SYNTHESIS AND POLYMERIZATIONS OF PHOSPHONATED-(METH)ACRYLATES AND (METH)ACRYLAMIDES

by

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To my family

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ABSTRACT

SYNTHESIS AND POLYMERIZATIONS OF PHOSPHONATED-(METH)ACRYLATES AND (METH)ACRYLAMIDES

In the first part of this work, three phosphonate containing (meth)acrylamides (1-3) were synthesized. Monomers 1 and 3 were synthesized by amidation reaction of acryloyl chloride with diethyl amino(phenyl)methylphosphonate and diethyl 1-aminoheptylphosphonate. Monomer 2 was synthesized via the reaction of methacryloyl chloride with diethyl amino(phenyl)methylphosphonate. Monomers 1 and 2 were white solids with melting points of 154 ^{o}C and 114 ^{o}C but monomer 3 was a yellow viscous liquid. Thermal homopolymerizations of monomers 1 and 2 in methanol and monomer 3 in bulk using 2 mol% of 2,2'-azobis(isobutyronitrile) (AIBN) at 65 ^{o}C gave polymers with M_n values of 8700, 9600 and 81494. Addition of these monomers (5 mol%) to 2-hydroxyethyl methacrylate (HEMA) did not change its photopolymerization kinetics. In the second part of this work, one reference urea monomer (4) and two new phosphonate-containing urea methacrylates (5 and 6) were synthesized from the reaction of of 2-isocyanatoethyl methacrylate (IEM) and benzyl amine (4), diethyl 1-aminomethylphosphonate (5) and diethyl amino(phenyl)methylphosphonate (6). Monomers 4 and 6 were obtained as white solids with melting points of 70 ^{o}C and 72 ^{o}C, whereas monomer 5 was a colorless viscous liquid. Monomers were homo and copolymerized with HEMA, triethylene glycol dimethacrylate (TEGDMA) and bisphenol A-glycolate methacrylate (BISGMA) using photo-DSC with 2,2'-dimethoxy-2-phenyl acetophenone (DMPA) as photoinitiator. These monomers were found to have significantly high polymerization rate and degree of conversion despite having one double bond and gave crosslinked polymers. Their photopolymerization reactivities were found to be higher or comparable to commercial dental crosslinkers such as Bis-GMA and TEGDMA, indicating their potential as reactive diluents or crosslinkers in dental systems.

ÖZET

FOSFONATLI (MET)AKRİLATLARIN VE (MET)AKRİLAMİTLERİN SENTEZLERİ VE POLİMERİZASYONLARI

Bu çalışmanın ilk bölümünde, fosfonat içeren üç (met)akrilamit sentezlenmiştir. Monomer 1 ve 3 akriloil klorürün dietil amino(fenil)metil fosfonat ve dietil 1-aminoheptil fosfonat ile amidasyon reaksiyonundan sentezlenmiştir. Monomer 2 ise metakriloil klorürün dietil amino(fenil)metil fosfonat ile reaksiyonundan sentezlenmiştir. Monomer 1 ve 2 erime noktaları 154 ^{o}C ve 114 ^{o}C olan beyaz katı maddelerken monomer 3 sarı viskoz bir sıvıdır. Monomer 1 ve 2'nin metanolde ve monomer 3'ün kütle homopolimerizasyonları, 65 ^{o}C'de 2 mol% AIBN kullanılarak, sayısal ortalamalı molekül ağırlıkları 8700, 9600 ve 81494 olan polimerler vermiştir. Bu monomerlerin 2-hidroksietil metakrilat (HEMA)'ya (5 mol%) eklenmeleri onun polimerizasyon kinetiğini değiştirmemiştir. Çalışmanın ikinci bölümünde, bir referans üre momomeri (4) ve iki yeni fosfonat içeren monomer (5 ve 6) 2-isosiyanatoetil metakrilat (IEM)'ın benzil amin (4), dietil aminometil fosfonat (5) ve dietil amino(fenil)metil fosfonat (6) ile reaksiyonundan sentezlenmiştir. Monomer 4 ve 6 erime noktaları 70 ^{o}C ve 72 ^{o}C olan beyaz katıyken, monomer 5 renksiz viskoz bir sıvıdır. Monomerler foto diferansiyel taramalı kalorimetre ile 2,2'-dimetoksi-2-fenil asetofenon (DMPA) kullanılarak homopolimerize ve HEMA, trietilin gikol dimetakrilat (TEGDMA) ve bisfenol A-glikolat metakrilat (BISGMA) ile kopolimerize edildi. Bu monomerlerin tek çift bağa sahip olmalarına rağmen yüksek polimerizasyon hız ve verimleri gösterdikleri ve çapraz bağlı polimerler verdikleri bulunmuştur. Bu monomerlerin fotopolimerizasyon reaktifliklerinin Bis-GMA ve TEGDMA gibi diş çapraz bağlayıcılarından daha yüksek ya da onlara benzeri oldukları bulunmuştur. Bu sonuç ise, bu monomerlerin diş sistemlerinde reaktif seyreltici veya çapraz bağlayıcı olarak kullanılabileceğini göstermektedir.

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LIST OF ACRONYMS/ABBREVIATIONS

AIBN	2,2’-azobisisobutyronitrile
Bis-GMA	2,2-Bis[4-(2-hydroxy-3-methacryloyloxy propyloxy) phenyl] propane
DSC	Differential Scanning Calorimetry
FT-IR	Fourier Transform Infrared Spectroscopy
GPC	Gel Permeation Chromatography
HEMA	2-Hydroxyethyl methacrylate
Irgacure 651	2,2’-dimethoxy-2-phenylacetophenone
NMR	Nuclear Magnetic Resonance Spectroscopy
Rp	Rate of polymerization
TEA	Triethylamine
TEGDMA	Triethyleneglycol dimethacrylate
Tg	Glass transition temperature

1. INTRODUCTION

Some of the most broadly-used polymers are based on (meth)acrylates and (meth)acrylamides. Their distinguishing property is relatively high reactivity, leading to their preferred use in applications where fast polymerization is required, such as dental and other adhesives and coatings.

Another important class of polymers are based on phosphorus-containing monomers. Because of their broad application areas, such monomers and polymers have been the subject of intense research.

The applications include, but are not limited to, fire retardants, metal binders, corrosion inhibitors, adhesives including for dental materials, fuel-cell membranes, etc. In particular, their biocompatible nature makes them especially suited for biomedical applications, including tissue engineering and bone targeting.

In this work, we propose to combine the advantages of these two classes of monomers by synthesizing and polymerizing phosphorus-containing acrylate and acrylamide monomers.

In the next section, we give more detail about the properties of (meth)acrylate monomers. The second section focuses on phosphorus-containing monomers. The third section summarizes the synthesis methods of alpha-aminophosphates.

1.1. Advantages and Applications of (Meth)acrylate and (Meth)acrylamide Monomers and Polymers

Acrylates and methacrylates are the most commonly used monomers in photoinitiated polymerizations due to their high reactivities and excellent polymer properties, especially optical and mechanical properties. The main application areas involve dental restorative materials, biomaterials, coatings, adhesives and photolithography [1-3]. (Meth)acrylamides are also another class of highly reactive monomers commonly

used in biomedical and pharmaceutical applications. Because of the wide variety of application areas, extensive research has been conducted to understand the relationship between the monomer structure and reactivity with the aim of facilitating development of monomers with enhanced reactivity.

In recent years, several factors leading to the enhanced reactivity of (meth)acrylates were hypothesized. These are hydrogen abstraction from labile hydrogens in monomers, hydrogen bonding and electronic effects (dipole moment, secondary functionalities).

Decker and Bowman found that new mono acrylate monomers with carbonate, cyclic carbonate, carbamate, and oxazolidone groups that react extremely rapidly to give crosslinked polymers. This high reactivity can be explained by crosslinking due to hydrogen abstraction reactions which cause an increase in viscosity and earlier gelation [4-11].

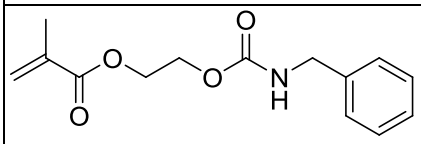
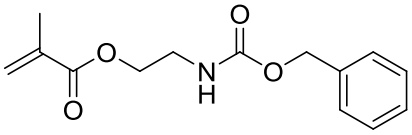
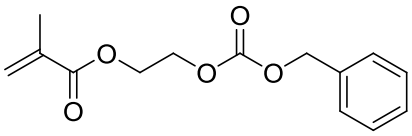
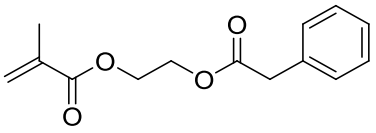
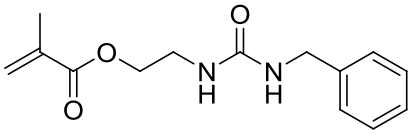
Hoyle *et al.* showed that the degree of hydrogen bonding and the rate of polymerization of hydroxyalkyl acrylates are directly related and both decrease with increasing temperature. Although they could not find a quantitative relationship between hydrogen bonding and termination rate constants, they claimed that highly hydrogen-bonded systems behave as multifunctional monomers and have low termination constants [12].

Jansen *et al.* also indicated the importance of hydrogen bonding on the rate of photopolymerization of different acrylates containing amide, urethane, 'inverted' urethane and urea groups. It was found that the monomers capable of forming hydrogen bonds show 3-6 times higher polymerization rates compared to their non-hydrogen bonded analogues possessing ester and carbonate groups [13].

Among the hydrogen bonded monomers urea-containing ones were found to the most reactive. For example, rate of photopolymerization of ethyl N, N-urea ethyl acrylate (25.2 $mol.ls^{-1}$) was higher than ethyl O-urethane-N-ethyl acrylate (16.1 $mol.ls^{-1}$) and ethyl ester ethyl acrylate (4.4 $mol.ls^{-1}$). Similar results were observed by Berchtold *et al.* and a benzyl-substituted urea monomer was evaluated as the most reactive of any urethane, carbonate,

cyclic carbonate, ester, and hydroxyl monomers studied (Table 1.1) [8]. The high reactivities were suggested to be due to pre-organization via hydrogen bonding to bring the double bonds close to each other, enhancing propagation, although reduction in termination rate may also be involved or be the cause.

Table 1.1. Photopolymerization results of aromatic urea-methacrylates at 25 ^{o}C/67^{o}C.

Monomer	$R_{p,\ 10\%\ Conv}$ (s^{-1})	$R_{p,\ Max}$ (s^{-1})
 Benzyl NCO MA	0.033/0.022	0.045/0.049
 Benzyl OCN MA	0.017/0.016	0.028/0.036
 Benzyl OCO MA	0.004/0.007	0.009/0.009
 Benzyl Ester MA	0.005/0.005	0.009/0.006
 Benzyl NCN MA	0.061[m]	0.082[m]

*m: polymerization at 70 ^{o}C.

Jansen *et al.* also investigated the effect of monomer polarity on the rate of polymerization using monomers which are not capable of hydrogen bonding and found a direct correlation between the maximum rate of polymerization and the dipole moment for the monomers having dipole moments higher than 3.5 Debye [13]. However, Kilambi *et al.*

found no monotonic correlation between monomer reactivity and molecular dipole moment during bulk polymerization of various acrylate monomers capable of hydrogen bonding [7].They suggested that a low dipole moment conformation of some monomers may be more reactive due to intermolecular hydrogen bonding than a conformation with a higher dipole moment.

1.2. Advantages and Applications of Phosphonated Monomers and Polymers

1.2.1. Fire Redardant Materials

Phoshorous-containing compounds are more useful candidates as flame retardants when compared with the halogen-containing compounds. They are environmentally friendly because of the fact that they generate less toxic gases and smoke than the halogen-based flame retardants [14]. In general organic phosphorous compounds provide fire retardant activity through a combination of condensed phase reactions, polymer carbonization promotion, and char formation to protect the surface from further burning [15, 16].

Some examples of polymers with fire retardant property are given in Figure 1.1.

1.2.2. Adhesives

Phosphorous-containing compounds are also important for adhesion to metals, bone and dental tissues [17, 18].

1.2.2.1. Metals. In coatings technology, certain additives comprising amine, silane, titanate, and phosphoric or carboxylic acid groups are used to improve adhesion on substrate. Boutevin *et al.* were synthesized (meth)acrylic monomers containing phosphonic esters, phosphonic acids, and semisalts and investigated the applicability of these monomers in the field of additives for adhesives (Figure 1.2) [19].

Phosphonic acids and phosphonate esters are well known complexing agents. They interact with a various transition and nontransition metal salts in order to form different

monomeric and polymeric complexes in aqueous solutions. In these complexes a coordination bond is formed between the phosphoryl oxygen and the metal component of a metal salt [─C─P=O →M].

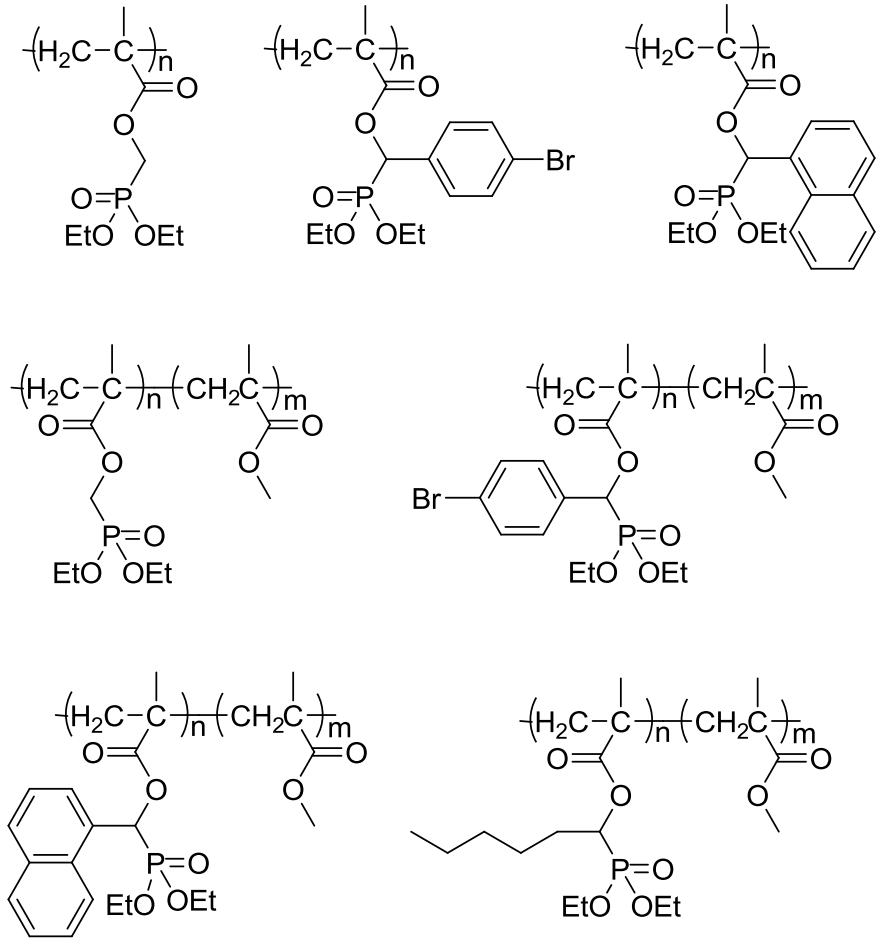


Figure 1.1. Examples of polymers with fire retardant property.

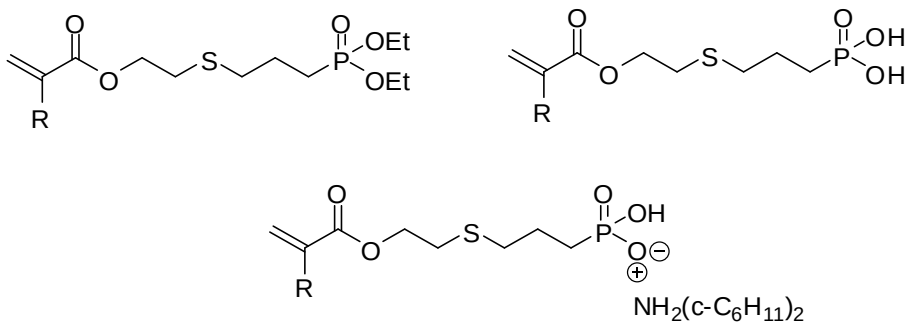


Figure 1.2. Structure of some phosphonated monomers used in coatings.

Metal binding ability of phosphonated polymers is very promising in medicine because of the fact that the control of the physical and chemical properties of material surfaces is very crucial when devoloping medicinal devices and biosensors. Indeed, when no specific surface treatment is applied on artificial materials, their direct expossure to biological fluids results generally in uncontrolled processes such as nonspecific adsorption of proteins followed by the formation of a biofilm. Furthermore, there is a substantial need to develop novel surface systems with long-term robustness under a variety of conditions (e.g., low/high pH and high ionic strength) and formation of a dense interfacial (brush) layer of hydrophilic polymer chains (e.g., with polyethylene glycol, PEG) imparting nonfouling properties to the artificial material and device surface. For example, Zoulalian *et al.* synthesized a terpolymer by polymerization of alkyl-phosphonated, butyl, and PEG methacrylates in the presence of a chain transfer agent. The resulting PEG-poly(phosphonate)-terpolymer molecules self-assembled on TiO_2 surface according to an organized scheme shown in Figure 1.3 were investigated. That four-layer system characterized the binding of phosphonate groups to TiO_2 substrate and the formation of a PEG-brush layer at the outermost surface of the coating. The stability of this terpolymer adlayer, after exposure to solutions of pH 2, 7.4 and 9 up to 3 weeks and also its nonfouling property when exposed to full blood serum were evaluated. Results demonstrated an overall stability improvements of this coating against desorption in contact with aqueous solutions in comparison with reference self-assembly systems.Additionally, the PEG-terpolmer adlayer proved to impart to TiO_2 substrate nonfouling properties when subjected to blood serum [20].

Phosphonate-containing polymers are also considered to act as excellent adhesive and anticorrosive compounds because of the fact that they form coatings without the use of a hydrophobic polymer matrix and solvents. Chougrani *et al.* prepared two novel phosphonated methacrylate monomers and subsequently incorporated into adhesive/anticorrosive coatings (Figure 1.4). The anticorrosive behaviors of the synthesized monomers were evaluated with the salt sprey test which is widely accepted as the most intense of the anticorrosive/adhesive test methods. The result related to bisphosphonic acid containing monomer without nitrogen showed enhanced anticorrosive property [21].

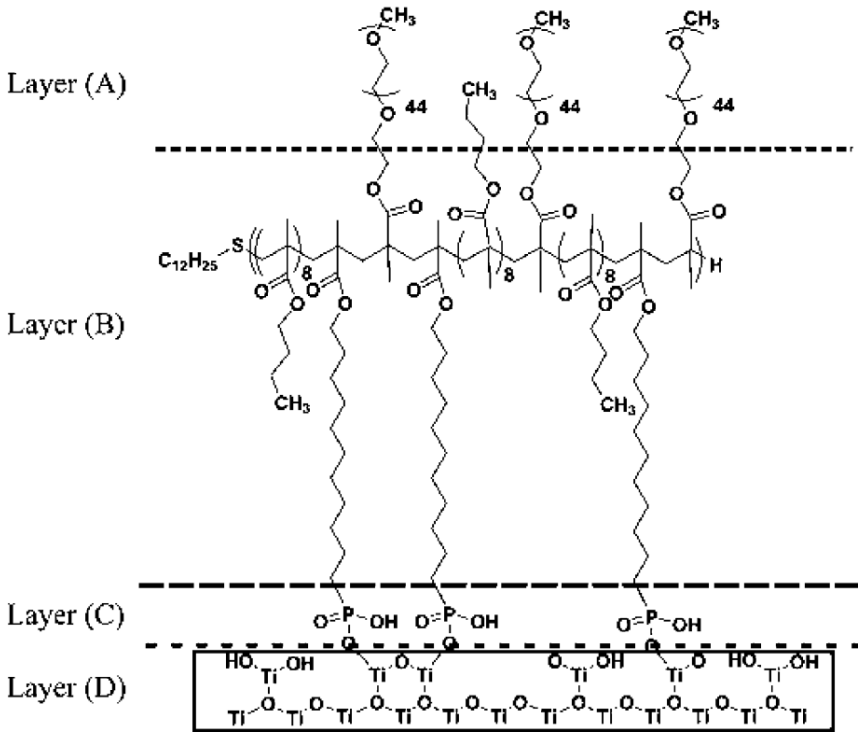


Figure 1.3. The PEG-poly(alkyl phosphonate) terpolymer on a TiO_2 surface in a four-layer system.

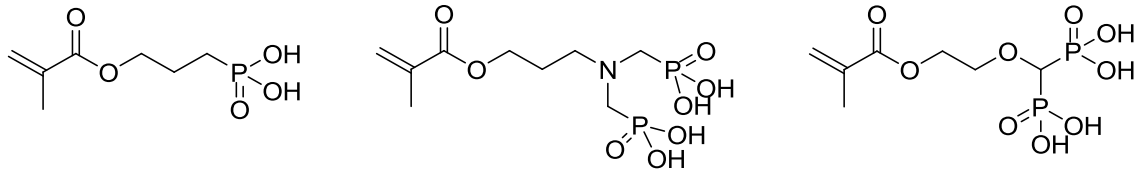


Figure 1.4. Structures of monomers with anticorrosive property.

Ion exchange and adsorption are well-established techniques for the removal of trace amount of toxic metal pollutants from potable water and waste water. Various functional groups on the carbon surface are responsible for the improved selectivity towards certain metal ions such as Pb^{+2}. The phosphorous functionality gives hydrophilicity and resistance towards oxidation as well as improving the ion exchange properties of the carbon surface [22]. Reidelsberger *et al.* were synthesized water soluble aminoethylphosphonic acids and the corresponding polymers in order to investigate the chelating abilities of them (Figure 1.5) [23, 24].

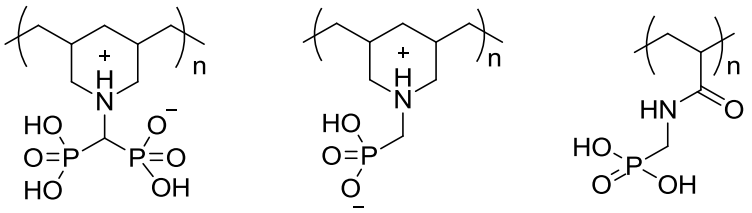


Figure 1.5. Polymeric aminoethyl phosphonic acids.

