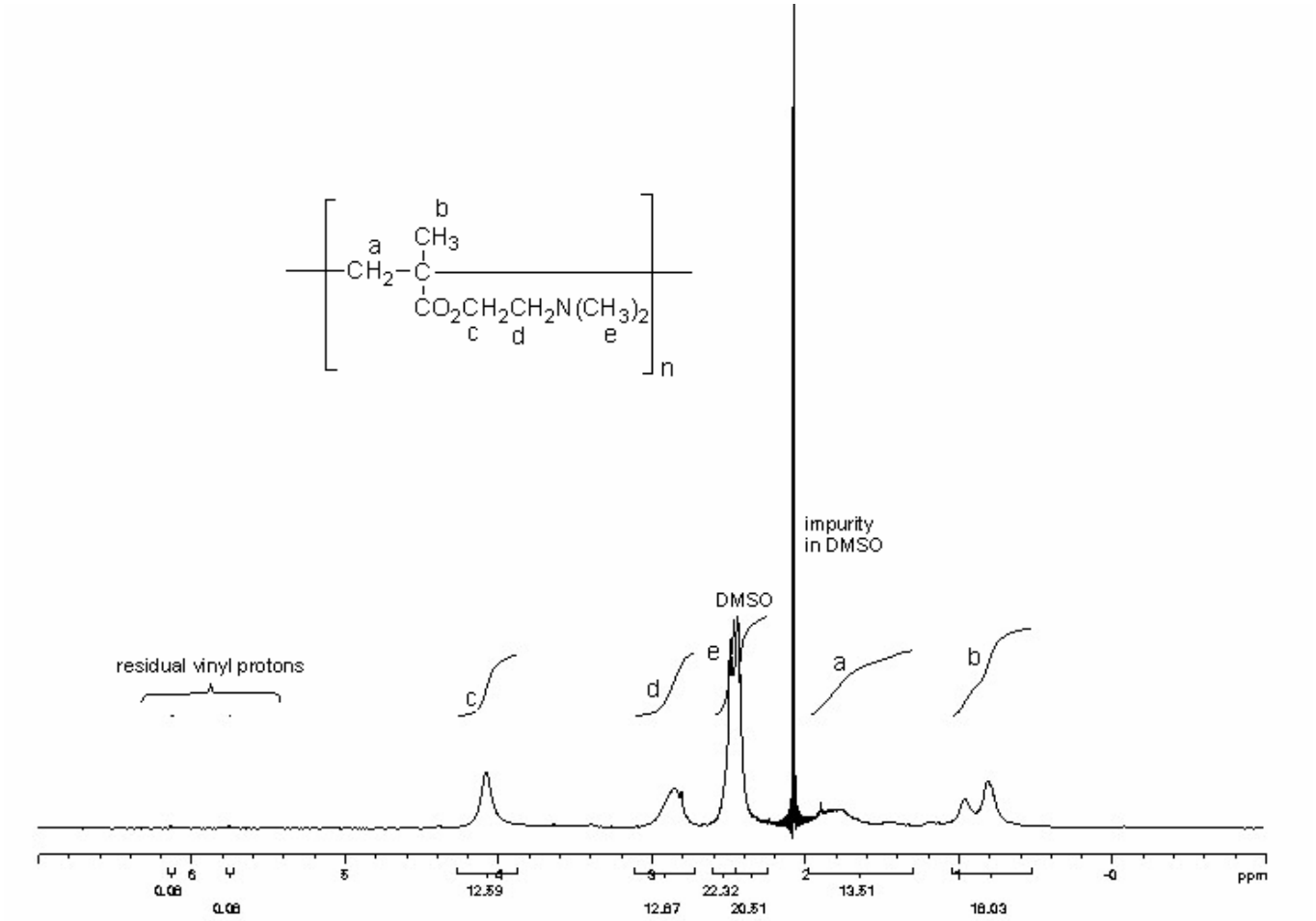

Figure 10. ^{1}H NMR spectrum of poly[2-(*N,N*-dimethylaminoethyl)methacrylate] in DMSO-d_6.

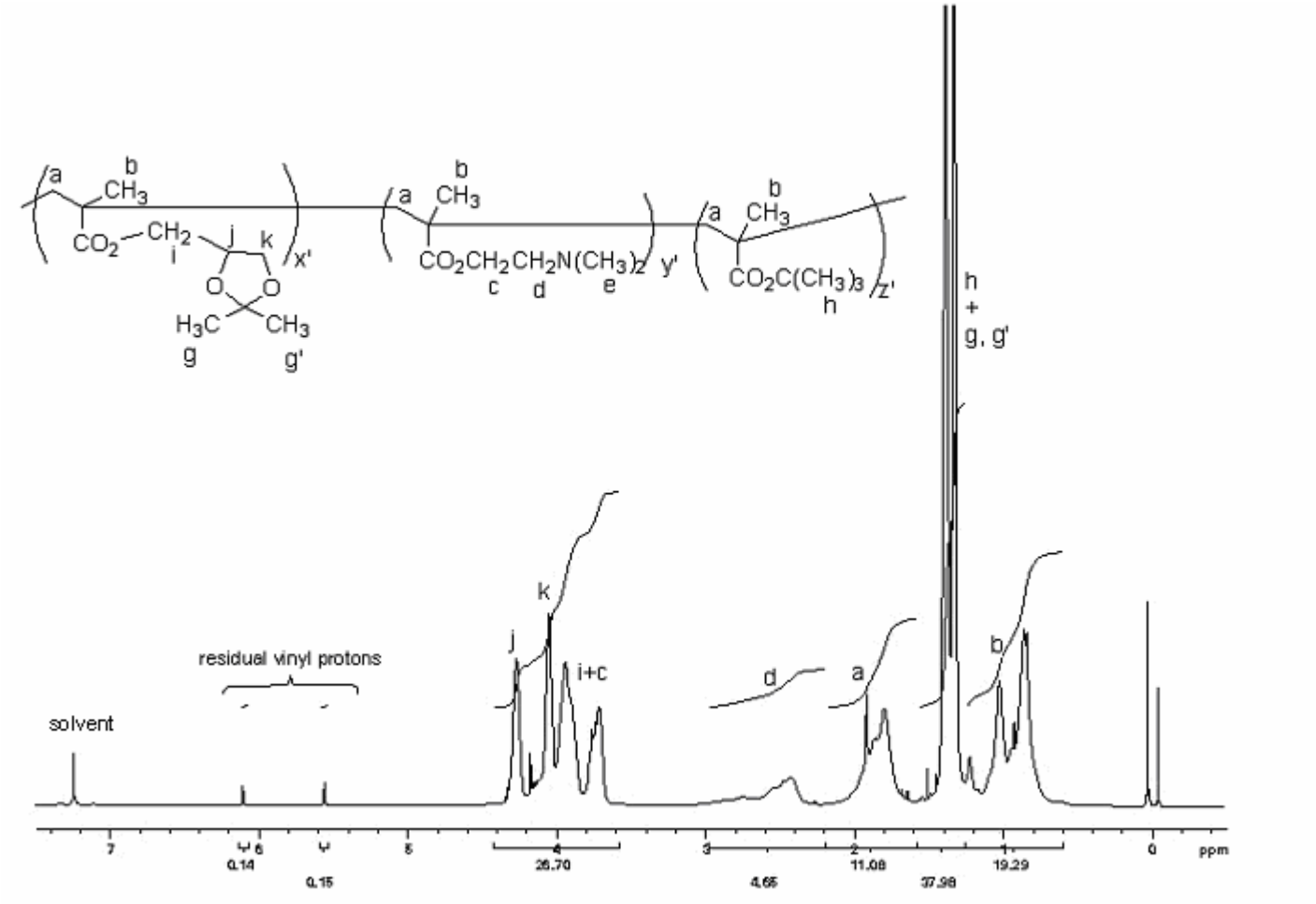

Figure 11. ^{1}H NMR spectrum of sample 6652 terpolymer (DP 98) in $CDCl_3$.