1.2.2.2. Dental Adhesives. Formation of a strong and permanent bond between composite filling materials and tooth substances improves the long-term durability of dental materials. Self-etching adhesive systems have been utilized to enable a strong and stable bond between filling material and the tooth substance for more than ten years [25].Commercial self-etching enamal-dentin adhesives are composed of a mixture of self-etching adhesive monomers, crosslinkers, additional monofunctional co-monomers and additives [25-29].

The general structure of self-etching dental adhesive monomers is shown in Figure 1.6. They contain a polymerizable group, which can react both with other monomers in the adhesive and filling composites by copolymerization, an adhesive group, such as strong acidic groups, which provides the desired adhesion to tooth substance, and a spacer group R [30, 31].

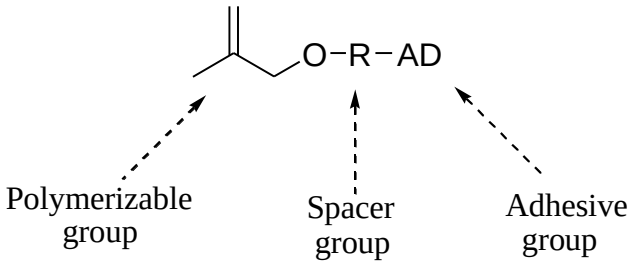


Figure 1.6. General structure of self-etching adhesive monomers.

As polymerizable groups, generally free radically polymerizable (meth)acrylates and (meth)acrylamides are used. Spacer groups have crucial effect on both the properties of monomer such as volatility, solubility, viscosity, wetting and the properties of the corresponding polymer such as hydrophilicity, swelling, and flexibility.Adhesive groups include mono- or dihydrogenphosphate, phosphonic or carboxylic acid groups [31-42].

These acidic monomers remove the smear layer, demineralize the dentin and enamel, and diffuse into collagen fibrils to form a hybrid layer, providing the desired adhesion.

Some examples of commercially available self-etching adhesive monomers are the glycerol dimethacrylate ester of phosphoric acid (GDMP), 10-methacryloyloxy methacrylate (MDP), methacryloyloxyethyl phenyl hydrogen phosphate (MEP-P) and methacryloyloxyethyl dihydrogen phosphate (MEP, HEMA-phosphate) (Figure 1.7) [43].

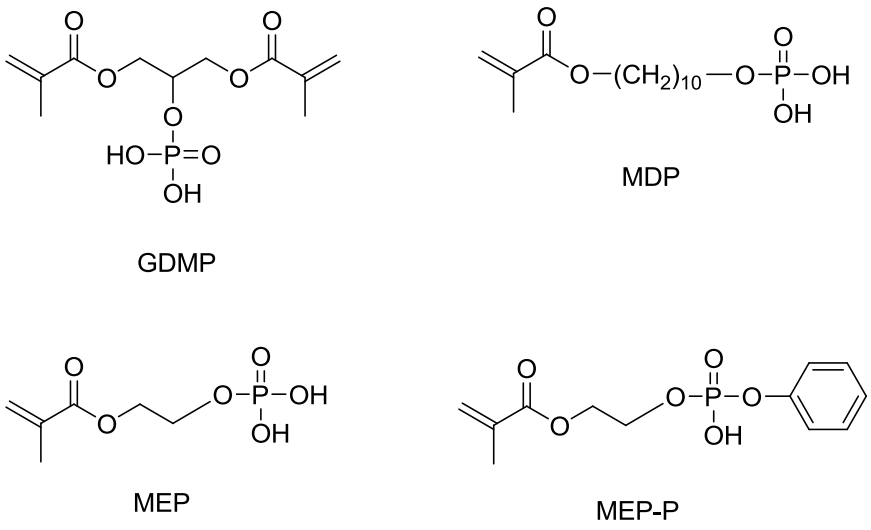


Figure 1.7. Examples of commercially available self-etching adhesive monomers.

As mentioned above, phosphorus-containing compounds are effectively used in dental applications because of the fact that the incorporation of the phosphorous functionality leads to a better adhesion on the tooth tissues owing to the formation of complexes with calcium ions in hydroxyapatite and the increased biocompatibility.

1.2.3. Biomedical Applications

Moreover, phosphorous-containing compounds are also received a great interest in the tissue engineering and drug delivery applications. The presence of phoshorous in the structures of the polymers (polyphosphates, polyphosphonates, polyphosphoesters, phosphonated, poly(meth)acrylates) improves the controlled biodegradability, biocompatibility, and processibility of polymers used in the biomedical applications by

enhancing the desired properties of the biopolymers. According to different results reported in the literature, phosphorous-containing polymers have already been successfully involved in many examples dealing with the biomedical field [44].

Some examples of polymers used in tissue engineering and drug delivery applications are shown in Figure 1.8 and Figure 1.9.

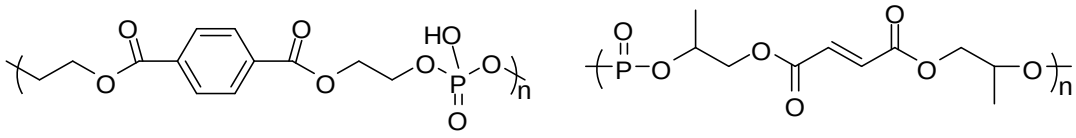


Figure 1.8. Poly(phosphoester) structures used in tissue engineering applications.

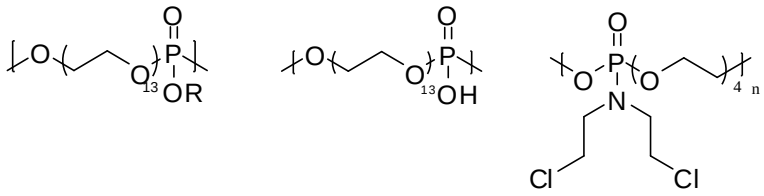
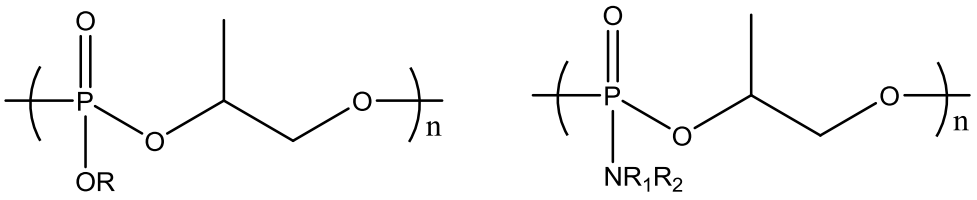


Figure 1.9. Poly(phosphoester) structures used in drug delivery applications.

Polyphosphoesters (PPE) and polyphosphoamidates (PPA) are important phosphorous-containing polymers which are effectively involved in the biomedical applications. The unique characteristic of biodegradation, biocompatibility and structure versatility of these compounds enables to develop various phosphonated-polymers for drug delivery, tissue engineering and gene delivery [45].

Huand *et al.* reviewed the recent advances in polyphosphoester- and polyphosphoramidate-based biopolymers and they reached the following results. The ring-opening polymerization and polycondensation are the two methods for the synthesis of these phosphonate-based polymers. Especially enzymatic ring-opening polymerizations are more favorable compared to the reactions initiated by organometallic initiators. Polyphosphonates, as a components of copolymers, can enhance their solubility in common organic solvents and lower the glass transition temperature of the copolymers.

Consequently, the processibility of copolymers can be greatly improved. Generally polyphosphoesters and polyphosphoramidates are hydrophobic and water insoluble. In order to make them hydrophilic and water soluble, amino and hydroxyl groups are incorporated into them (Figure 1.10) As a result, degradation rate of these polymers is increased. Finally, in contrast to polyphosphoesters containing amino groups, polyphosphoesters containing hydroxyl groups show very low cytotoxicity [45].



PPE

PPA

$R = CH_2CH_2NH_3^+Cl^-$
$R = CH_2CH_2NH_2^+(Me)Cl^-$
$R = (CH_2)_6NH_3^+Cl^-$
$R = CH_2CH_2OH$

$NR_1R_2 = NHCH_2CH_2NH_2$
$NR_1R_2 = NH(CH_2)_4NH_2$
$NR_1R_2 = NHCH_2CH_2NH(Me)$
$NR_1R_2 = NHCH_2CH_2N(Me)_2$
$NR_1R_2 = NHCH_2CH_2N(Et)_2$
$NR_1R_2 = NHCH_2CH_2N^+(Me)_3Cl^-$

Figure 1.10. Water soluble polyphosphoesters and polyphosphoramidates.

Phosphonated-hydrogels, another class of biomaterials that exhibit various properties, have a variety of applications, ranging from biomacromolecule separation to contact lenses, coatings of blood contacting materials, controlled drug delivery devices, as well as tissue engineering scaffolds [46-48].

For example, Wang *et al.* synthesized poly(ethylene glycol) di-[ethyl phosphatidyl (ethylene glycol) methacrylate], ‘‘PhosPEG-dMA’’, in order to produce a novel biodegradable and biocompatible photopolymerizing hydrogel. It may exhibit biological activity that increases tissue development in musculoskeletal tissue engineering applications.Synthesis, photogelation and degration process of PhosPEG-dMA are shown in Figure 1.11 [47].

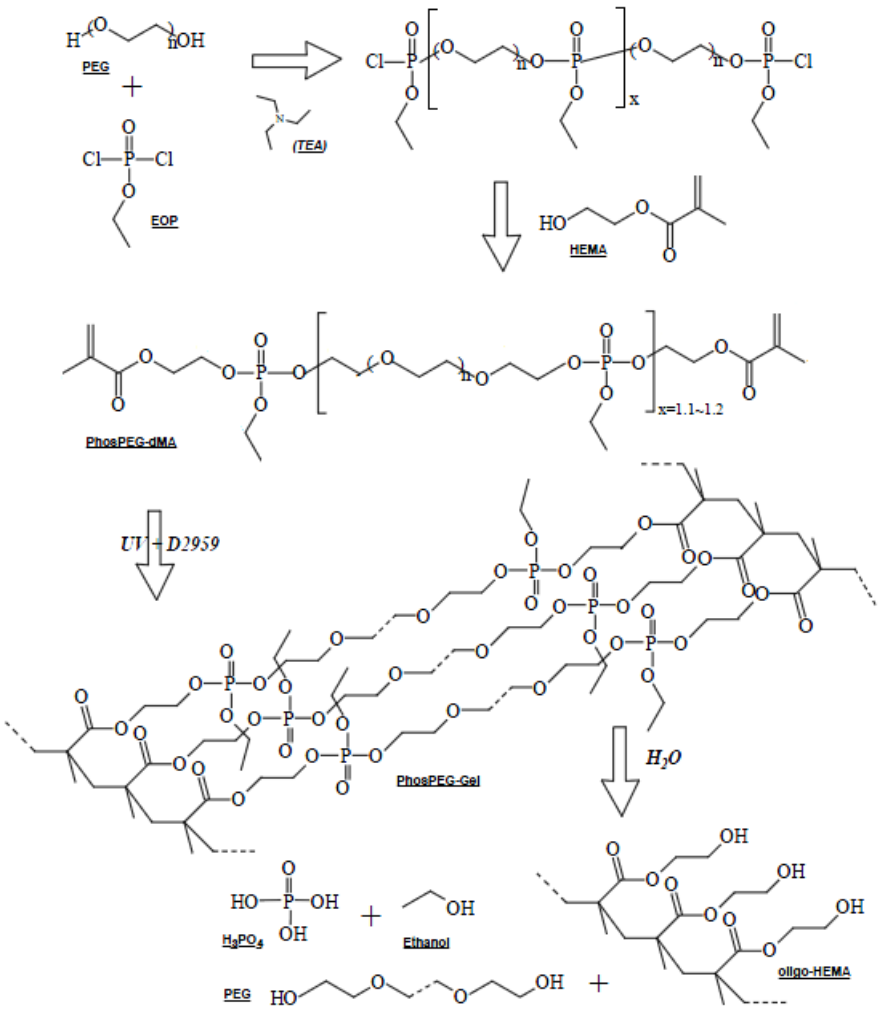


Figure 1.11. Schematic diagram for synthesis, photogelation and degration of PhosPEG-dMA.

Bisphosphonates (BPs) are structural analogues of naturally existing pyrophosphate (Figure 1.12) with increased chemical and enzymatic stability due to the replacement of the oxygen in P-O-P by a carbon, resulting in a P-C-P structure [49]. They have strong affinity for bone mineral, hydroxyapatite (HAP), enabling them to chelate calcium ions and prevents bone dissolution.

Bisphosphonates have been used as drugs for bone diseases including osteoporosis, Paget's disease, bone cancer, etc [49]. They can inhibit bone resorption [50, 51], be used to deliver small molecule drugs [52-55], imaging agents [56, 57] peptides or proteins to the bone [58, 59]. The polymers carrying bisphosphonic acid groups are used as drug carriers

to bone. Bone-targeting drug conjugates based on poly(ethylene glycol) and poly[N-(2-hydroxypropyl)methacrylamide] containing alendronate as bone targeting groups were tested [60, 61], a hydrogel prepared from copolymer of N-acrylpamidronate and N-isopropylacrylamide was used as scaffold for mineralization of HAP [62], bisphosphonate derivatives of cationic polymers such as poly(l-lysine) and poly(ethylenimine) were tested for affinity to HAP [63] and bisphosphonate-modified polyurethanes were prepared to resist calcification around implants [64]. More recently bisphosphonate-containing monomers were investigated for self-etching dental adhesive applications [65, 66] which facilitate adhesion of dental restoratives and orthodontic appliances to dental tissue.

Figure 1.12. Naturally existing pyrophosphate and its synthetic analogues, bisphosphonates.

1.3. α-Aminophosphonates

1.3.1. General Structure and Application Areas of α-Aminophosphonates

As indicated in the litrature, α-aminophosphonate derivatives (I) have been correlated to α-amino acids (II) due to their structural similarity (Figure 1.1).

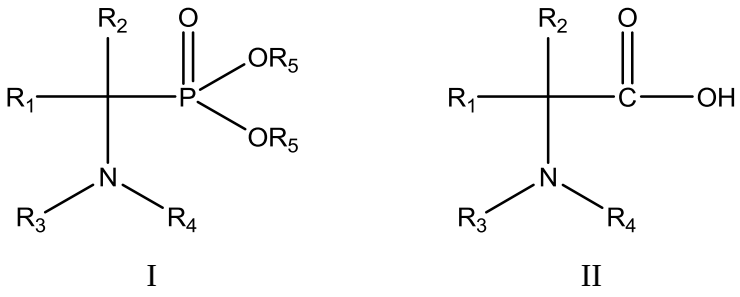


Figure 1.13. General structure of α-aminophosphonates and α-amino acids.

As mentioned above, α-aminophosphonates are structural analogs of the corresponding α-amino acids as well as heterocyclic phosphonates [67] and ω-aminophosphonates [68]. They have a wide range of applications in the areas of industrial, agricultural, and medicinal chemistry owing to their biological and physical properties as well as their utility as synthetic intermediates [67, 69–72]. As a kind of natural amino acid analogues, α-aminophosphonates constitute an important class of compounds with diverse biological activities. The activity of α-aminophosphonates as peptidomimetics [73], enzyme inhibitors [74], pharmacogenic agents [75], haptens of catalytic antibodies [76], herbicidals [77], inhibitors of serine hydrolases [78], inhibitors of UDP-galactopyranose mutase [79] and antitumor agents [80–83] is reported in literature.

1.3.2. Mechanistic Details and General Scope of The Kabachnik-Fields Reaction

Various synthetic methods for α-aminophosphonates have been reported [84-90] and the straightforward one is the addition of the compounds, containing P-H bond to the C=N-bond of imines (Figure 1.14) [91]. In fact, dialkyl phosphites are able to undergo many addition reactions, including addition to the C=O bond to give α- hydroxyphosphonates (Figure 1.15) [91, 92].

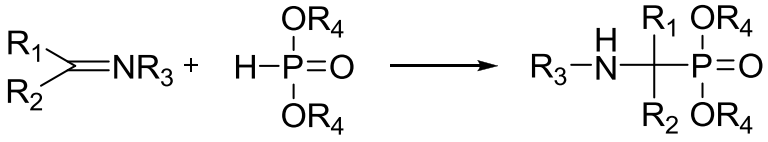


Figure 1.14. Pudovik reaction.

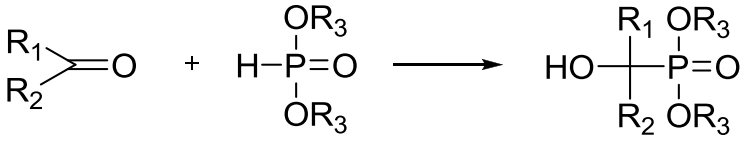


Figure 1.15. Abramov reaction.

However, the most remarkable pathway to the synthesis of α-aminophosphonates is the Kabachnik-Fields reaction which is a one-pot, three-component procedure using carbonyl compound, amine and dialkyl phosphite (Figure 1.16) [91].

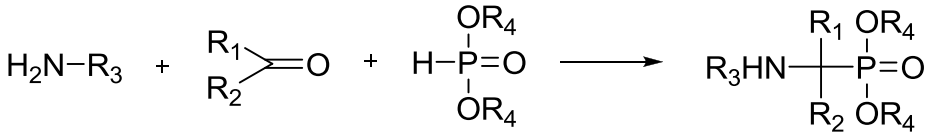


Figure 1.16. Kabachnik-Fields reaction.

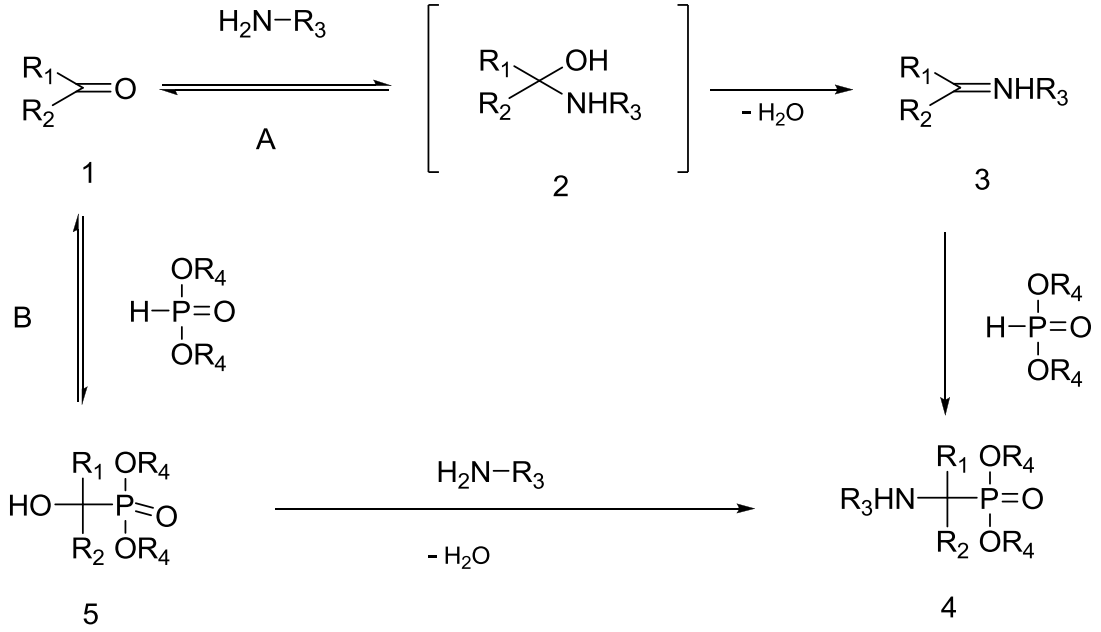


Figure 1.17. Mechanism of Kabachnik-Fields reaction.

This reaction is a multistep procedure having quite complex mechanism (Figure 1.17). The first step is the formation of the corresponding imine 3 (Figure 1.17, path A). The elimination of the water formed is heplful for the whole process because its formation is a reversible process. The second step is the addition of the compounds having P─H bond to the transient imine 3 following with Pudovik type of addition (Figure 1.17, 3→4) to give aminophosphonate 4 as the final product [91].

One possible complication of the Kabachnik-Fields reaction is that the dialkyl phosphites are able to undergo Abramov addition to C=O bond, giving α-

hydroxyphosphonates 5 (Figure 1.17, path B). Therefore, in the case of three component process it is possible to face with competitive addition of either N─H or P─H fragments to to C=O bond. It is claimed that the Abramov pathway can also lead to the product 4 and even considered the direct nucleophilic substitution of the hydroxyl in α-hydroxyphosphonates by amino component (Figure 1.17, 5→4) [91, 93, 94].

1.3.3. One Step-Three Component Synthesis of α-Aminophosphonates

One of the most reliable methods for the synthesis of α-aminophosphonates is the three component reaction that takes place when a carbonyl compound (aldehyde or ketone), a primary or secondary amine, and a dialkyl or trialkyl phosphites are reacted. In most of the cases it requires an electrophilic activation brought about by a Lewis or Broensted acid. However, it has been recently shown that the reaction can occur even without catalyst. Another great improvement concerns the elimination of the solvent that, in addition to represent an advance in the sustainable chemistry, also makes the reaction more efficient [83, 84, 95, 96].

1.3.3.1.Catalyzed Syntheses. As reported in the Table 1.2 and Table 1.3, several new electrophilic activators have been introduced in order to improve the reaction yields and scope. Among this group a further option concerns the solvent and the solvent-free alternative [96].

In the presence of a solvent the choice of the catalyst seems to be really huge: from simple $LiClO_4$ to lanthanide derivatives, from Amberlyst-15 to ammonium salts. The phosphorous moiety can be alternatively a trialkyl or dialkyl phosphite without appreciable difference. The solvent is often a classic organic solvent, but some examples of ionic liquid use have been reported [96].

Solvent-free reactions are more appealing because they eliminate the need of treating the reaction waste. Also in this group there is a great variety of catalysts, from silica gel to sulfonium salts, from $Mg(ClO_4)_2$ to TiO_2. Some examples of microwave activation (MW), in addition to the catalyst, have been also reported showing an impressive acceleration of

the reaction. It is remarkable that in this reaction group the phosphorous component choice is diethyl phosphite [96].

1.3.3.2. Catalyst and Solvent Free Syntheses. Recent examples of Kabachnik-Fields reactions show that it is possible to carry out the reaction in absence of both catalyst and solvent. In one of them the MW activation of the mixture is required with the result of lowering the reaction time. All show good scope and yields [96-100].