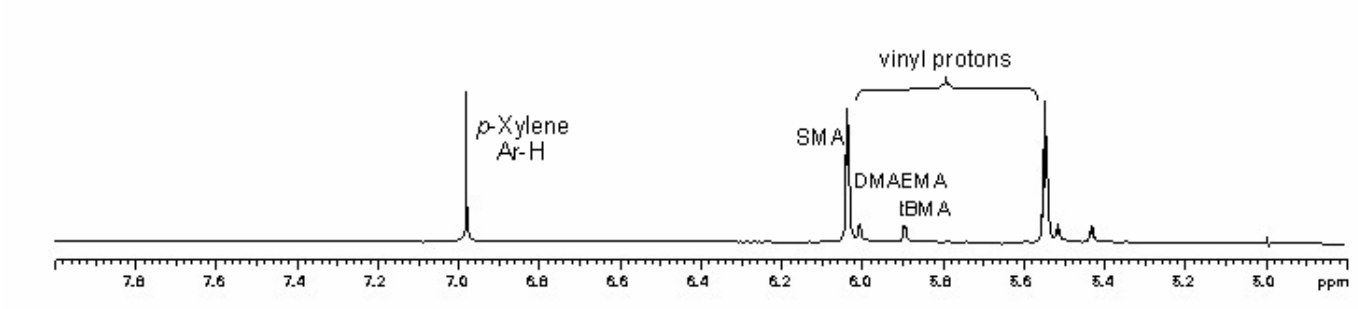

Figure 12. ^{1}H NMR spectrum for the determination of monomer conversions in 1,4-dioxane-d_8.