Some examples of one-pot three component synthesis of α-aminophosphonates are shown in Table 1.4.

1.3.3.3. Synthesis of Monomers from α-Aminophosphonates. As indicated in the literature, there are a variety of synthetic routes to introduce α-aminophosphonates into monomer structure. One of the most effectively used methods to synthesize monomers bearing phosphorous functionality is amidation reaction of α-aminophosphonates derivatives with (meth)acryloyl chloride in the presence of triethyl amine in an anhydrous environment [137-139]. Some examples of monomers are given in Figure1.18.

Gomy *et al.* reported the synthesis of bis-ureated monomers from bis α-aminophosphonates for use in molecular imprinting applications (Figure 1.19). They are used for the imprinting of the dicarboxylate moiety of chemotherapeutic drugs due to their highly enhanced binding [140].

Table 1.2. Catalyzed Kabachnik-Fields reactions using solvents.

Catalyst	**Solvent**	**T (^{0}C)**	**Time**	**Carbonyl Component**	**Yield Range**	**Special Conditions**	**Refs.**
$La(OTf)_3$	Butylmethyl Imidazolium (bmim)X	20	2-27 h	Aromatic Aldehyde	90-100	–	[101]
$TaCl_5$-SiO_2	CH_2Cl_2	rt	18-24 h	Aldehyde & Ketone	81-94	N_2	[88]
$LiClO_4$	Et_2O	rt	0.5 h	Aromatic Aldehyde	85-97	Ar	[102]
$LiClO_4$	Et_2O	rt	1.5 h	Aldehyde	86-95	Hydrazine Hydroxyamie	[103]
bmim	bmimX	rt	7.5-12 h	Aldehyde	71-87	–	[104]
Phthalo Cyanine	CH_2Cl_2, EtOH,Toluene	bp	12-24 h	Ketones	0-98	Hindered ketone	[105,106]
SmI_2	CH_3CN	45-100	24 h	Aromatic Aldehyde	18-96	4 A^0-ms , Ar	[107]
$In(OTf)_3$	THF	bp	12-54 h	Aldehyde	16-99	N_2	[108]
$AlCl_3$	bmimCl	rt	2-4 h	Aromatic Aldehyde	80-95	N_2	[109]
CH_3COOH	EtOH	55	1-3 d	Heterocyclic Ketone	50-90	–	[110]

Table 1. 2. Catalyzed Kabachnik-Fields reactions using solvents. (Continued)

Catalyst	**Solvent**	**T (^{0}C)**	**Time**	**Carbonyl Component**	**Yield Range**	**Special Conditions**	**Refs.**
–	Benzene	0	6 h	Aromatic Aldehyde	72-89	Uses Cl-Phosphites	[111]
$PhNMe_3Cl$	CH_2Cl_2	bp	3 h	Aldehyde	65-98	TMSCl	[112]
$H_3PW_{12}O_{40}$	CH_2Cl_2	rt	30 min	Aldehyde	83-98	–	[113]
Amberlyst-15	CH_3CN	rt	25-90 min	Aldehyde	83-96	–	[114]
$SbCl_3$-Al_2O_3	CH_3CN	rt	2.5-5 h	Aromatic Aldehyde	49-92	5 A^0-ms , Amino Acid Esters	[115]
CH_3COCl	CH_3COCl	rt	8 h	Aldehyde & Ketone	38-72	The N compound is a phosphor amidate	[116]
Cu(ll)	Water	80	0.5-3 h	Aromatic Aldehyde	90-98	Complex copper catalyst	[117]
CH_3COOH	CH_3COOH	rt	12-48 h	Aromatic Aldehyde	65-98	–	[118]
$Sc(O_3SOC_{12}H_{25})_3$	Water	30	20 min-2 h	Aldehyde	53-88	–	[90]
In/HCl	Water	rt	0.5-1.5 h	Aldehyde & Ketone		Aromatic Nitro Compounds as amine source	[119]

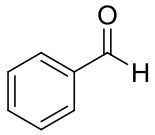
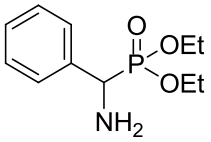
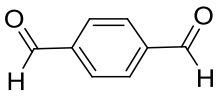
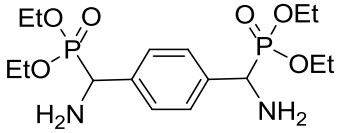
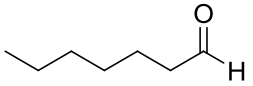
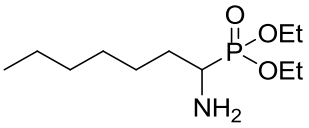
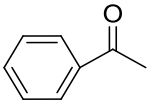
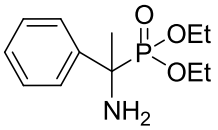
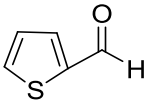
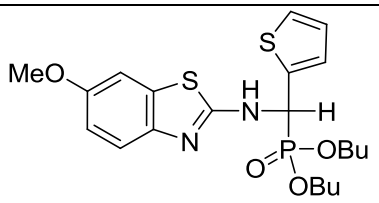
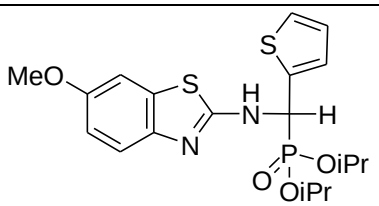
Table 1.3. Solvent free catalyzed Kabachnik-Fields reactions.

Catalyst	**T (^{0}C)**	**Time**	**Carbonyl Compoud**	**Yield Range**	**Special Conditions**	**Refs.**
Al_2O_3	rt	3-6 min 5-8 h	Aldehyde	65-90	MW HCO_2NH_4	[120]
CF_3COOH	rt	24 h	Aldehyde	81-100	–	[121]
$M(OTf)_3$ M=Li, Mg, Al, Cu, Ce	80	5 min-6 h	Aromatic Aldehyde & Ketone	60-98	–	[122]
SiO_2	rt	3-15 min	Aldehyde & Ketone	80-95	MW	[123]
Me_2SBrBr	rt	15-25 min	Aromatic Aldehyde	87-95	–	[124]
$Bi(NO_3)_3$	rt	1-4 min 5-10 h	Aromatic Aldehyde	80-98	MW	[125]
$Mg(ClO_4)_2$	rt or 80	2 min-6 h	Aldehyde & Ketone	75-98	–	[85]
$BF_3.Et_2O$	110	0.5-2 h	Aromatic Aldehyde	70-85	–	[126]
TiO_2	50	1-7 h	Aldehyde & Ketone	50-98	–	[127]
Sulfamic Acid	rt	0.25-4 h	Aldehyde	74-94	–	[128]

Table 1. 3. Solvent free catalyzed Kabachnik-Fields reactions. (Continued)

$ZrOCl_2$	rt	5min-6 h	Aldehyde & Ketone	70-95	–	[129]
Amberlite-IR 120	rt	1-3 min	Aldehyde & Ketone	11-98	MW	[130]
$H_2C_2O_4$	50	2 h	Aldehyde	83-98	–	[131]
$LiClO_4$	rt	15-45 min	Aromatic Aldehyde	80-92	HMDS source of amine	[132]
$Al(OTf)_3$	100	5 min-3 h	Aldehyde & Aliphatic Ketone	65-98	$(NH_4)_2CO_3$ or CH_3COONH_4 source of amine	[133]
$FeCl_3$.THF	60		Aromatic Aldehyde	53-96	–	[134]
NBS or CBr_4	rt or 50	3-24 h	Aldehyde	60-99	–	[135]

Table 1.4. Examples of Kabachnik-Fields synthesized α-aminophosphonates.

Carbonyl Compound	**Product**	**Refs.**
		[133]
		
		
		[88]
		[136]
		

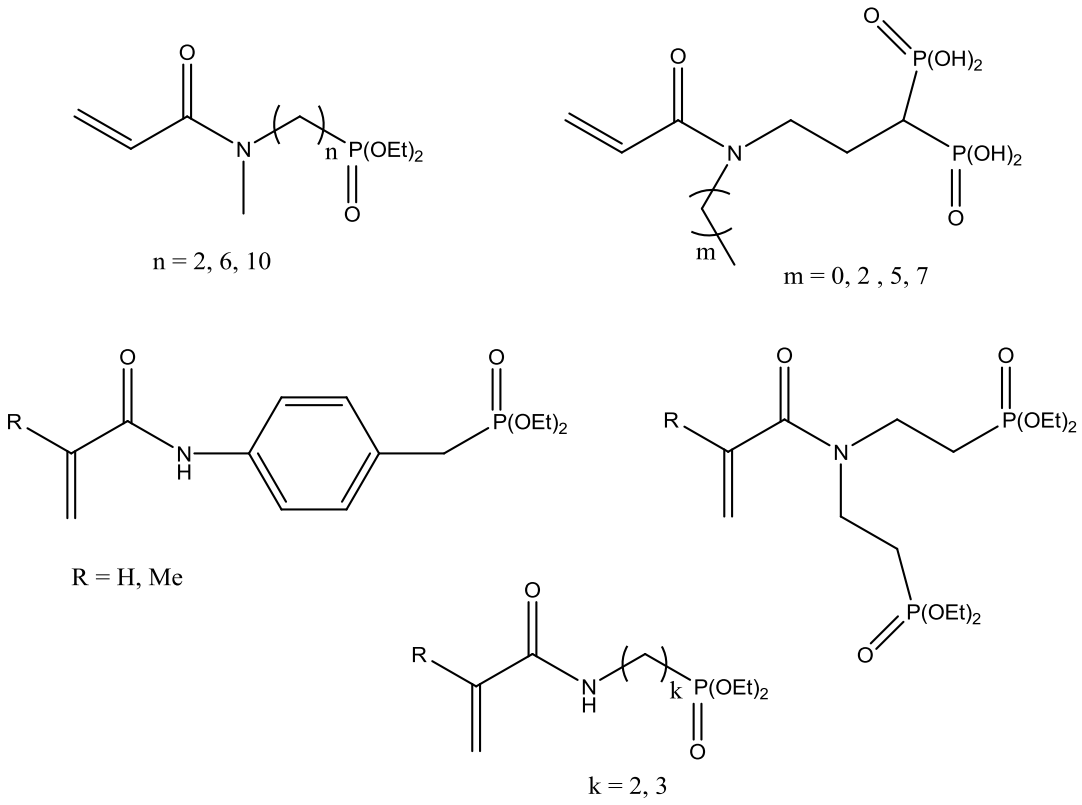


Figure 1.18. Examples of monomers obtained from α-aminophosphonates.

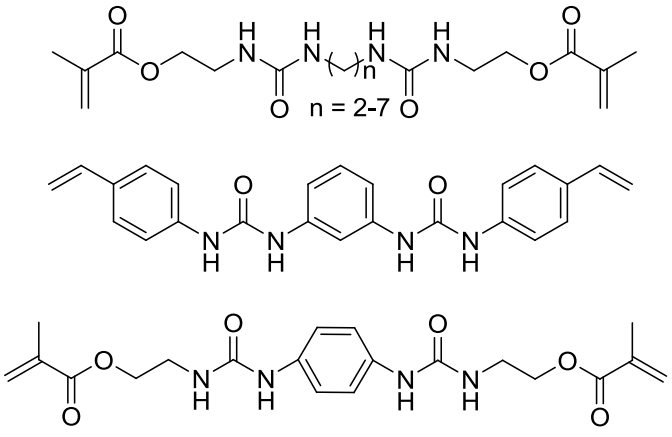


Figure 1.19. Examples of bis-ureated (meth)acrylates.

2. OBJECTIVES

The purpose of this thesis is to design, synthesize, characterize and evaluate novel, highly reactive, biocompatible monomers for mainly dental applications, investigation of the relationship between structure and reactivity of monomers. For high reactivity we choose methacrylate and (meth)acrylamide functionalities, for biocompatibility we add phosphonate groups. Some of the monomers are also hydrolysis resistance due to amide linkages instead of ester as in currently used commercial monomers.

Therefore the objectives of this thesis are (i) synthesis of α-amino phosphonates, (ii) attachment of these amines to methacrylates and methacrylamides to obtain novel monomers desired, (iii) polymerization of the monomers and evaluation of their reactivities and polymer properties.

3. EXPERIMENTAL

3.1. Materials and Apparatus

3.1.1. Materials

Diethyl aminomethylphosphonate, diethyl amino(phenyl)methylphosphonate, and diethyl 1-aminoheptylphosphonate were prepared according to literature procedures [133, 141]. Triethyl amine (TEA, Merck), 2-hydroxyethyl methacrylate (HEMA, Aldrich), bisphenol A-glycolate methacrylate (BISGMA, Aldrich), triethylene glycol dimethacrylate (TEGDMA, Aldrich), 2-isocyanatoethyl methacrylate (IEM, Aldrich), 1-heptaldehyde (Fluka), benzaldehyde (Aldrich), diethyl phosphite (Across Organics), ammonium carbonate (it contains ammonium carbamate, Merck), aluminum trifluoromethane sulfonate (Aldrich), sodium chloride (Merck), sodium hydroxide (Merck), sodium sulfate (Merck), sodium hydrogen carbonate (Merck), hydrochloric acid (Merck), anhydrous toluene (Aldrich), hexane (Merck), diethyl ether (Merck), 2,2'-azobis(isobutyronitrile) (Aldrich), and 2,2-dimethoxy-2-phenylacetophenone (Aldrich) were used without further purification. Acrloyl chloride (Aldrich), and methacrloyl chloride (Fluka) were passed through neutral aluminum oxide before used. Dichloromethane and chloroform were dried over molecular sieves.

3.1.2. Apparatus

^{1}H-, ^{13}C- and ^{31}P-NMR spectroscopy (Varian Gemini 400 MHz) and Fourier transform infrared (FTIR) spectroscopy (T380) were used for monomer characterization. The photo-polymerizations were performed on a TA Instruments Q100 differential photocalorimeter (DPC). Thermogravimetric analysis was done with a TA Instrument Q50. Elemental analyses were obtained from Thermo Electron SpAFlashEA 1112 elemental analyser (CHNS separation column, PTFE; 2 m; 6 x5 mm) .Gel permeation chromatography (Viscotek) was carried out with THF solvent using polystyrene standarts.

3.2. Synthesis of Novel Phosphonated Monomers

3.2.1. Synthesis of Primary α-Aminophosphonates

3.2.1.1. Synthesis of diethyl 1-aminomethylphosphonate [141]. Diethyl phthalimidomethylphosphonate (4.869 g, 16.38 mmol), hydrazine hydrate (1.12 ml, 35.68 mmol) and ethanol (69.4 ml) was mixed into a 250 ml of round bottom flax. The mixture was stirred and refluxed at 76 ^{o}C for one hour. White precipitate was obtained in the mixture. After ethanol was evaporated, $CHCl_3$ was added and filtered out. The organic solvent was evaporated and finally the crude product was distilled under reduced pressure. Pure product was obtained as a colorless liquid in 58% yield.

^{1}H NMR ($CDCl_3$): 1.29 (t, 6H, CH_3), 2.96 (d, 2H, CH_2P), 4.02-4.19 (m, 4H, CH_2O).

FT-IR:3382,3303 (N–H), 2981-2898 (C–H), 1229 (P=O), 1019 and 952 (P–O–Et) cm^{-1}.

^{31}P NMR ($CDCl_3$): 28.0 ppm.

3.2.1.2. Synthesis of diethyl amino(phenyl)methylphosphonate [133]. $Al(OTf)_3$ (95 mg, 0.2 mmoL) was added to a mixture of benzaldehyde (4mL, 40 mmol), $(NH_4)_2CO_3$ (3.143 g, 20 mmol), and diethyl phosphite (5 mL, 40 mmol). The resulting mixture was placed in a preheated oil bath at 100 ^{0}C and stirred for 5 min under open atmosphere. The reaction mixture was cooled to room temperature and acidified to pH 1 by $HCl_{(aq)}$. The solution was extracted with diethyl ether (4x100 mL). The aqueous phase was then made alkaline with $NaOH_{(aq)}$, and the product was extracted with diethyl ether (4x100 mL). The combined organic phase was dried over Na_2SO_4 and concentrated under reduced pressure. The pure product was obtained as a colerless liquid in 60% yield.

^{1}H-NMR ($CDCl_3$): 1.10, 1.21 (t, 6H, $OCH_2C\mathit{H}_3$), 1.81 (s, 1H, NH), 3.75-4.02 (m, 4H, $OC\mathit{H}_2CH_3$), 4.17, 4.21 (d, 1H, CH-P), 7.18-7.40 (m, 5H, Ar-H) ppm.

^{13}C-NMR ($CDCl_3$): 15.49 ($OCH_2\mathit{C}H_3$), 52.08, 53.78 (CH–P), 61.72 ($O\mathit{C}H_2CH_3$), 126.66, 126.78, 127.35, 136.74 (Ar-C) ppm.

FTIR:3371, 3294 (N-H), 3064, 3025 (Ar-H), 2981, 2928,2901 (C–H), 1235 (P=O), 1017 and 955 (P–O) cm^{-1}.

3.2.1.3. Synthesis of diethyl 1-aminoheptylphosphonate [133]. $Al(OTf)_3$ (95 mg, 0.2 mmoL) was added to a mixture of heptanal (6 mL, 40 mmol), $(NH_4)_2CO_3$ (3.143 g, 20 mmol), and diethyl phosphite (5 mL, 40 mmol). The resulting mixture was placed in a preheated oil bath at 100 ^{0}C and stirred for 35 min under open atmosphere. The reaction mixture was cooled to room temperature and acidified to pH 1 by $HCl_{(aq)}$. The solution was extracted with diethyl ether (4x100 mL). The aqueous phase was then made alkaline with $NaOH_{(aq)}$, and the product was extracted with diethyl ether (4x100 mL). The combined organic phase was dried over Na_2SO_4 and concentrated under reduced pressure. The pure product was obtained as a colerless liquid in 65% yield.

^{1}H-NMR ($CDCl_3$):0.83 (t, 3H, $CH_2C\mathit{H}_3$), 1.13-1.30 (m, 14H, $OCH_2C\mathit{H}_3$, $C\mathit{H}_2C\mathit{H}_2C\mathit{H}_2C\mathit{H}_2$), 1.53, 1.73 (m, 2H, $CHC\mathit{H}_2$), 2.88 (t of d, 1H, CH-P), 4.09 (m, 4H, $OC\mathit{H}_2CH_3$) ppm.

^{13}C-NMR ($CDCl_3$): 13.94 ($\mathit{C}H_3$), 16.56 ($OCH_2\mathit{C}H_3$), 22.67, 25.94, 28.93, 31.01, 31.56 ($\mathit{C}H_2\mathit{C}H_2\mathit{C}H_2\mathit{C}H_2\mathit{C}H_2$), 47.95, 49.48 ($\mathit{C}$H–P), 61.96 ($O\mathit{C}H_2CH_3$) ppm.

FTIR: 3376, 3298 (N-H), 2957, 2927,2827 (C–H), 1235 (P=O), 1022 and 955 (P–O) cm^{-1}.

3.2.2. Synthesis of Phosphonated-(Meth)acrylamides

3.2.2.1.Synthesis of monomer 1. A solution of acryloyl chloride (0.80 mL, 10 mmol) diluted in anhydrous toluene (2 mL) was added dropwise, under N_2, to a mixture of diethyl amino(phenyl)methylphosphonate (1.95 g, 8.02 mmol), and triethylamine (1.30 mL, 9.00 mmol) in anhydrous toluene (7 mL) in an ice bath. Thereafter, more toluene (5 mL) was poured into the flask and the mixture was stirred at room temperature two more hours. The reaction was terminated by addition of distilled water (10 mL). The mixture was

filtered.The filtered solid was dissolved in chloroform (113 mL) and extracted with distilled water (3x40 mL), 2M HCl (3x40 mL), saturated $NaHCO_3$ (3x40 mL), and distilled water (3x40 mL). The combined organic layer was dried over Na_2SO_4. After removal of solvent, monomer 1 was obtained as white solid in 30% yield (mp=154 ^oC).

^{1}H-NMR ($CDCl_3$): 1.02, 1.24 (t, 6H, OCH_2CH_3), 3.64, 3.83, 4.11 (m, 4H, OCH_2CH_3), 5.50 (d, 1H, CH-P), 5.61 (d of d, 1H, CH_1H_2=CH), 6.23 (d, 1H, CH_1H_2=CH), 6.25 (d, 1H, CH_1H_2=CH), 7.21-7.46 (m, 5H, Ar-H), 8.22 (bs, 1H, NH) ppm.

^{13}C-NMR ($CDCl_3$): 16.31 (OCH_2CH_3), 48.92, 51.04 (CH–P), 63.24 (OCH_2CH_3), 126.85, 128.46, 128.52, 135.07 (Ar-C), 128.02 ($CH=CH_2$), 130.41 ($CH=CH_2$), 165.19, 165.27 (C=O) ppm.

FTIR: 3262 (N-H), 3052, 3027 (Ar-H), 2985, 2935 (C–H), 1672 (C=O), 1630 (C=C), 1540 (NH), 1216 (P=O), 1015 and 954 (P–O) cm^{-1}.

ELEM. ANAL., Calcd. for $C_{14}H_{20}NO_4P$: C, 56.56%; H, 6.78%; N, 4.71%; O, 21.53%; P, 10.42%. Found: C, 57.62%; H, 7.20%; N, 4.97%.

3.2.2.2. Synthesis of monomer 2. A solution of methacryloyl chloride (0.60 mL, 6 mmol) diluted in anhydrous toluene (1.2 mL) was added dropwise, under N_2, to a mixture of diethyl amino(phenyl)methylphosphonate (1.20 g, 5. mmol), and triethylamine (0.8 mL, 5.5 mmol) in anhydrous toluene (4.2 mL) in an ice bath. Thereafter, more toluene (3 mL) was poured into the flask and the mixture was stirred at room temperature two more hours. The reaction was terminated by addition of distilled water (6 mL). The mixture was filtered. The filtered solid was dissolved in chloroform (57 mL) and extracted with distilled water (3x20 mL), 2M HCl (3x20 mL), saturated $NaHCO_3$ (3x20 mL), and distilled water (3x20 mL). The combined organic layers was dried over Na_2SO_4. After removal of solvent, monomer 2 was obtained as white solid in 40% yield (mp=114 ^oC).