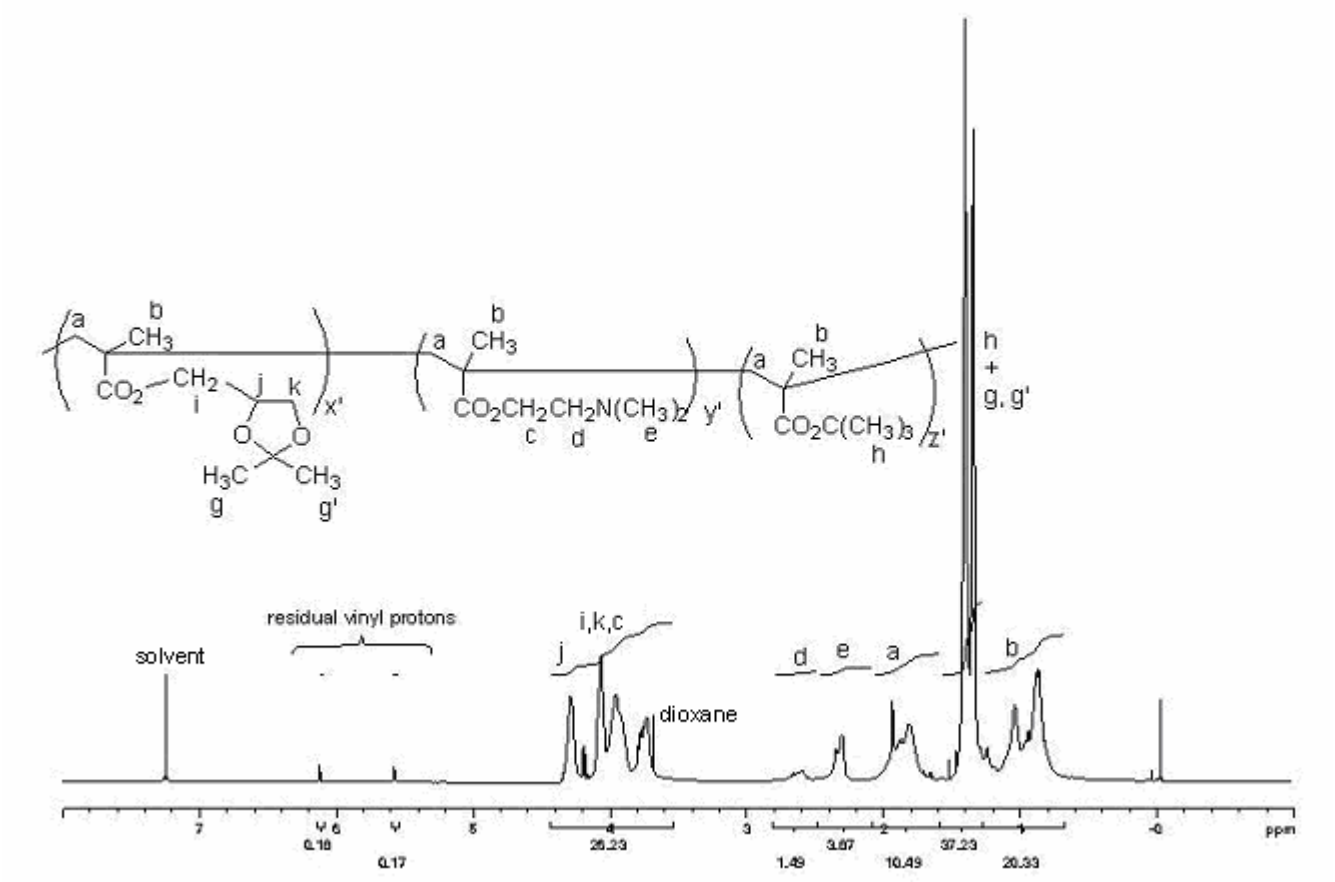

Figure 13. ^{1}H NMR spectrum of sample 7341 terpolymer (DP 135) in $CDCl_3$.

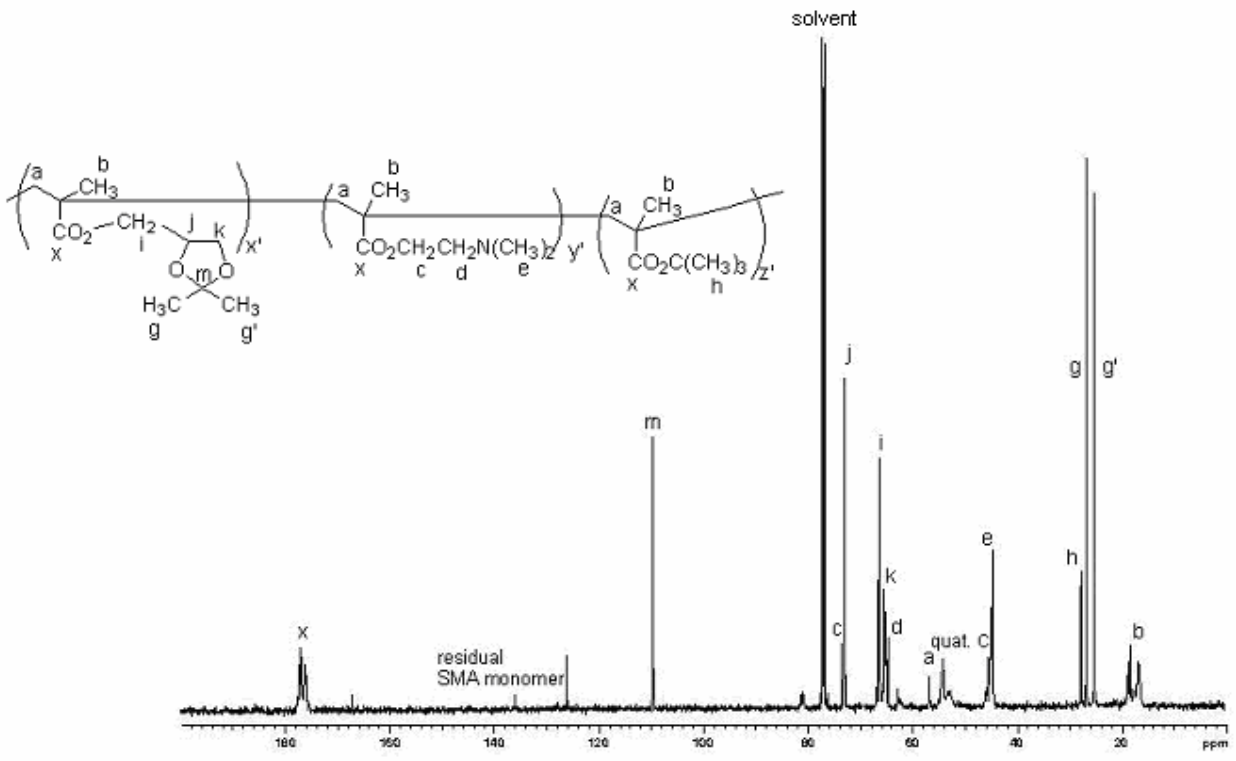

Figure 14. ^{13}C NMR spectrum of sample 7341 terpolymer (DP 135) in $CDCl_3$.