^{1}H-NMR ($CDCl_3$): 1.05, 1.27 (t, 6H, OCH_2CH_3), 1.93 (s, 3H, CH_3), 3.67, 3.89, 4.11 (m, 4H, OCH_2CH_3), 5.32, 5.71 (s, 2H, CH_2=C), 5.53 (d, 1H, CH-P), 7.06 (bs, 1H, NH), 7.27-7.46 (m, 5H, Ar-H) ppm.

^{13}C-NMR ($CDCl_3$): 16.35 ($OCH_2\mathit{C}H_3$), 18.97 (CH_3), 49.84, 51.26 (CH–P), 63.36 ($O\mathit{C}H_2CH_3$), 120.59 ($\mathit{C}H_2$=C), 128.30, 128.41, 128.80, 135.45 (Ar-C), 140.43 (CH_2=C), 167.89, 167.97 (C=O).

FTIR: 3280 (N-H), 3048, 3029 (Ar-H), 2982, 2908 (C–H), 1659 (C=O), 1621 (C=C), 1524 (NH), 1234 (P=O), 1021 and 960 (P–O) cm^{-1}.

ELEM. ANAL., Calcd. for $C_{15}H_{22}NO_4P$: C, 57.87%; H, 7.12%; N, 4.50%; O, 20.56%; P, 9.95%. Found: C, 57.82%; H, 7.55%; N, 4.43%.

3.2.2.3. Synthesis of monomer 3. A solution of acryloyl chloride (0.33 mL, 4.06 mmol) diluted in anhydrous dichloromethane (3.3 mL) was added dropwise, under N_2, to a mixture of diethyl 1-acrylamidoheptylphosphonate (0.64 g, 2.53 mmol), and triethylamine (0.5 mL, 3.43 mmol) in anhydrous dichloromethane (7.4 mL) in an ice bath. Thereafter, the mixture was stirred at room temperature two more hours. The reaction was terminated by addition of distilled water (3.3 mL). After addition of chloroform (35mL), the mixture was extracted several times with distilled water (12 mL), 2M HCl (12 mL), saturated $NaHCO_3$ 12 mL), and distilled water (12 mL). The combined organic layers was dried over Na_2SO_4. After removal of solvent, monomer 3 was obtained as a yellow viscous liquid in 49% yield.

^{1}H-NMR ($CDCl_3$): 0.79 (t, 3H, $CH_2C\mathit{H_3}$), 1.13-1.30 (m, 14H, $OCH_2C\mathit{H_3}$, $C\mathit{H_2}C\mathit{H_2}C\mathit{H_2}C\mathit{H_2}$),1.58, 1.73 (m, 2H, $CHC\mathit{H_2}$), 4.06 (m, 4H, $OC\mathit{H_2}CH_3$) 4.47 (m, 1H, CH-P), 5.58 (d of d, 1H, CH_1H_2=CH), 6.25 (d, 1H, $C\mathit{H_1}H_2$=CH), 6.27 (d, 1H, $CH_1\mathit{H_2}$=CH), 7.45, 7.48 (d, 1H, NH) ppm.

^{13}C-NMR ($CDCl_3$): 12.78 ($\mathit{C}H_3$), 15.58 ($OCH_2\mathit{C}H_3$), 21.66 ($CH\mathit{C}H_2$), 24.87, 27.84, 28.51, 30.54 ($\mathit{C}H_2\mathit{C}H_2\mathit{C}H_2\mathit{C}H_2$), 43.31, 44.79 ($\mathit{C}$H–P), 61.19, 62.08 ($O\mathit{C}H_2CH_3$), 125.47(CH=$\mathit{C}H_2$), 129.59 ($\mathit{C}$H=$CH_2$), 164.59, 164.64 (C=O) ppm.

FTIR: 3253 (N-H), 2980, 2928 (C–H), 1664 (C=O), 1630 (C=C), 1539 (NH), 1222 (P=O), 1022 and 959 (P–O) cm^{-1}.

3.2.3. Synthesis of Phosphonated-Urea-Methacrylates

3.2.3.1. Synthesis of monomer 4 [142]. To a solution of benzyl amine (0.5 g, 4.67 mmol) in 17 mL of dry chloroform, 2-isocyanatoethyl methacrylate (0.68 mL, 4.83 mmol) was added dropwise in an ice bath under N_2. After stirring overnight at room temperature, the solution was extracted with 1 wt% of NaOH (3x70 mL), with 1 wt% of HCl (3x70 mL), and brine (3x70 mL). After drying the organic phase with anhydrous Na_2SO_4, the solvent was evaporated. The crude product was recrystallized from diethyl ether and monomer 4 was obtained as a white solid in 75% yield (mp = 70 ^oC).

^{1}H-NMR ($CDCl_3$): 1.82 (s, 3H, CH_3), 3.33 (t, 2H, $OCH_2C\mathit{H_2}$), 4.07 (t, 2H, $OC\mathit{H_2}$ CH_2), 4.21 (s, 2H, CH_2─Ar), 5.12, 5.26 (bs, 2H, NH), 5.46, 5.98 (s, 2H, $C=CH_2$), 7.16-7.24 (m, 5H, Ar─H)

^{13}C-NMR ($CDCl_3$): 18.34 (CH_3), 39.58 ($OCH_2\mathit{C}H_2$), 44.47 (NH─CH_2), 64.08 ($O\mathit{C}H_2CH_2$), 125.96 ($\mathit{C}H_2$=C), 135.96 (CH_2=C), 127.30, 127.36, 128.60, 139.10 (Ar─C), 158.21 (HN─C=O), 167.53 (O─C=O) ppm.

FTIR: 3321 (N−H), 3060, 3062 (Ar─H), 2960, 2928,2890 (C−H), 1711 (C=O), 1628 (C=C), 1587 (N−H) cm^{-1}.

3.2.3.2. Synthesis of monomer 5. To a solution of diethyl aminomethylphosphonate (0.2 g, 1.20 mmol) in 4 mL of dry chloroform, 2-isocyanatoethyl methacrylate (0.22 mL, 1.56 mmol) was added dropwise in an ice bath under N_2. After stirring overnight at room temperature, the solution was extracted with 1 wt% of NaOH (3x18 mL), with 1 wt% of HCl (3x18 mL), and brine (3x18 mL). After drying the organic phase with anhydrous Na_2SO_4, the solvent was evaporated. Monomer 5 was obtained as a colorless viscous liquid in 77% yield.

^{1}H-NMR ($CDCl_3$): 1.25 (t, 6H, OCH_2 $C\mathit{H_3}$), 1.87 (s, 3H, CH_3), 3.43 (t, 2H, OCH_2 $C\mathit{H_2}$), 3.60 (m, 2H, CH_2−P), 4.04 (m, 4H, $OC\mathit{H_2}CH_3$), 4.13 (t, 2H, $OC\mathit{H_2}$ CH_2), 5.50, 6.05 (s, 2H, $C=CH_2$), 5.77, 5.90 (bs, 2H, NH) ppm.

^{13}C-NMR ($CDCl_3$): 15.36 ($OCH_2\mathit{C}H_3$), 17.17 (CH_3), 33.21, 34.95 (CH_2─P), 38.15 ($OCH_2\mathit{C}H_2$), 61.60 ($O\mathit{C}H_2CH_3$), 63.31 ($O\mathit{C}H_2CH_2$), 124.76 ($\mathit{C}H_2$=C), 135.14 (CH_2=C), 157.59 (HN─C=O), 166.28 (O─C=O) ppm.

FTIR : 3349 (N−H), 2983, 2929,2901 (C−H), 1716, 1686 (C=O), 1644 (C=C), 1561 (N−H), 1160 (P=O), 1020, 949 (P−O−Et) cm $^{-1}$.

^{31}P-NMR ($CDCl_3$): 24.44 ppm.

3.2.3.3. Synthesis of monomer 6. To a solution of diethyl amino(phenyl)methylphosphonate (0.5 g, 2.06 mmol) in 7.4 mL of dry chloroform, 2-isocyanatoethyl methacrylate (0.30 mL, 2.13 mmol) was added dropwise in an ice bath under N_2. After stirring overnight at room temperature, the solution was extracted with 1 wt% of NaOH (3x30 mL), with 1 wt% of HCl (3x30 mL), and brine (3x30 mL). After drying the organic phase with anhydrous Na_2SO_4, the solvent was evaporated. The crude product was recrystallized from diethyl ether and washed with hexane. Monomer 6 was obtained as a white solid in 70% yield (mp = 72 ^{o}C).

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^{1}H-NMR ($CDCl_3$): 1.07, 1.35 (t, 6H, OCH_2 CH_3), 1.84 (s, 3H CH_3), 3.40 (t, 2H, $OCH_2C\mathit{H}_2$), 3.65, 3.83, 4.07 (m, 4H, $OC\mathit{H}_2CH_3$), 4.21 (t, 2H, $OC\mathit{H}_2CH_2$), 5.43, 5.98 (s, 2H, C=CH_2), 5.48 (m, 1H, CH−P), 7.11 (bs, 2H, NH), 7.24-7.48 (m, 5H, Ar─H) ppm.

^{13}C-NMR ($CDCl_3$): 16.16 ($OCH_2\mathit{C}H_3$), 18.05 (CH_3), 38.73 ($OCH_2\mathit{C}H_2$), 49.87, 51.51 (CH─P), 63.18 ($O\mathit{C}H_2CH_3$), 64.01 ($O\mathit{C}H_2CH_2$), 125.44 ($\mathit{C}H_2$=C), 136.03 (CH_2=C), 127.81, 127.99, 128.34, 135.96 (Ar─C), 157.77 (HN─C=O), 167.13 (O─C=O) ppm.

FTIR: 3379, 3317 (N−H), 3060, 3032 (Ar─H), 2987, 2929, 2907 (C−H), 1721, 1684 (C=O), 1639 (C=C), 1545 (N−H), 1160 (P=O), 1012, 976 (P−O−Et) cm $^{-1}$.

^{31}P-NMR ($CDCl_3$): 23.22 ppm.

ELEM. ANAL., Calcd. for $C_{18}H_{27}N_2O_6P$: C, 54.27%; H, 6.83%; N, 7.03%; O, 24.10%; P, 7.77%. Found: C, 54.54%; H, 7.31%; N, 7.31%.

3.3. Photopolymerizations

3.3.1. Photopolymerization Procedure

All the photopolymerizations were carried out on a TA Instrument Q 100 Photo-DSC equipped with a mercury arc lamp as the light source and using 2,2-dimethoxy-2-phenyl acetophenone (Irgacure 651) as the photoinitiator. The photoinitiator (~8 mg) was first dissolved in methylene dichloride (5 mL). 3-4 mg sample was placed in aluminum DSC pan. A methylene dichloride solution of the photoinitiator was added with a microsyringe to give a final concentration in the monomer of 2 mol% after evaporation of the solvent. The sample and the reference pans were placed in the DSC chamber, the system was puged with nitrogen flow to remove air and methylene dichloride for 10 min before polymerization and purging was continued during polymerization. The samples were irradiated for 10 min at 40 ^{o}C, 55 ^{o}C, and 72 ^{o}C with an incident light intensity of 20 mW/cm^2. The heat flux as a fuction of time was monitored using DSC under isothermal conditions and both the rates of polymerization (Rp) and conversions were calculated as a fuction of time. The rates of polymerizations were calculated according to the following formula:

$$\text{Rate} = \frac{(Q/s)\, M}{n\, \Delta H_p\, m}$$

where Q/s is the heat flow per second, M is the molar mass of the monomer, n is the number of double bonds per monomer molecule, ΔH_p is the heat released per mole of double bonds reacted and m is the mass of monomer in the sample. The theoretical value used for $\Delta H_p$was 13.12 kcal/molfor methacrylamide double bonds [143].

3.4. Free Radical Polymerizations in Bulk and Solution

3.4.1. Polymerization Procedure

The homopolymerizations of monomers 1 and 2 were carried out in methanol at 65 ^{o}C with 2 mol% AIBN as an initiator. For example, monomer 1 (179.5 mg, 0.600 mmol) and AIBN (2 mg, 0.012 mmol) in methanol were added to a septum sealed tube. The tube was subjected to freeze-evacuate-thaw procedure and placed in a 65 ^{o}C oil bath. The polymer was purified by precipitating into diethyl ether with few drops of methylene dichloride in which monomer 1 was soluble and dried under vacuum.

The homopolymerization of monomer 3 was carried out in bulk at 65 ^{o}C with 2 mol% AIBN as an initiator. The purification of the polymer was performed by dissolving in methylene dichloride and precipitating into hexane with few drops of diethyl ether.

3.5. Calculation of Dipole Moments

Spartan ‘06 program was used to calculate the Boltzmann-average dipole moments of monomers 4, 5, and 6. For this purpose, all possible rotations around single bonds were considered for a given acrylate in order to generate all the conformations corresponding to stationary points. All these conformations were minimized at the PM3 level of theory. The unique structures were sorted in the order of increasing energy. The dipole moments of the first 100 conformers are Boltamann averaged at 298.15 K according to the following formula:

$$\langle \mu_{calc} \rangle = \sum_j D_j \frac{e^{\Delta H_j / RT}}{\sum_i e^{\Delta H_i / RT}} = \sum_j D_j p_j$$

where D_j is the dipole moment of the conformation j, ΔH_j is the heat of formation of conformation j, T is the absolute temperature, R is the Boltzmann constant and p_j is the probability of finding the monomer in conformation j at the temperature T [144].

4. RESULTS AND DISCUSSION

4.1. Synthesis and Characterizations of Primary α-Aminophosphonates

α-Aminophosphonates have attracted a good deal of attention in chemistry, medicine, and agricultural science because of the fact that they are structural analogs of naturally occuring α-amino acids [85]. As indicated in the literature, various methods are available for their synthesis [83]. The most efficient route for the synthesis of α-aminophosphonates is the one pot three component Kabachnik-Fields reaction.

Synthesis of three different primary α-aminophosphonates (diethyl amino(phenyl)methylphosphonate,diethyl diethyl 1-aminomethylphosphonate and diethyl 1-aminoheptylphosphonate) which were used as starting phosphonate compounds for the synthesis of monomers are shown in Figures 4.1 and 4.2. Two of them (diethyl amino(phenyl)methylphosphonate and diethyl 1-aminoheptylphosphonate) were prepared from one pot three component Kabachnik-Fields reaction in the presence of aluminum trifluoromethane sulfonate, $Al(OTf)_3$ as a catalyst under solvent-free condition by using two different aldehydes (benzaldehyde and 1-heptaldehyde), ammonium carbonate, and diethyl phosphite according to literature procedure (Figure 4.1) [133]. The other amine (diethyl 1-aminomethylphosphonate) was synthesized by Gabriel synthesis [141].

These primary α-aminophosphonates were obtained as colorless liquids. Their structures were confirmed by FTIR, ^{1}H, and ^{13}C NMR spectroscopy. ^{13}C NMR spectra of diethyl amino(phenyl)methylphosphonate and diethyl 1-aminoheptylphosphonate are shown in Figure 4.3. ^{1}H NMR spectrum of diethyl 1-aminomethylphosphonate is given in Figure 4.4. For instance, the characteristic peaks of the carbon atom adjacent to phosphorous atom are seen as a doublet at 52.08 and 53.78 ppm for diethyl aminomethylphosphonate, at 47.95 and 49.48 ppm for diethyl 1-aminoheptylphosphonate. The spectra also have characteristic peaks for methyl and methylene carbons around 16.0 and 61.72 ppm.

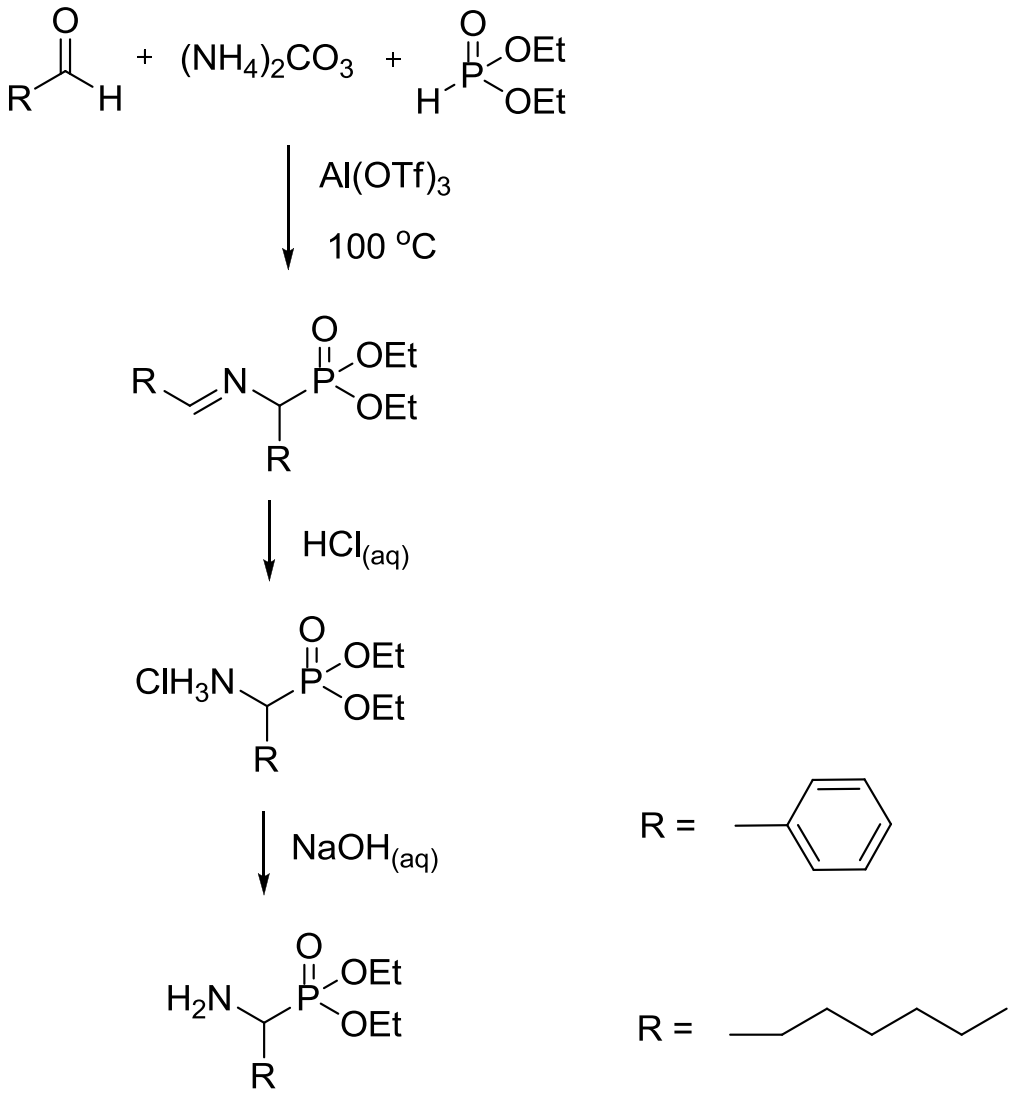


Figure 4.1. Synthesis of diethyl amino(phenyl)methylphosphonate and diethyl 1-aminoheptylphosphonate.

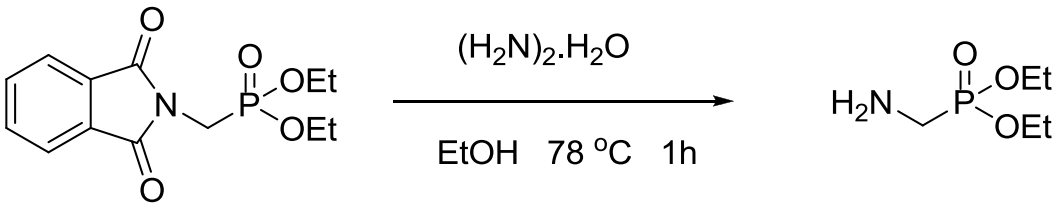


Figure 4.2. Synthesis of diethyl 1-aminomethylphosphonate.

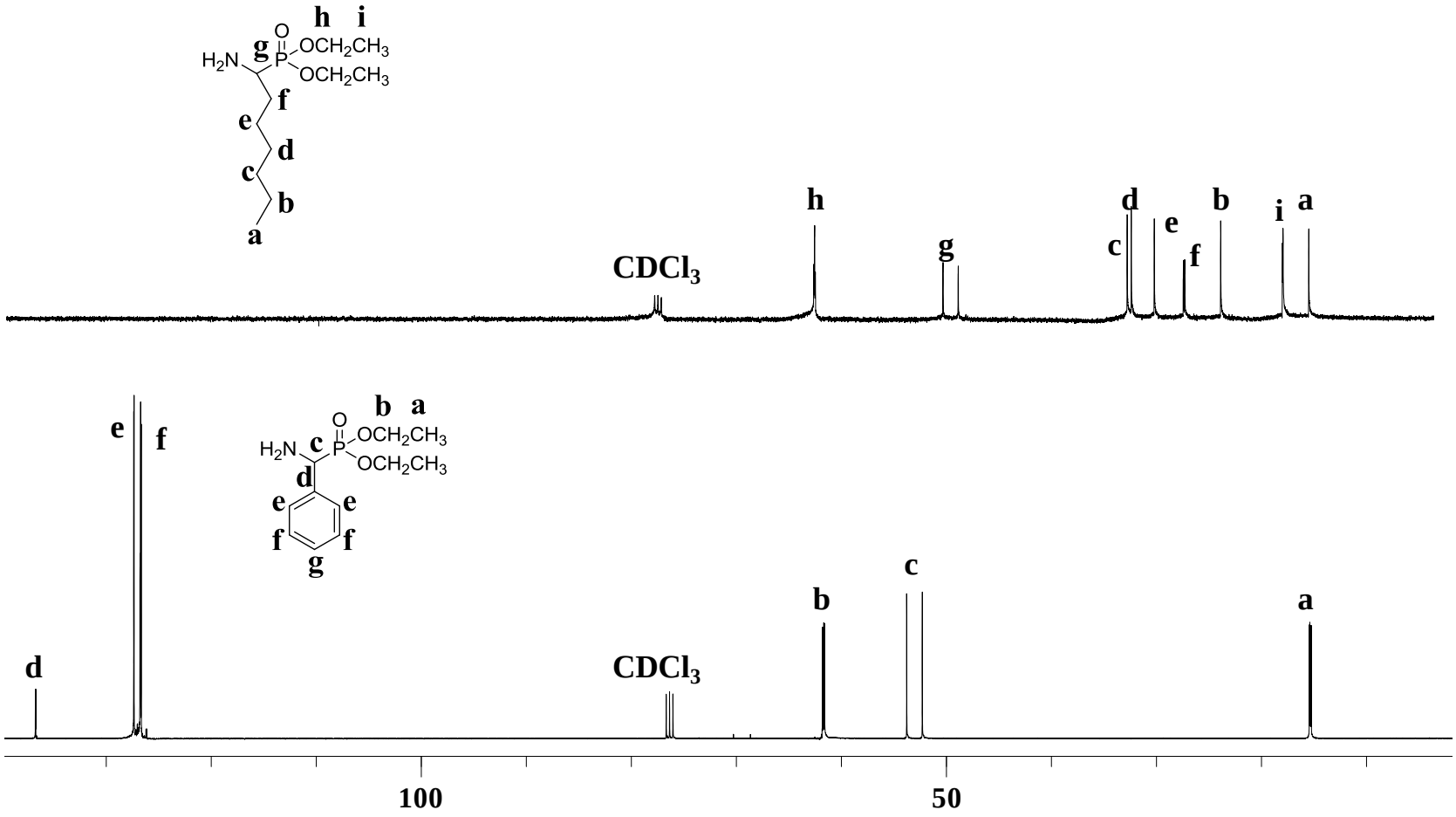


Figure 4.3. ^{13}C NMR spectra of diethyl amino(phenyl)methylphosphonate and diethyl 1-aminoheptylphosphonate.

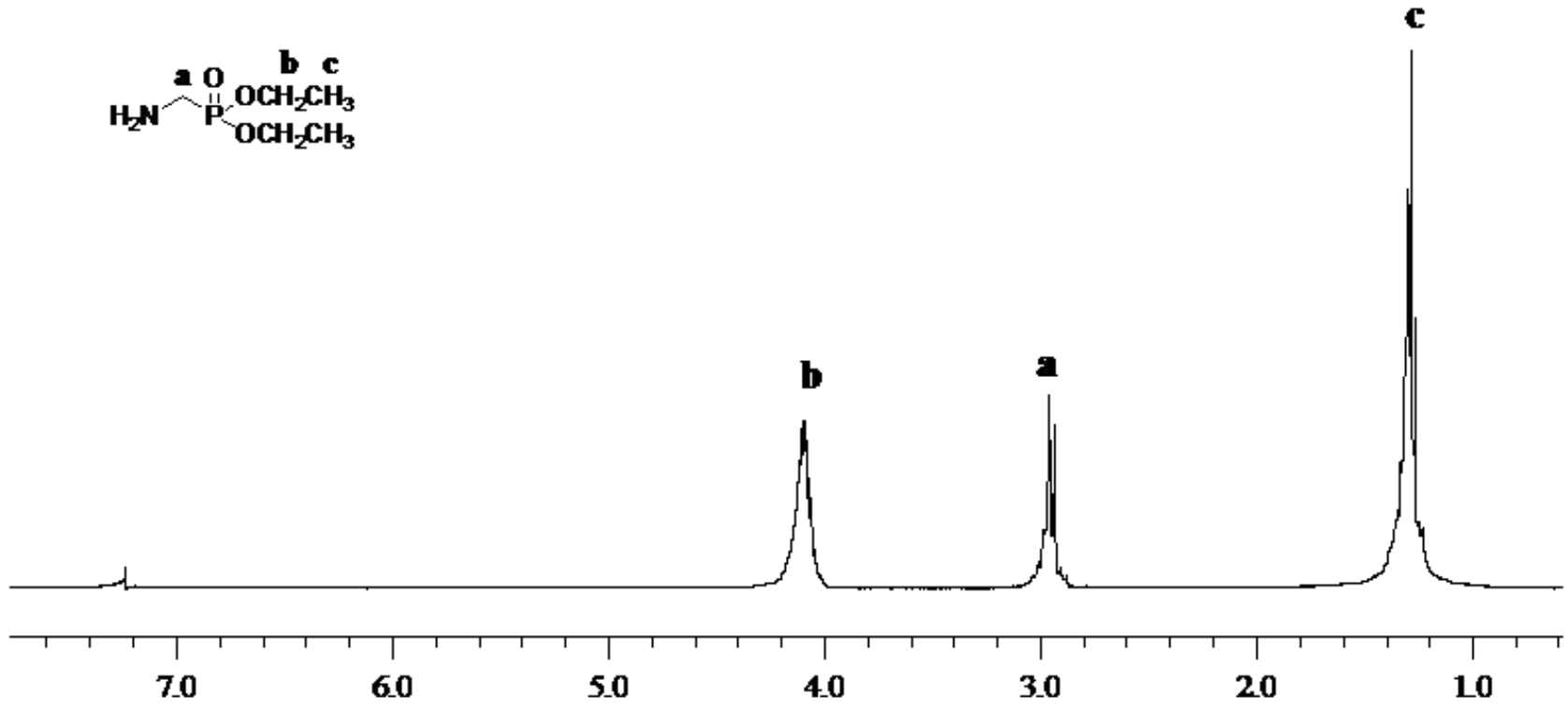


Figure 4.4. ^{1}H NMR spectrum of diethyl 1-aminomethylphosphonate.

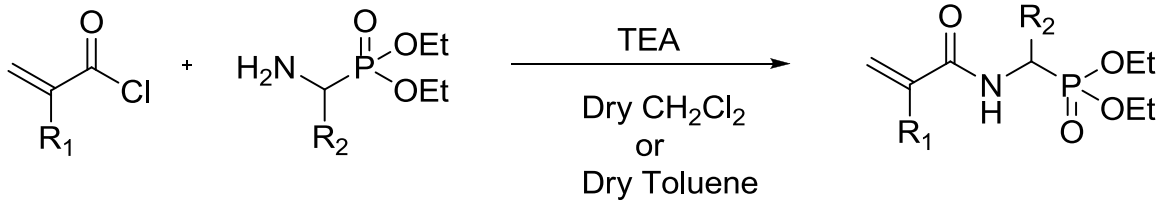
4.2. Synthesis and Polymerizations of Phosphonated-(Meth)acrylamides

As discussed in the introduction, (meth)acrylamides are highly reactive monomers preferred for various polymerization applications, and phosphorus-containing monomers have their own advantages. Here we report on phosphonated (meth)acrylamide monomers which are hoped to combine good properties of both groups.

4.2.1. Synthesis and Characterizations of Phosphonated-(Meth)acrylamides

New phosphonated (meth)acrylamides (1-3) were synthesized in one step by the reaction of (meth)acryloyl chloride with diethyl amino(phenyl)methylphosphonate and diethyl 1-aminoheptylphosphonate in the presence of triethylamine (Figure 4.5). Monomers 1 and 2 were obtained as white solids with melting points of 154 ^{o}C and 114 ^{o}C in 30% and 40% yields, respectively. Monomer 3 was obtained as a yellow viscous liquid in 49% yield.

The solubility of the monomers in common solvents are given in Table 4.1. For example, all the monomers were soluble in methylene dichloride, diethyl ether and methanol but insoluble in water.



R_1 = H, CH_3 R_2 = Ph, C_6H_{13}

1 : R_1 = H, R_2 = Ph
2 : R_1 = CH_3, R_2 = Ph
3 : R_1 = H, R_2 = C_6H_{13}

Figure 4.5. Synthesis of monomers 1, 2 and 3.

The structures of the monomers were confirmed by FTIR, ^{1}H, ^{13}C NMR spectroscopies and elemental analysis. For example, the ^{13}C NMR spectra of monomer 1,2

and 3 show characteristic peaks for the carbon attached to phosphorous at around 45 and 52 ppm as doublet (Figure 4.6). This splitting can also be seen for methyl and methylene carbons of the ethyl ester of phosphonate groups.

Table 4.1. Solubility of monomers 1, 2 and 3.

Monomer	Solvents						
	H_2O	Methanol	THF	Acetone	Diethyl ether	CH_2Cl_2	Hexane
1	–	+	–	–	+	+	–
2	–	+	+	+	+	+	–
3	–	+	+	+	+	+	+

The ^{1}H NMR spectra of synthesized monomers are shown in Figure 4.7. In the ^{1}H NMR spectrum of monomers 1 and 2, we observe two different triplet peaks for methyl protons and three different multiplets for methylene protons,indicating special conformations of these monomers. The rigid structure of the molecule provided by the benzyl group may be the reason for this behavior. Therefore two methylene protons seem to be different and appeared at different chemical shift values of 4.11 and 3.67, 3.89 ppm (for monomer1). Also, diastereotopic protons of one methylene at 3.67 and 3.89 ppm (for monomer 1) were observed and this methylene might be more rigid than the other methylene protons, therefore we observed diastereotopic protons for only one methylene. Moreover, monomers 1 and 2 also have a peak seen as doublet of doublet for single proton adjacent to phosphorus due to phosphorus and resonance form of amide linkage.

The FTIR spectrum of monomer 3 shows absorptions for N–H at 3253 cm^{-1} (amide V region), C=O at 1664 cm^{-1}(amide I region), 1539 cm^{-1} (amide II region), C–H at 2980 and 2928 cm^{-1}, C=C at 1630 cm^{-1}, P=O at 1222 cm^{-1}, and P–O–Et at 1022 and 959 cm^{-1} (Figure 4.8).

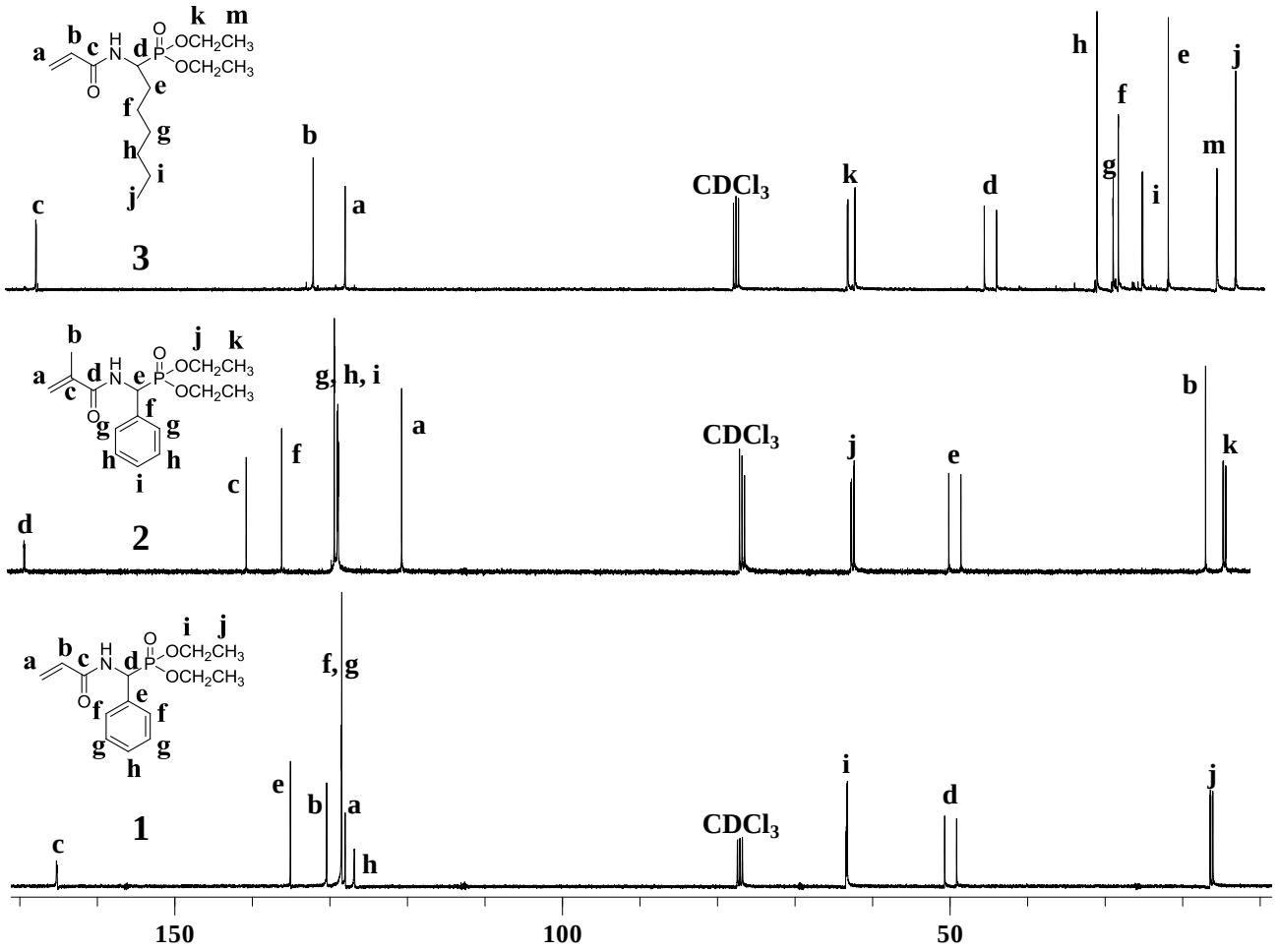


Figure 4.6. ^{13}C NMR spectra of monomers 1, 2 and 3.

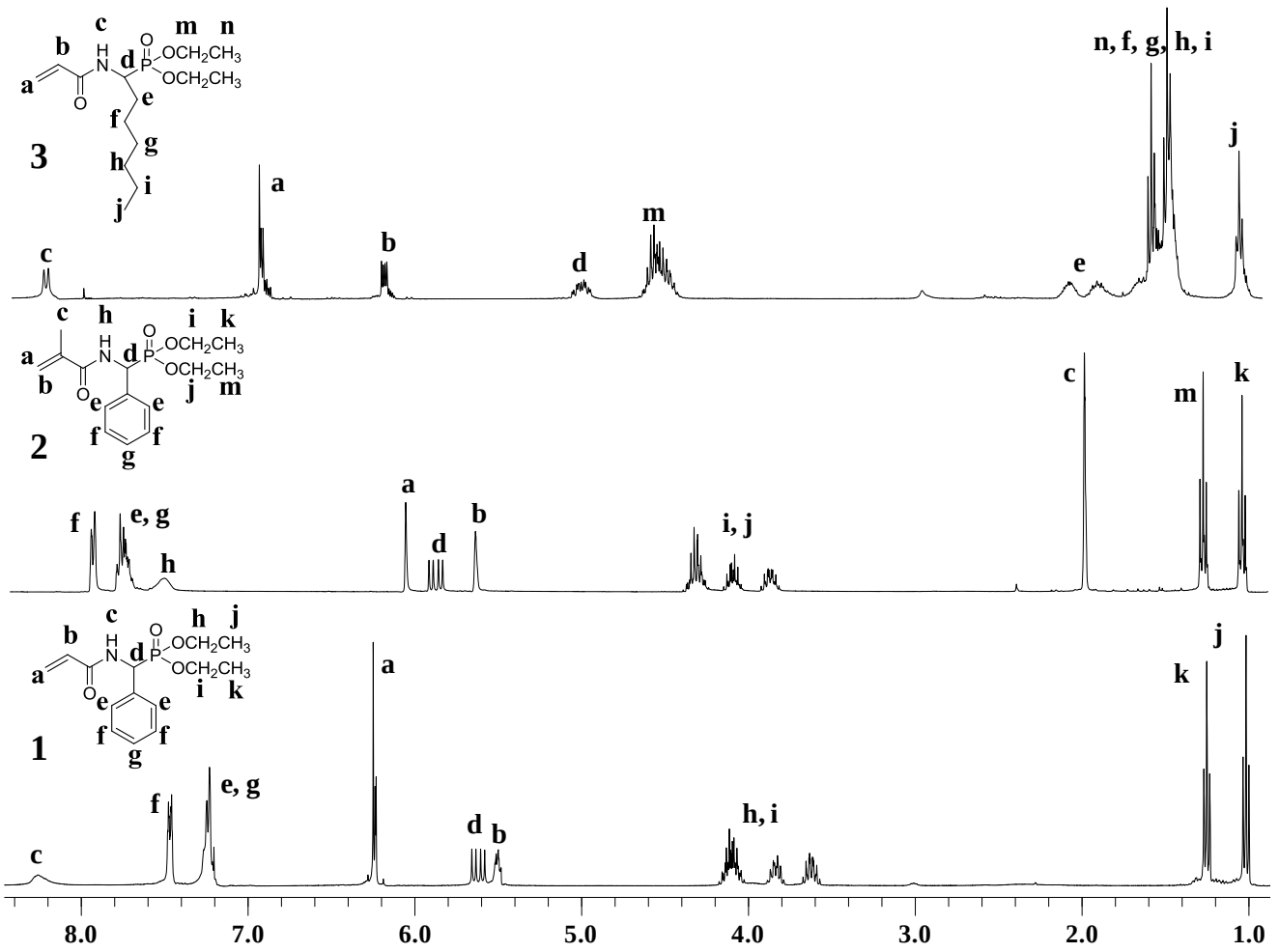


Figure 4.7. ^{1}H NMR spectra of monomers 1, 2 and 3.

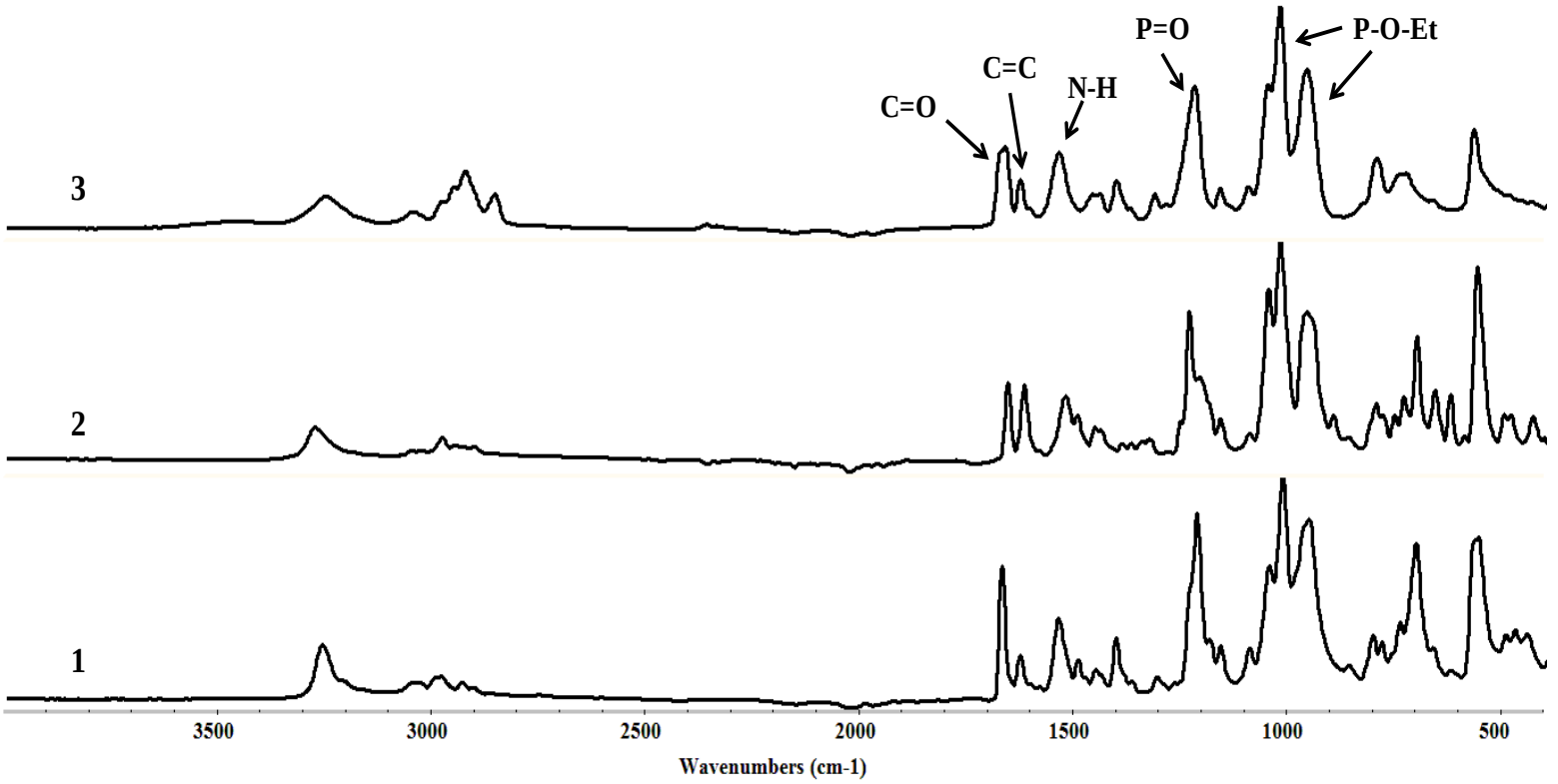


Figure 4.8. FTIR spectra of monomers 1, 2 and 3.

4.2.2. Thermal Polymerizations of Phosphonated (Meth)acrylamides

Thermal homopolymerizations of monomers 1 and 2 were performed in methanol in the presence of 2 mol% of AIBN at 65 ^{o}C using standard freeze-evacuate-thaw procedures (Figure 4.9). The solution polymerizations of monomers 1 and 2 gave soluble polymers in 24 hours with 52% and 33% conversions. The corresponding polymers (poly-1 and poly-2) were obtained as white solids after the precipitation into diethyl ether with a few drops of methylene chloride. The polymers were soluble in methylene chloride and acetone but insoluble in hexane.

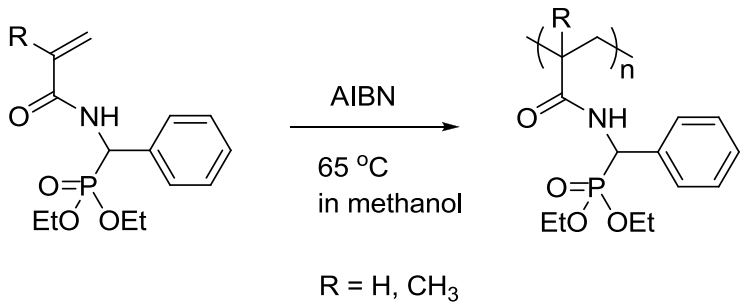


Figure 4.9. Polymerizations of the monomers 1 and 2.

The ^{1}H NMR spectra of polymers 1, 2 and 3 are seen in Figure 4.10. The disappearance of the double bond peaks at 5.61, 6.23 and 6.25 ppm for monomer 1 and at 5.32 and 5.71 ppm for monomer 2 is shown after polymerization.