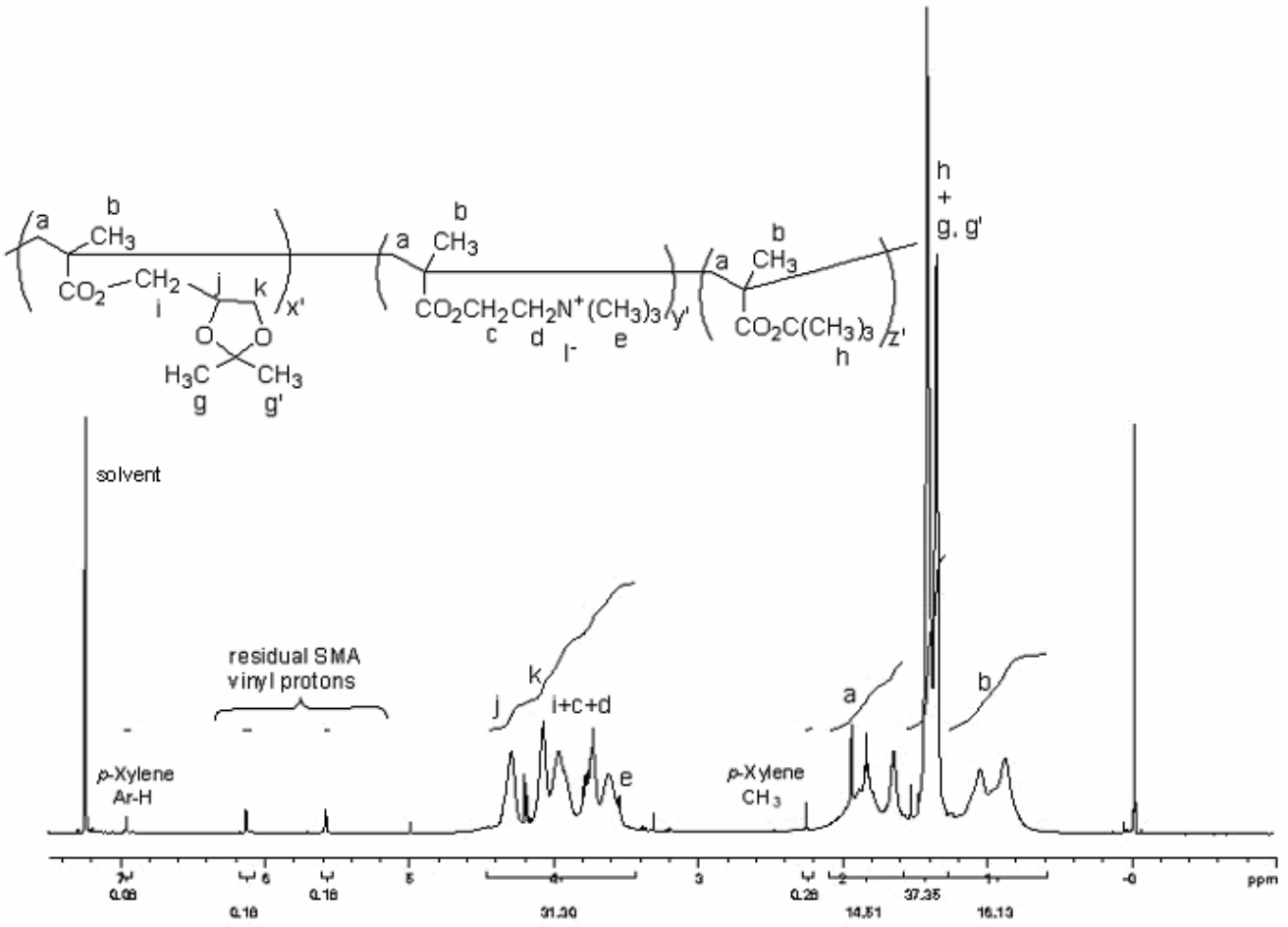

Figure 15. ^{1}H NMR spectrum of quaternized sample 7622 terpolymer (DP 532) in $CDCl_3$.