Thermal homopolymerization of monomer 3 was conducted with 2 mol% of AIBN in bulk at 65 ^{o}C (Figure 4.11). Polymerization gave a soluble polymer in 68 min with 14% conversion (Table 4.2). This indicates that monomer 3 is more reactive than monomers 1 and 2. The polymer (poly-3) was obtained as a yellowish solid after the precipitation into hexane with few drops of diethyl ether. The double bond peaks at 5.58, 6.25 and 6.27 ppm completely disappeared after the polymerization (Figure 4.10). The number average molecular weights of the poly-1, poly-2 and poly-3 were around 8700, 9600 and 81494, respectively. The reason for low moecular weight of poly-1 and poly-2 compared to poly-3 is the chain transfer from labile hydrogens between phosphonate and benzyl groups in monomer 1 and 2.

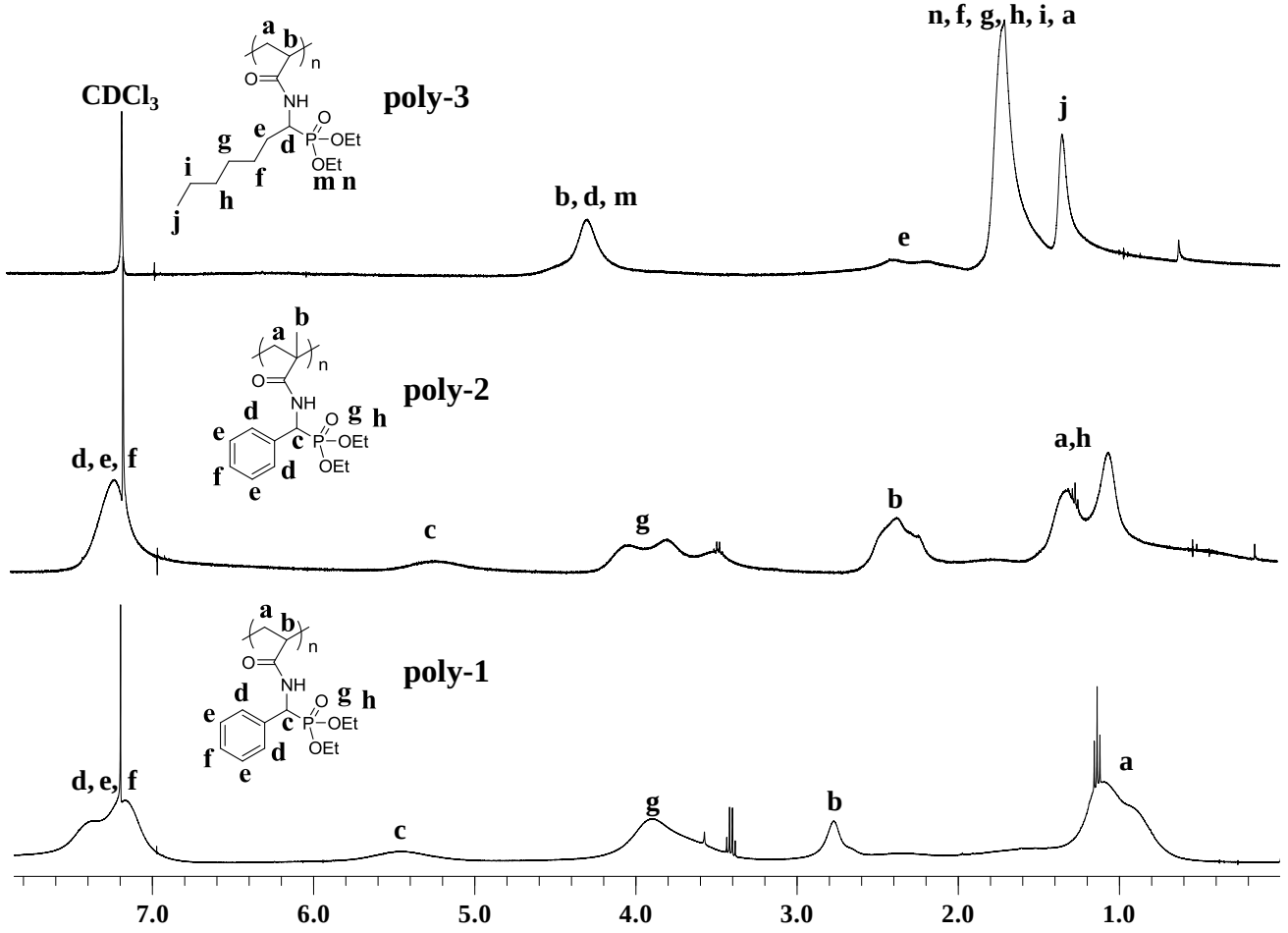


Figure 4.10. ^{1}H NMR spectra of polymers 1, 2 and 3.

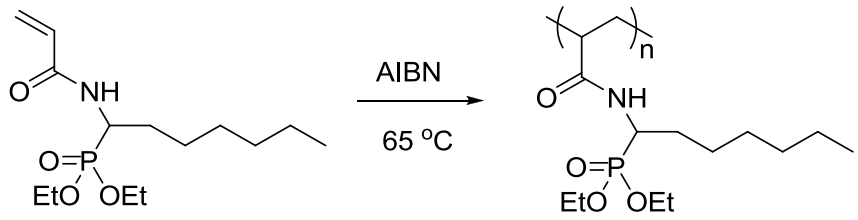


Figure 4.11. Polymerization of monomer 3.

Table 4.2. Solution and bulk polymerization results of monomers 1, 2 and 3.

Monomer	[M]	[AIBN] (mol%)	Solvent	Time (min)	T (^{o}C)	Conversion (%)	M_n
1	1	0.02	Methanol	1440	65	52	8700
2	1	0.02	Methanol	1440	65	33	9600
3	-	1.05 wt%	-	68	65	14	81494

4.2.3. Photopolymerizations of Phosphonated (Meth)acrylamides

Photopolymerization behaviors of the monomers 1, 2 and 3 were investigated with photodifferential scanning calorimetry to determine their relative rates of polymerizations. Because monomers 1 and 2 were solids with high melting points (154 ^{o}C and 114 ^{o}C) it was not possible to homopolymerize them at 40 ^{o}C. Therefore mixtures of these monomers and HEMA were prepared with monomer:HEMA ratios of 5:95 mol%.

Figure 4.12 shows the time dependences of polymerization rates and conversions for HEMA, 1-HEMA (5-95 mol%), 2-HEMA (5-95 mol%) and 3-HEMA (5-95 mol%) at 40 ^{o}C. The results are given in Table 4.3. It was observed that addition of 5 mol% of the synthesized monomers to HEMA did not change both its rate and conversion significantly.

Table 4.3. The maximum rates and conversions of 1-HEMA, 2-HEMA, 3-HEMA and HEMA at 40 ^{o}C.

Monomers	$R_p(s^{-1})$	Conversion (%)
1-HEMA (5-95 mol%)	0.344	84.3
2-HEMA (5-95 mol%)	0.337	84.5
3-HEMA (5-95 mol%)	0.318	82.0
HEMA	0.341	82.2

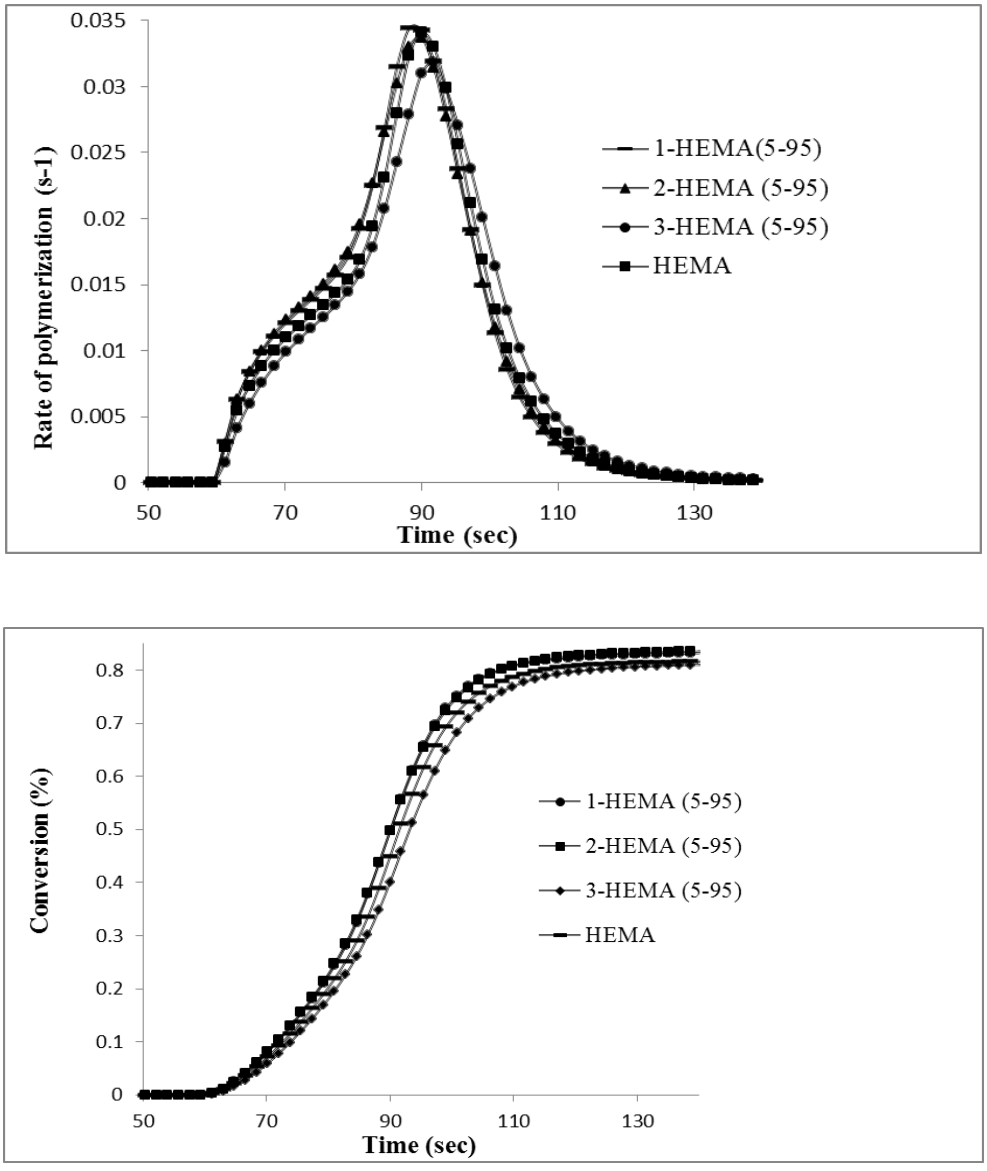


Figure 4.12.Rate-time and conversion-time curves for 1-HEMA (5:95 mol%), 2-HEMA (5:95 mol%), 3-HEMA (5:95 mol%), and HEMA at 40 ^{o}C.

4.2.4. Outlook for Phosphonated (Meth)acrylamides

The monomers 1, 2 and 3 synthesized in this work have been shown to be (i) easy to synthesize (ii) polymerizable (iii) copolymerizable. They could be used as fire retardants; or in dental composites, since their amide likages and phosphorus content are expected to give them hydrolytic stability and biocompatibility. For the same reasons, hydrolysis of phosphonate groups using TMSBr to phosphonic acid, to be reported in other work, gives yet another group of monomers with great potential as dental adhesives.

4.3. Synthesis and Polymerizations of Phosphonated-Urea Methacrylates

In this part, we report synthesis and photopolymerizations of new urea-methacrylates containing phosphonate groups and evaluate the role of hydrogen bonding, hydrogen abstraction, π–π interactions and dipole moment on the reactivity (Figure 4.13).

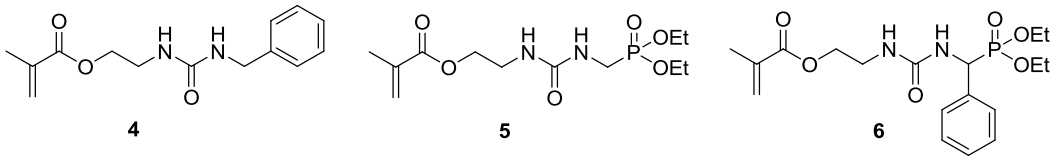


Figure 4.13. Phosphonated-urea-methacrylates.

4.3.1. Synthesis and Characterizations of Phosphonated-Urea Methacrylates

Three primary α-aminophosphonates (benzyl amine, diethyl 1-aminomethylphosphonate and amino(phenyl)methylphosphonate) were used as starting materials for each of the monomers synthesized in this part of the work. The monomers (4-6) were synthesized in one-pot reactions of the amines with IEM at room temperature for 12 h (Figure 4.14). The monomers 4 and 6 were obtained as white solids with melting points 70 ^{o}C and 72 ^{o}C, while monomer 5 is a viscous liquid, with yields over 75%, 77% and 70% respectively.The monomers characterized by using FTIR, ^{1}H, ^{13}C, ^{31}P NMR spectroscopies and elemental analysis.

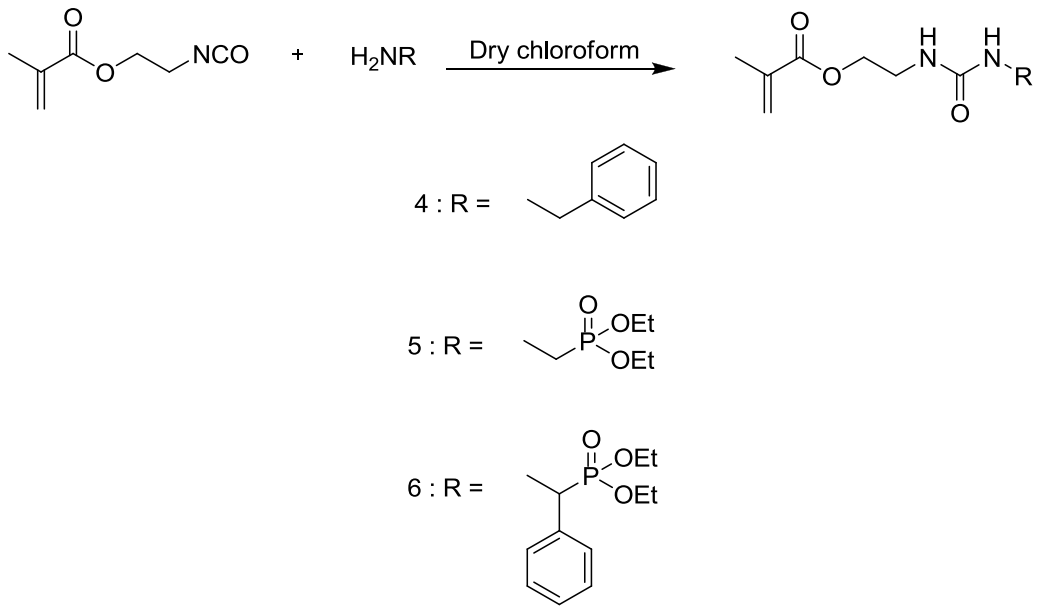


Figure 4.14. Synthesis of monomers 4, 5 and 6.

^{1}H NMR spectra of the monomers are shown in Figure 4.15. Monomer 5 has characteristic peaks for methyl protons at 1.25 and 1.87 ppm, methylene protons adjacent to nitrogen, phosphorous and oxygen at 3.43, 3.60, 4.04 and 4.13 ppm and double bond protons at 5.50 and 6.05 ppm. The NH protons are confirmed by the presence of two broad peaks which appear like a doublet at 5.77 and 5.90 ppm. The chemical shift values of the NH protons indicates the electron withdrawing properties of the substituents on the carbon next to the NH. Monomer 4 with one electron withdrawing phenyl group shows lower proton shift compared to monomer 6 with two (phenyl and phosphonate groups).

The ^{13}C NMR spectra of monomers 4, 5 and 6 are given in Figure 4.16. In the ^{13}C NMR spectra of monomers 5 and 6, the methine carbon attached to phosphorous is supported by the presence of a doublet. The ^{31}P NMR spectra of monomers 5 and 6 is seen in Figure 4.17. The purity of monomers 5 and 6 were confirmed by the single peaks in the ^{31}P NMR spectra.

The FTIR spectra of each monomer shows the NH stretching vibration peaks around 3320-3378 cm^{-1}due to hydrogen bonded urea groups (Figure 4.18). Monomer 6 displays two peaks owing to hydrogen bonded cis-trans isomers of urea groups. The presence of a single NH peak in monomers 4 and 5 is probably due to overlap of two peaks arising from

two isomers (monomer 5) or due to interconvertibility of the two conformations (monomer 4). The free NH stretching vibration which might appear as a shoulder around 3400 cm^{-1} is not obvious. The stretching vibrations of ester carbonyl groups are from 1711 (4) to 1721 (6) cm^{-1}. In the C=O regions of urea groups, monomer 4 shows one peak (1711 cm^{-1}) due to free urea C=O group, monomer 5 shows two peaks due to hydrogen-bonded (1680 cm^{-1}) and nonbonded (1717 cm^{-1}) C=O groups, monomer 6 shows two peaks owing to hydrogen-bonded (1684 cm^{-1}) and nonbonded (1721 cm^{-1}) C=O groups.

4.3.2. Photopolymerizations of Phosphonated-Urea Methacrylates

4.3.2.1. Homopolymerizations. In order to determine the effect of substituents on the rate of polymerization of the synthesized methacrylates, their polymerizations were investigated with photodifferential scanning calorimetry, using 2 mol% of 2,2-dimethoxy-2-phenylacetophenone (Irgacure 651) as photoinitiator. However, since only monomer 5 is liquid at room temperature the three could only be compared at 72 ^{o}C. For comparison, three commercial monomers HEMA, TEGDMA and BISGMA were also polymerized under the same conditions.

It was observed that photopolymerization behaviors of the monomers 4-6 are similar and different than those of HEMA and TEGDMA (Figure 4.19). The photopolymerizations of the synthesized monomers start at higher rates compared to HEMA and TEGDMA. For example, after 5 s of polymerization 53.7, 54.1, 39.5 and 16.3% of conversion were reached for monomers 4, 5, 6 and TEGDMA and only 4.5% for HEMA. These values indicate that autoacceleration, that is, an increase in polymerization rate, resulting probably from high viscosity due to hydrogen bonding of urea linkages or hydrogen abstraction reactions which leads to increase in propagation rates and decrease in termination rates occurs earlier in the synthesized monomers. This behavior is typical to multifunctional (meth)acrylates.

It is known that as the monomer functionality increases the rate of polymerization increases while the conversion decreases. Thus, dimethacrylates (Bis-GMA and TEGDMA) would be expected to have higher rates of polymerization than monomers 4-6. However, the maximum rates of the commercial and synthesized monomers follow the

order: 5~4 >6~TEGDMA > HEMA (Figure 4.19 and Table 4.4). The synthesized monomers with one double bond react very rapidly and give high double bond conversion. The overall conversions reached were found to be similar (85-92%) for monomers 4, 5 and TEGDMA. Although the maximum rate of polymerization of monomer 6 is similar to TEGDMA and higher than HEMA, conversion was found to be lower than both of them. This may be attributed to early autoacceleration and/or high T_g of its polymer and polymerization temperature close to the melting point of this monomer.

All of the synthesized monomers have the capability of hydrogen bonding due to urea linkages. Thermal bulk polymerization of these monomers using AIBN at gave crosslinked polymers, indicating importance of hydrogen abstraction reactions. Similar rate of polymerizations of monomers 4 and 5 and lower rate of polymerization of monomer 6 suggest that $\pi-\pi$ interactions have no important effect on the polymerization rate.

The synthesized monomers were evaluated to look for a relationship between polarity and polymerization reactivity. The Boltzmann-averaged dipole moments of the monomers were calculated for their minimum energy conformations as 3.27, 4.47 and 4.32 debye for monomers 4, 5 and 6 (Table 4.5).

No clear correlation of dipole moment to reactivity can be observed. The above-mentioned effects, that is, hydrogen bonding and hydrogen abstraction, seem to dominate over any effect that dipole moment may have.

4.3.2.2. Copolymerizations with Dental Monomers. In order to test the use these monomers as crosslinking monomers in dental adhesives and also reactive diluents in filling composites, we investigated copolymerization of them with HEMA, TEGDMA and BISGMA, which are important monomers in dental applications.

Figure 4.20 and Table 4.6 show the results of the copolymerizations of the synthesized monomers with HEMA. Addition of 10 mol% of monomers 4, 5 and 6 to HEMA increased its rate significantly because of the fact that hydrogen bonding ability of HEMA was enhanced due urea linkages of the monomers 4, 5 and 6. In addition, addition of 10 mol% of monomer 6 to HEMA increased its rate more than monomers 4 and 5 on

account of the fact that hydrogen abstraction ability of HEMA was improved due to two electron withdrawing groups (benzyl and phosphonate).On the other hand, addition of 10 mol% of monomer 6 to HEMA decreased its conversion significantly due to two steric effect of two bulky groups (benzyl and phosphonate). Additionally, the results clearly show that there is a shift in the maximum of HEMA by the addition of the monomers. This behavior typical to multifunctional methacrylates confirms the incorporation of monomers into the copolymers.

Figure 4.21 and Table 4.7 show the results of the copolymerizations of the synthesized monomers with TEGDMA. The mixtures of the synthesized monomers showed very similar photopolymerization behavior with TEGDMA. After 5 s of polymerizations, 89.4%, 89.0%, 82.1% and 62.2% conversions were reached for mixtures of monomers 4, 5, 6 and TEGDMA.This slight difference in conversion of TEGDMA can be observed by a small shift in the peak maximum towards left, indicating earlier gelation of the mixtures compared to TEGDMA. Addition of 10 mol% of monomers 4, 5 and 6 to TEGDMA improved both its rate and conversion. This increase in rate of polymerization was expected due to higher reactivity of the synthesized monomers. Unexpectedly, the mixture of monomer 6 and TEGDMA also showed higher conversion than TEGDMA. This results was probably due to decrease in rigidity of monomer 6.