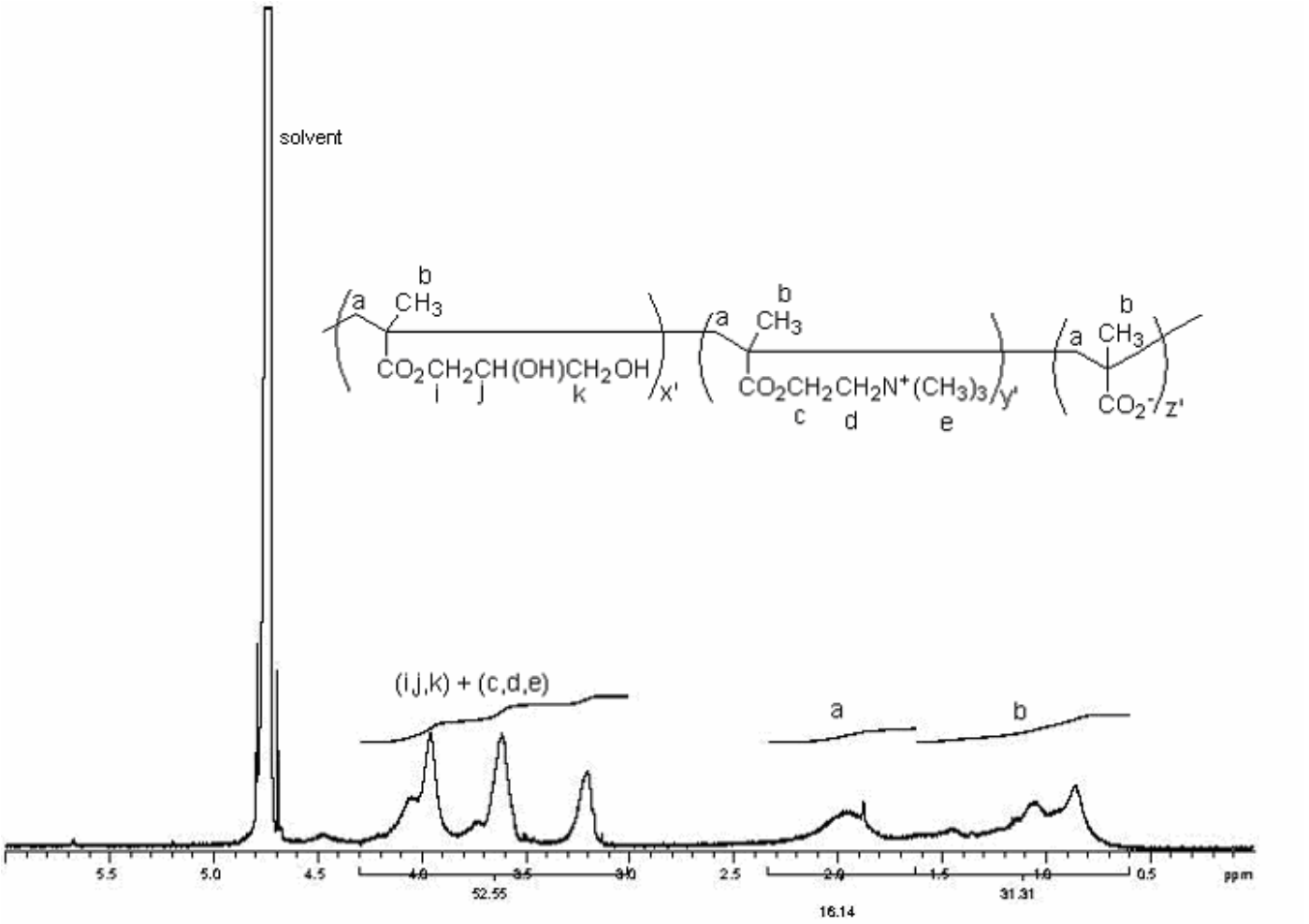

Figure 16. ^{1}H NMR spectrum of sample 6652-1 in D_2O.

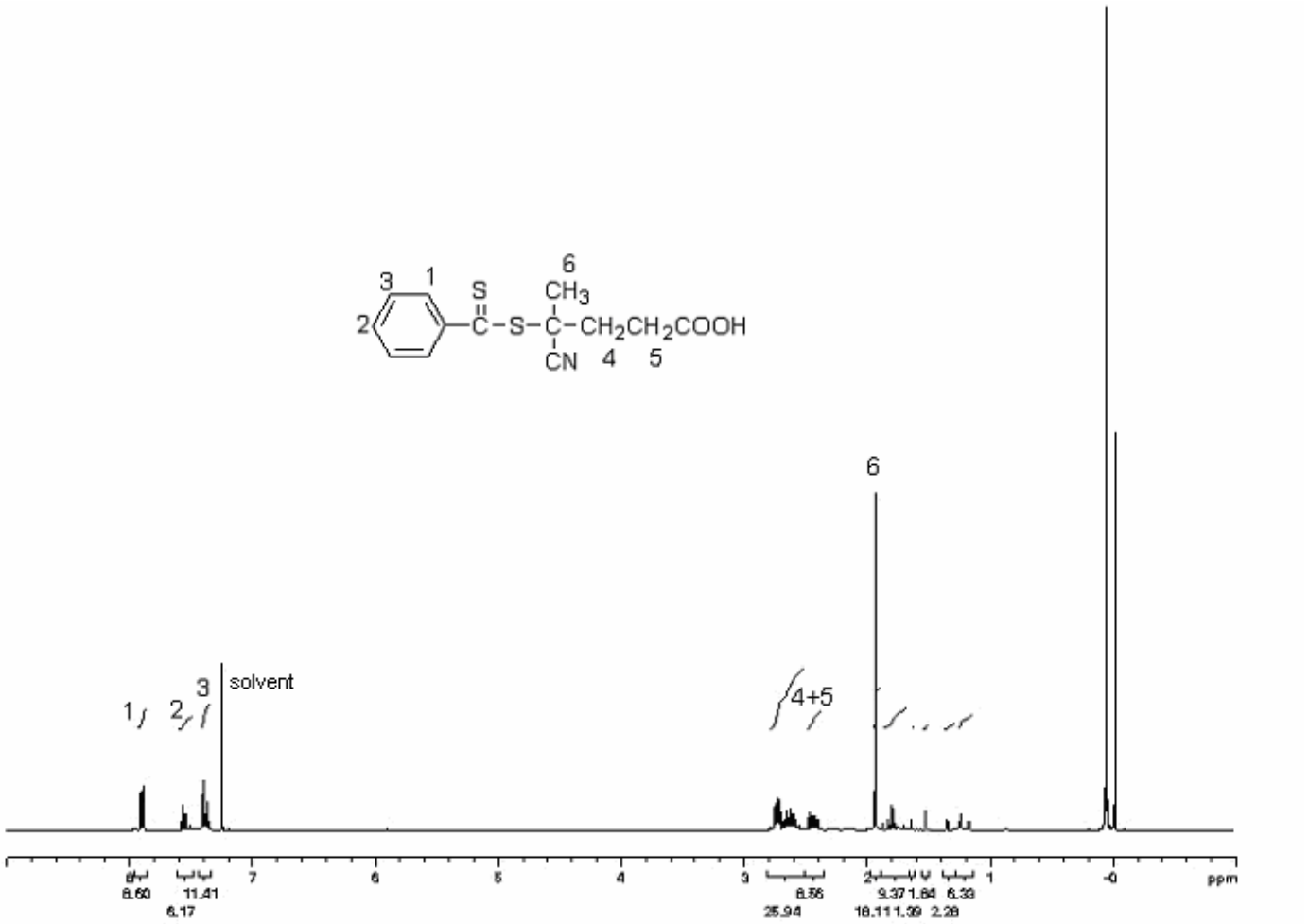

Figure 17. ^{1}H NMR spectrum of 4-cyano-4-dithiobenzoylthiylpentanoic acid in $CDCl_3$.