Dental composites are composed of dimethacrylate monomers such as BISGMA, an inorganic filler and polymerization initiator system. However, BISGMA has very low conversion due to its very high viscosity resulting from intermolecular hydrogen bonding between hydroxyl groups. A comonomer such as TEGDMA is used to decrease the high viscosity of BISGMA and increase conversion. BISGMA showed a maximum rate of polymerization of 0.0516 s^{-1} with a conversion of 64%, whereas TEGDMA showed a maximum rate of 0.0512 s^{-1} with a conversion of 75% due to its flexible structure (Figure 4.22, Figure 4.23, Table 4.8 and Table 4.9).In general, the compositions of BISGMA:TEGDMA used are in the range of 5-92%. It is reported that the maximum rate of polymerization and conversion of the mixtures increase up to 50 mol% Bis-GMA amount and decrease above this amount.

It was observed that addition of 10 and 50 mol% of TEGDMA to BISGMA improved its rate to 0.063 and 0.067 s^{-1}. The conversions were also improved by 71.5% and 65.8%. In order to see if our monomers can replace TEGDMA, 10 mol% of the synthesized monomers were added to BISGMA. The only liquid monomer 5 gave clear solutions, solid monomers 4 and 5 were not miscible with BISGMA. Therefore, we only studied the mixtures of Bis-GMA containing 10 and 50 mol% of monomer 5. It was observed that addition of 10 mol% of monomer 5 to BISGMA slightly decreased both rate of polymerization and conversion of BISGMA. However, when 50 mol% of monomer 5 was added both rate (0.0594 s^{-1}) and conversion (69%) was improved.

Both hydrogen abstraction reactions and hydrogen bonding contribute to enhanced polymerization rate. Hydrogen abstraction generates a site for reinitiation and may lead to crosslinking, reducing the rate of termination and increasing the polymerization rate. Generally, the activation energy for chain-transfer reactions is higher than that for propagation. If a crosslinking reaction caused by chain transfer is the main reason for increased polymerization rates of these monomers the rate of polymerization should probably increase with increasing temperature. However, if hydrogen bonding is operative in polymerization, then the rate will decrease with an increase in temperature. Because the associations present between monomer molecules due to hydrogen bonding will disappear with temperature.

To investigate the effect of temperature on the polymerization rate of the synthesized monomers, polymerization rate of monomer 5 at three different temperatures was measured using photo-DSC.The results of the polymerizations are shown in Table 4.10 and Figure 4.24. It can be clearly seen that the rate of polymerization of monomer 5 is slightly enhanced with increasing temperature. Based on this result, it is difficult to say whether hydrogen bonding or hydrogen abstraction is more effective on the polymerization rates of the synthesized monomers.

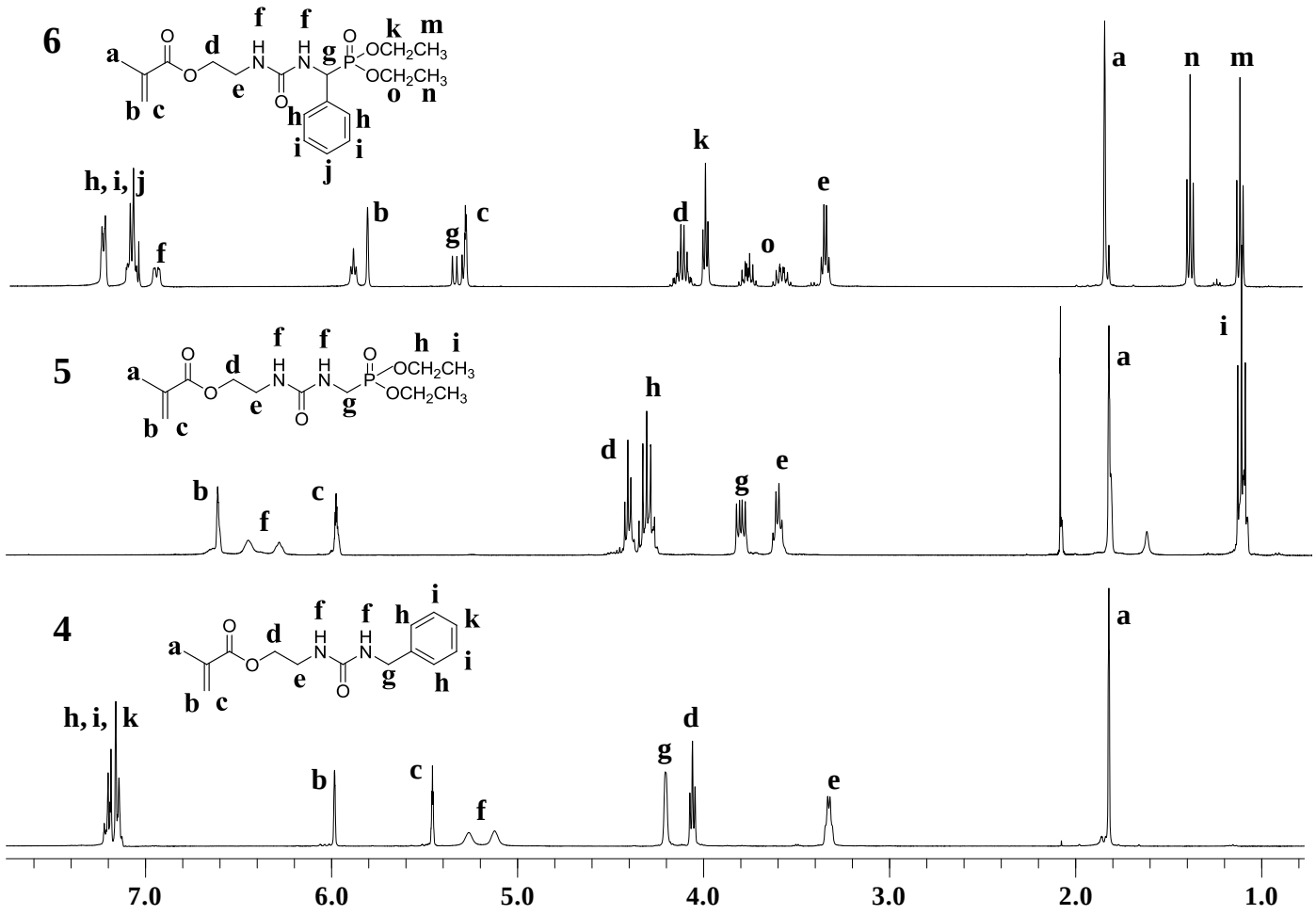


Figure 4.15. ^{1}H NMR spectra of monomers 4, 5 and 6.

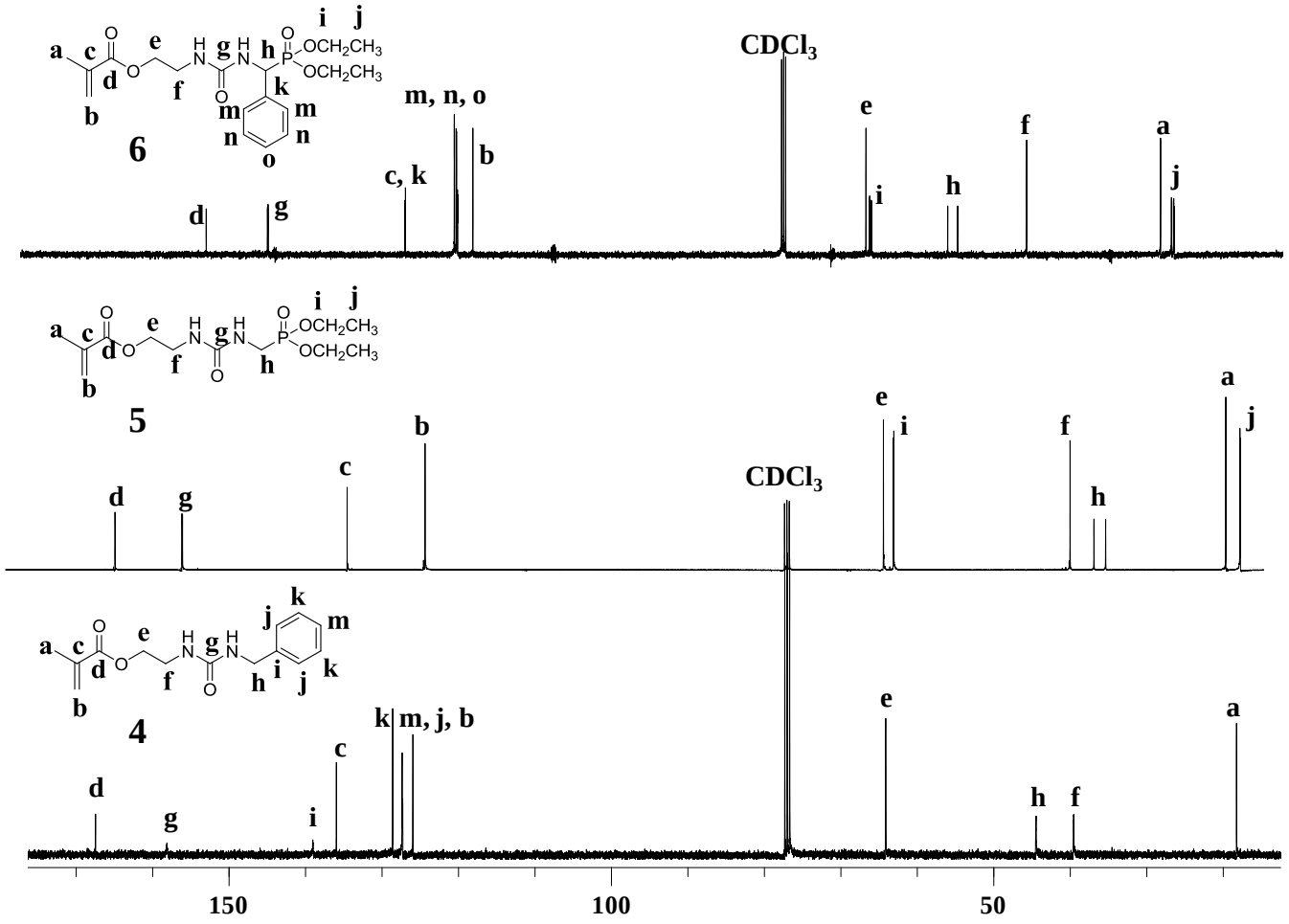


Figure 4.16. ^{13}C NMR spectra of monomers 4, 5 and 6.

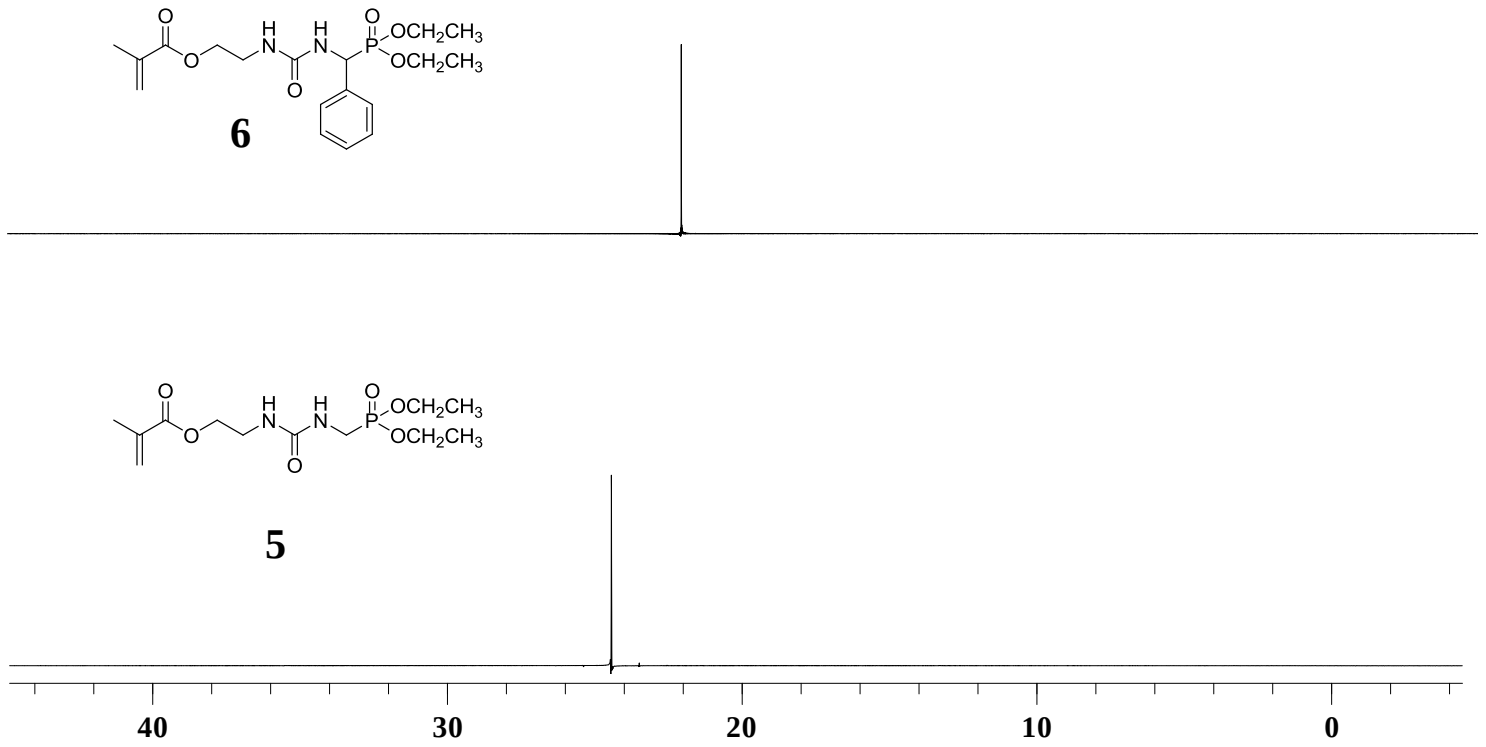


Figure 4.17. ^{31}P NMR spectra of monomers 5 and 6.

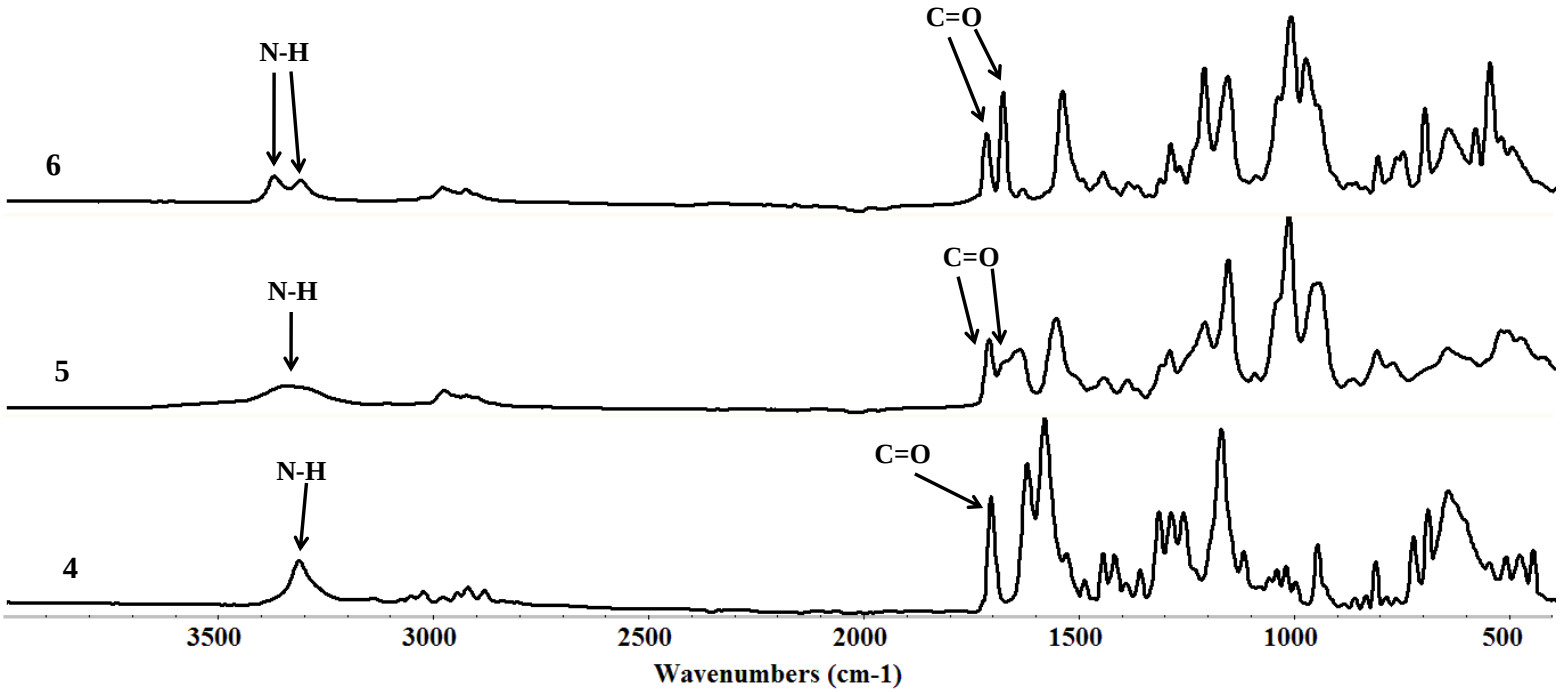


Figure 4.18. FTIR spectra of monomers 4, 5 and 6.

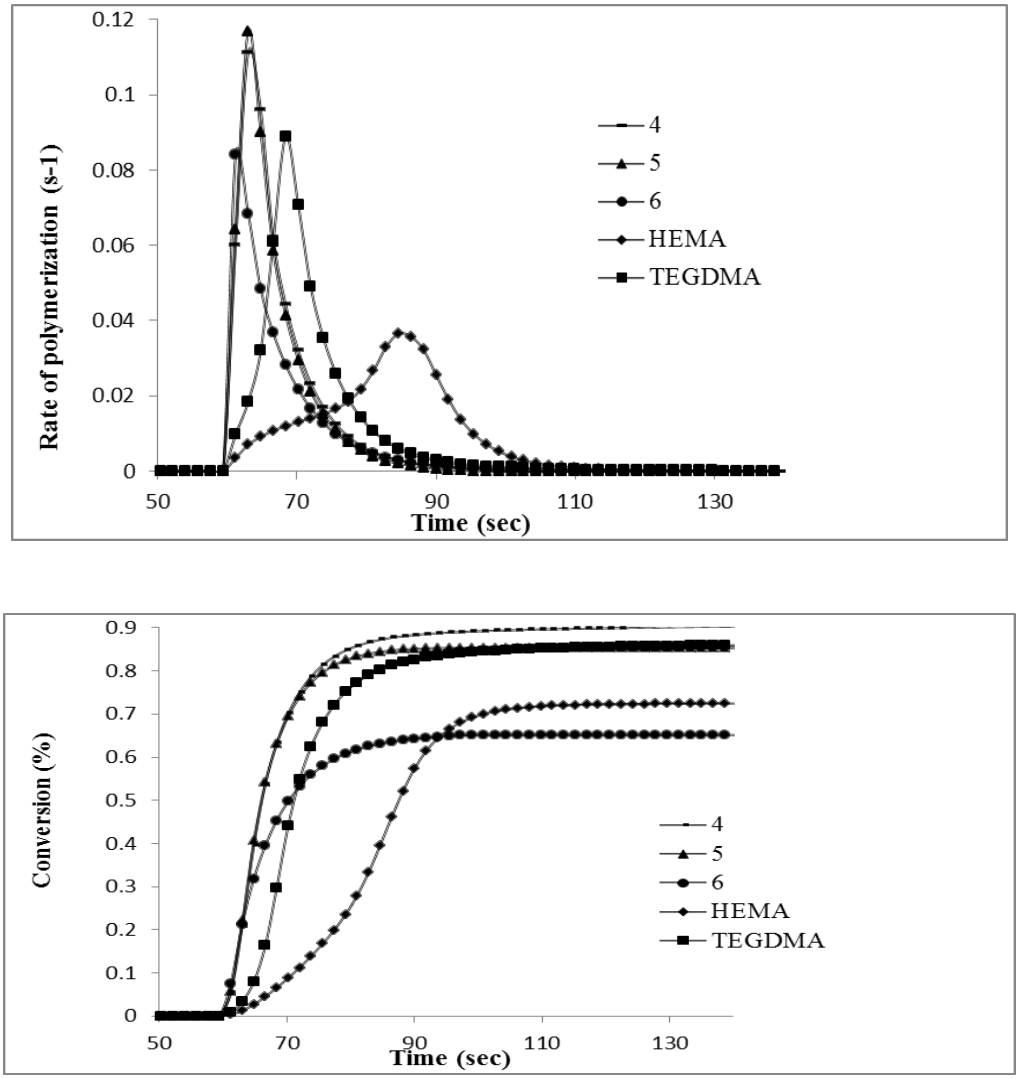


Figure 4.19. Rate-time and conversion-time curves in the polymerizations of 4, 5, 6, HEMA and TEGDMA at 72 ^{o}C.

Table 4.4. The maximum rates and conversions of 4, 5, 6, HEMA, and TEGDMA at 72 ^{o}C.

Monomers	$R_p(s^{-1})$	Conversion (%)
4	0.111	92.0
5	0.117	85.3
6	0.084	65.1
HEMA	0.036	73.0
TEGDMA	0.089	86.3

Table 4.5. The Boltzmann-averaged dipole moments of monomers 4, 5 and 6.