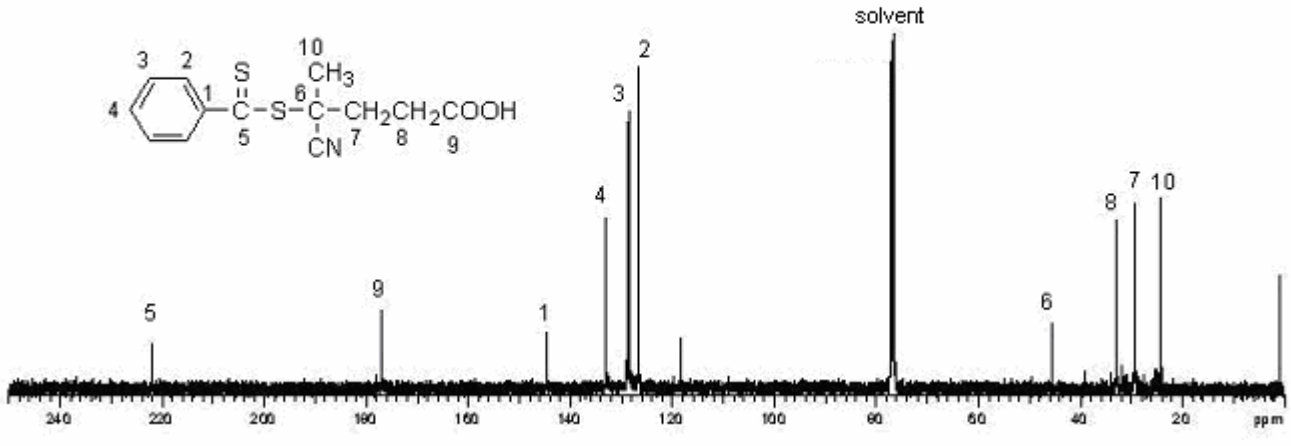

Figure 18. ^{13}C NMR spectrum of 4-cyano-4-dithiobenzoylthiylpentanoic acid in $CDCl_3$.

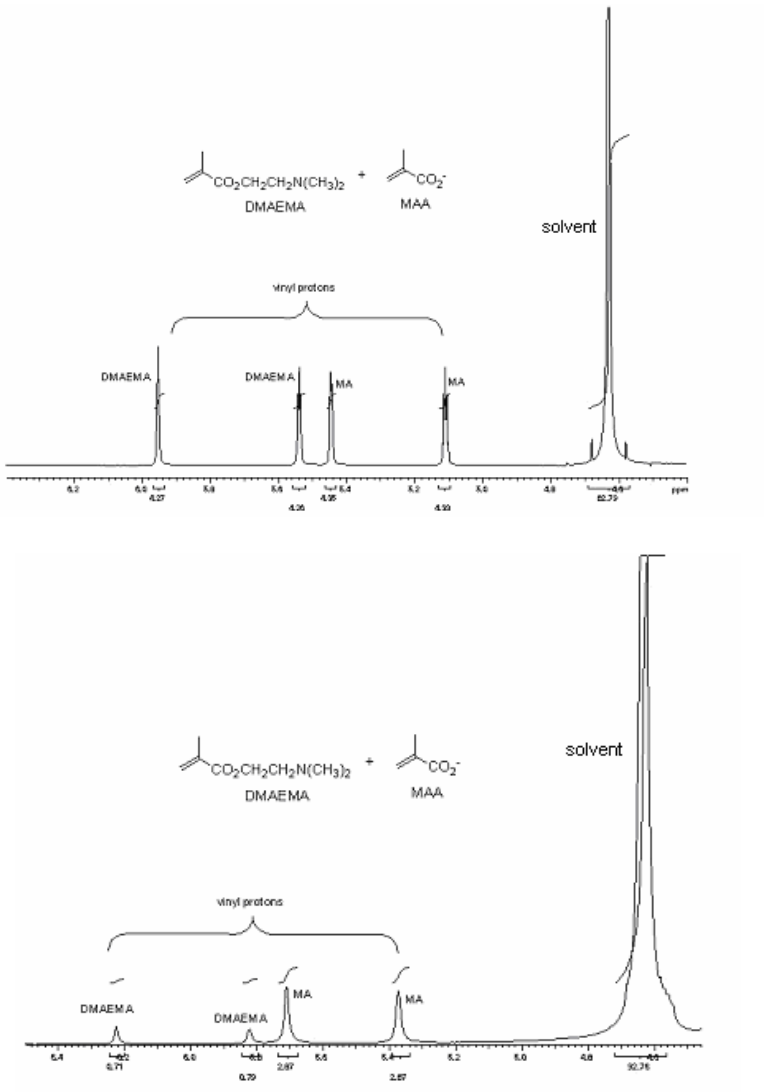

Figure 19. a. ^{1}H NMR room temperature spectrum of DMAEMA and MAA in D_2O and b. ^{1}H NMR spectrum of DMAEMA and MAA after 1 h at 50 ^{o}C in D_2O.

VITA

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