Monomer	Dipole moment (debye)	R_p (s^{-1})
4	3.27	0.111
5	4.47	0.117
6	4.32	0.084

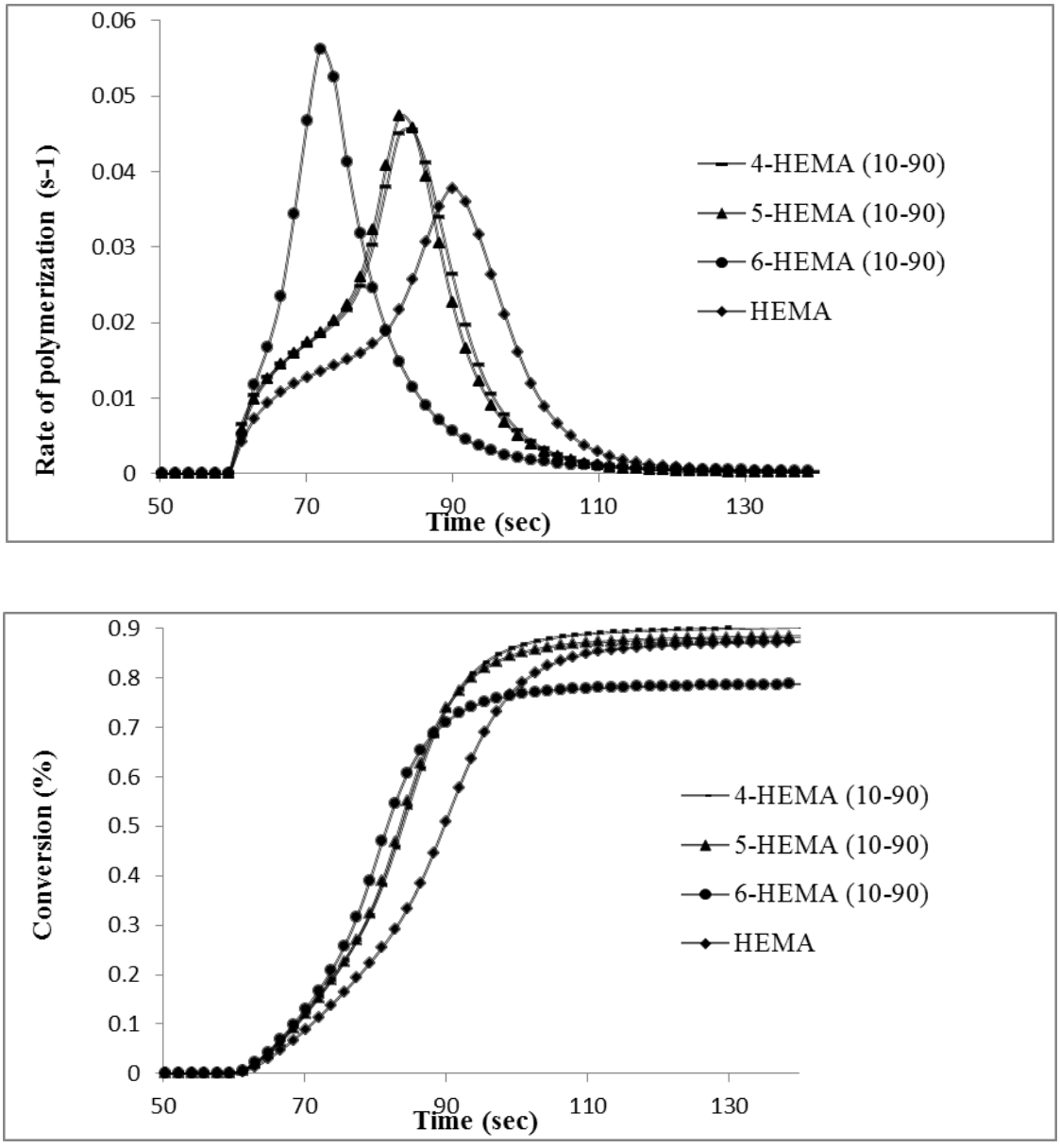


Figure 4.20. Rate-time and conversion-time curves in the polymerizations of 4-HEMA (10-90 mol%), 5-HEMA (10-90 mol%), 6-HEMA (10-90 mol%), HEMA at 40 ^{o}C.

Table 4.6. The maximum rates and conversions of 4-HEMA (10-90 mol%), 5-HEMA (10-90 mol%), 6-HEMA (10-90 mol%), and HEMA at 40 ^{o}C.

Monomer	$R_p(s^{-1})$	Conversion (%)
4-HEMA (10-90 mol%)	0.045	91.0
5-HEMA (10-90 mol%)	0.047	89.1
6-HEMA (10-90 mol%)	0.056	79.1
HEMA	0.038	88.4

Table 4.7. The maximum rates and conversions of 4-TEGDMA (10-90 mol%), 5-TEGDMA (10-90 mol%), 6-TEGDMA (10-90 mol%), and TEGDMA at 40 ^{o}C.

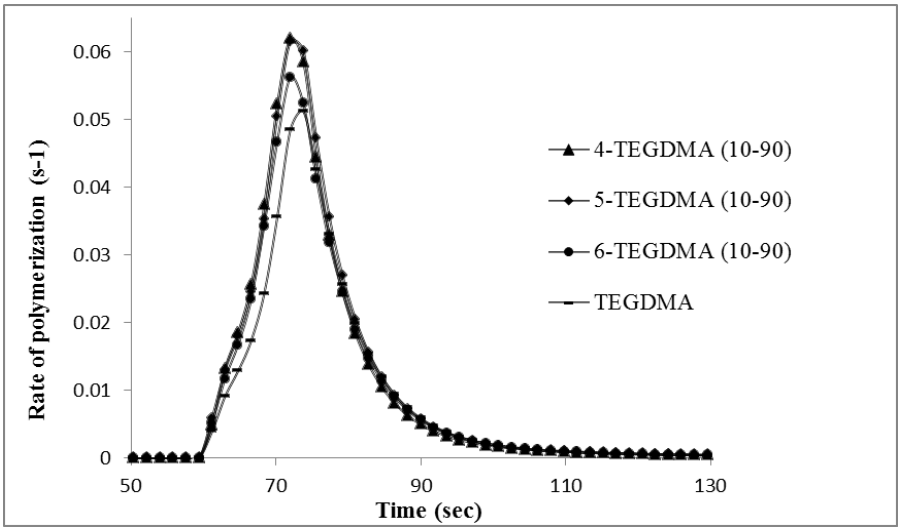
Monomer	$R_p(s^{-1})$	Conversion (%)
4-TEGDMA (10-90 mol%)	0.062	86.0
5- TEGDMA (10-90 mol%)	0.060	90.0
6- TEGDMA (10-90 mol%)	0.056	82.0
TEGDMA	0.051	75.0

Table 4.8. The maximum rates and conversions of 5-BISGMA (10-90 mol %), TEGDMA-BISGMA (10-90 mol %), TEGDMA and BISGMA at 40 ^{o}C.

Monomer	$R_p(s^{-1})$	Conversion (%)
5-BISGMA (10-90 mol%)	0.0440	60.5
TEGDMA-BISGMA (10-90 mol%)	0.0630	71.5
TEGDMA	0.0512	75.0
BISGMA	0.0515	64.0

Table 4.9. The maximum rates and conversions of 5-BISGMA (50-50 mol%), TEGDMA-BISGMA (50-50 mol%), TEGDMA and BISGMA at 40 ^{o}C.

Monomer	$R_p(s^{-1})$	Conversion (%)
5-BISGMA (50-50 mol%)	0.0594	69.0
TEGDMA-BISGMA (50-50 mol%)	0.0672	65.8
TEGDMA	0.0512	75.0
BISGMA	0.0516	64.0



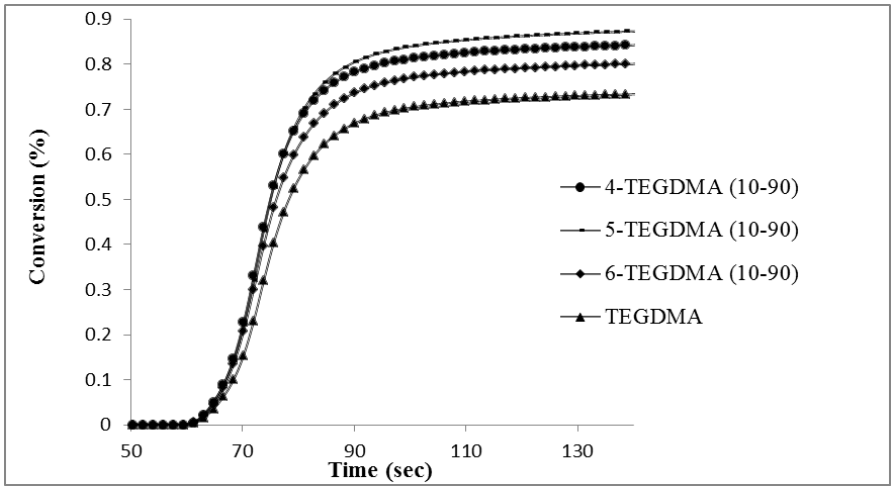
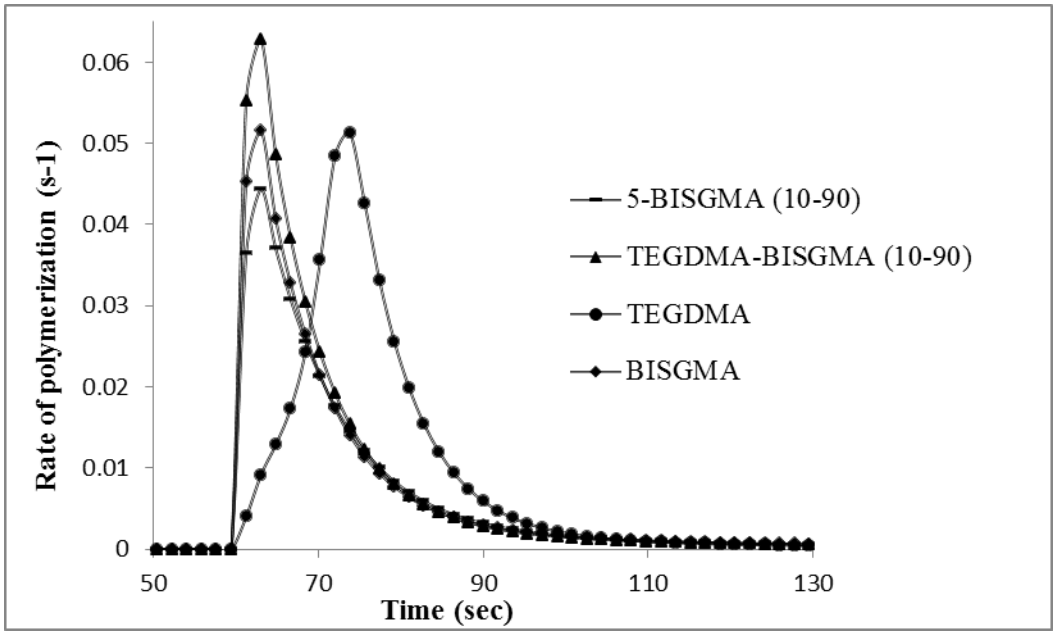


Figure 4.21. Rate-time and conversion-time curves in the polymerizations of 4-TEGDMA (10-90 mol%), 5-TEGDMA (10-90 mol%), 6-TEGDMA (10-90 mol%), TEGDMA at 40 ^{o}C.



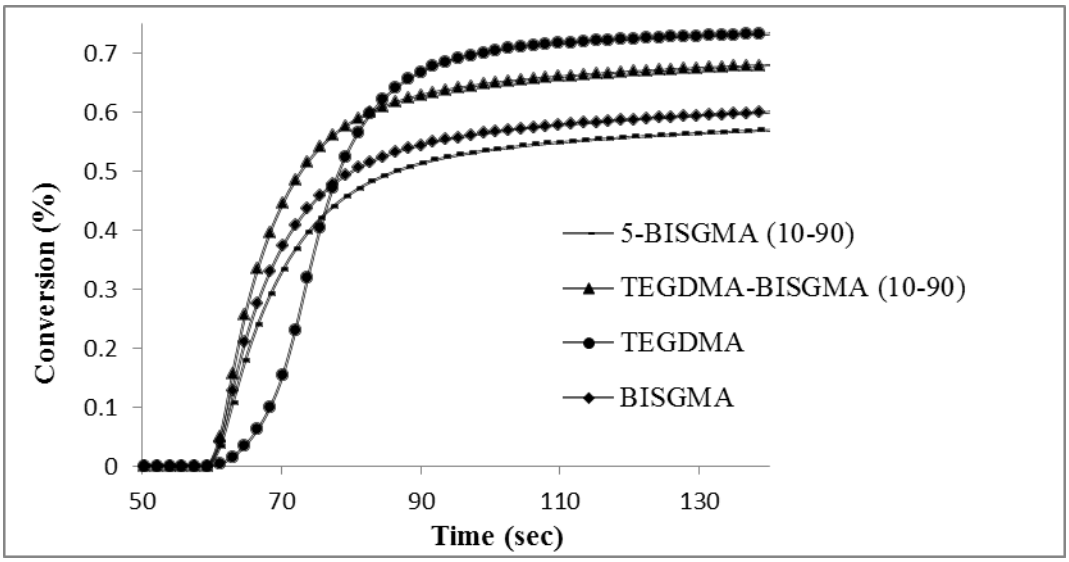
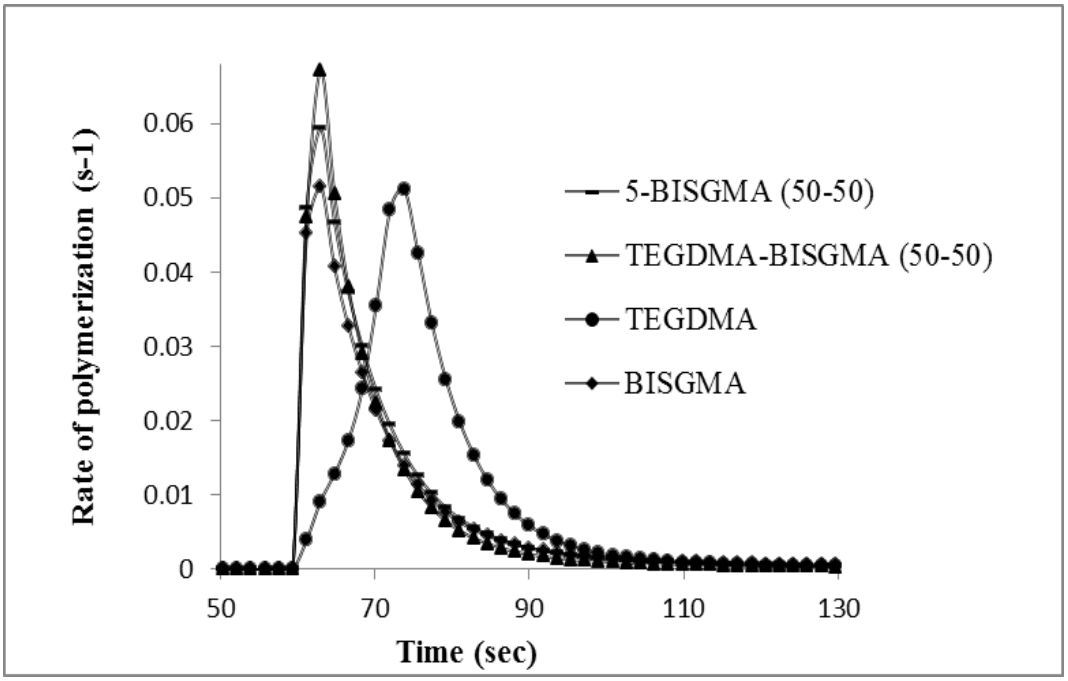


Figure 4.22. Rate-time and conversion-time curves in the polymerizations of 5-BISGMA (10-90 mol%), TEGDMA-BISGMA (10-90 mol%), 6-TEGDMA, BISGMA at 40 ^{o}C.

Table 4.10. The maximum rates and conversions of 5 at 40, 55 and 72 ^{o}C.

Monomer	$R_p(s^{-1})$	Conversion (%)
5 (40 ^{o}C)	0.083	76.0
5 (55 ^{o}C)	0.098	96.0
5 (72 ^{o}C)	0.112	85.3



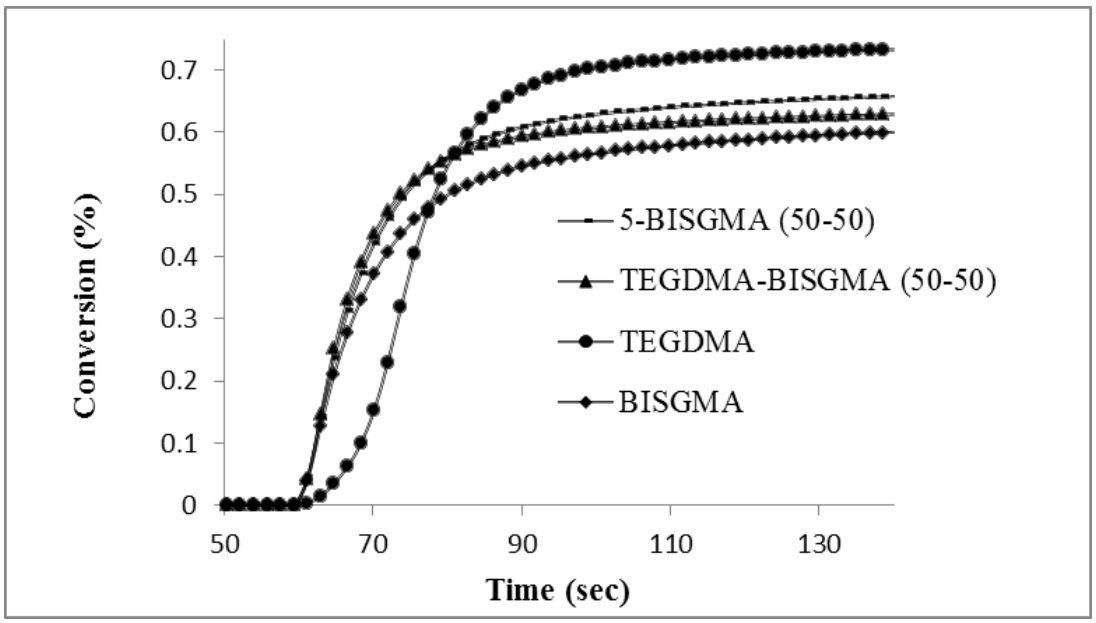


Figure 4.23. Rate-time and conversion-time curves in the polymerizations of 5-BISGMA (50-50 mol%), TEGDMA-BISGMA (50-50 mol%), 6-TEGDMA, BISGMA at 40 ^{o}C.

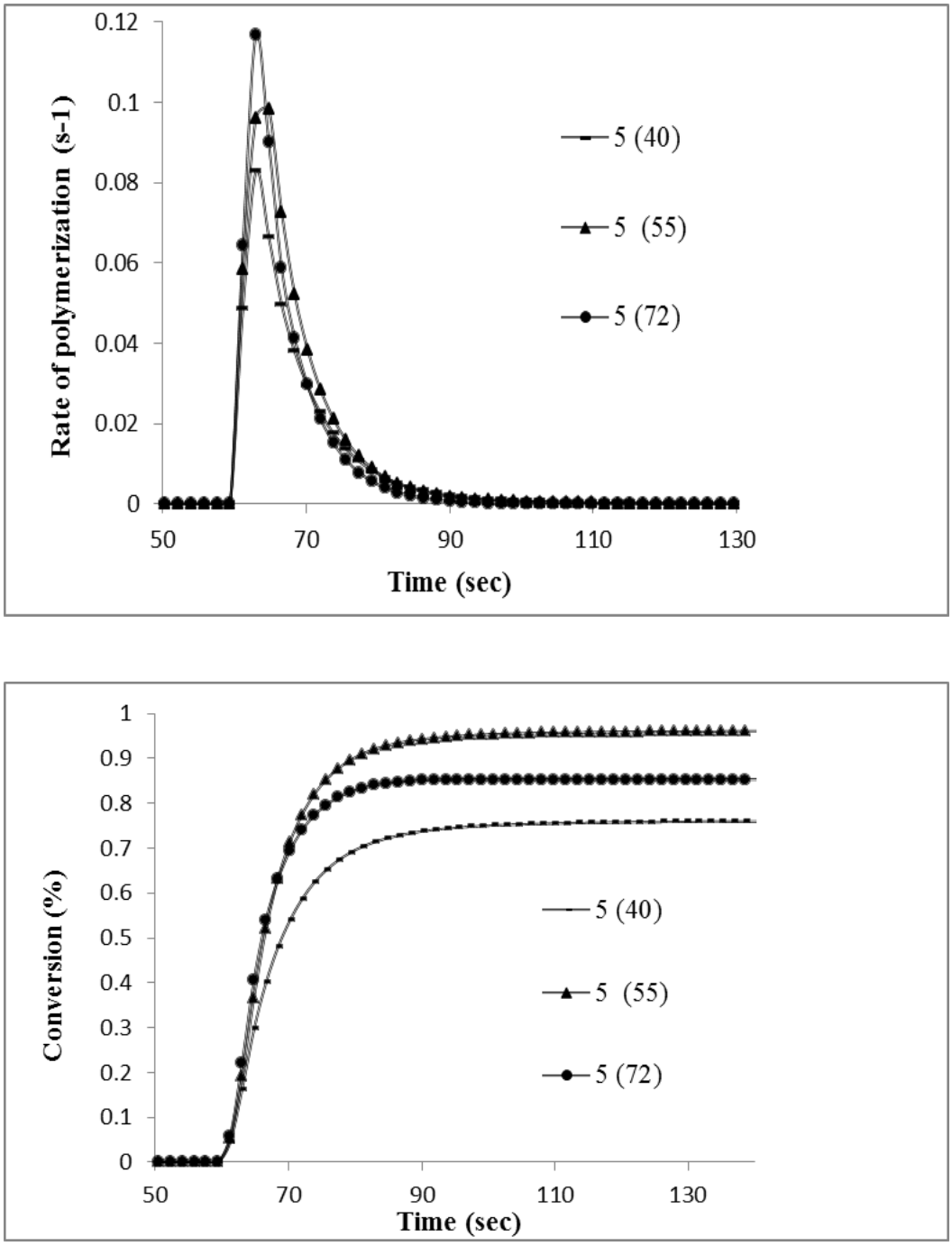


Figure 4.24. Rate-time and conversion-time curves in the polymerizations of 5 at 40, 55 and 72^{o}C.

5. CONCLUSION

In the first part of this work, three new hydrolytically stable phosphonated (meth)acrylamide monomers were successfully synthesized. The homo- and copolymerizability of the monomers were investigated. It was shown that by changing the structure of α-aminophosphonates, it is possible to produce polymers with different properties. Further studies of the phosphonic acid derivatives of these monomers are continuing to obtain novel self-etching adhesive monomers.

In the second part of this work, the reactions of IEM with primary phosphonated amines were found to be an easy method to prepare new phosphonated-urea-methacrylates. These monomethacrylate monomers have significantly high polymerization rate and degree of conversion despite having one double bond. Their photopolymerization reactivities were found to be higher or comparable to commercial dental crosslinkers such as Bis-GMA and TEGDMA. The increased curing efficiency will be obtained with reduced irradiation times, light intensities and initiator concentrations by using these monomers. Moreover, their high crosslinking tendencies will enhance mechanical properties of the cured materials. As a result, these monomers are very promising to be used as reactive diluents or crosslinkers in dental systems.

The phosphonic acid derivatives of phosphonated-urea-methacrylate monomers may have potential in self-etching dental adhesives.

APPENDIX A: SPECTROSCOPY DATA

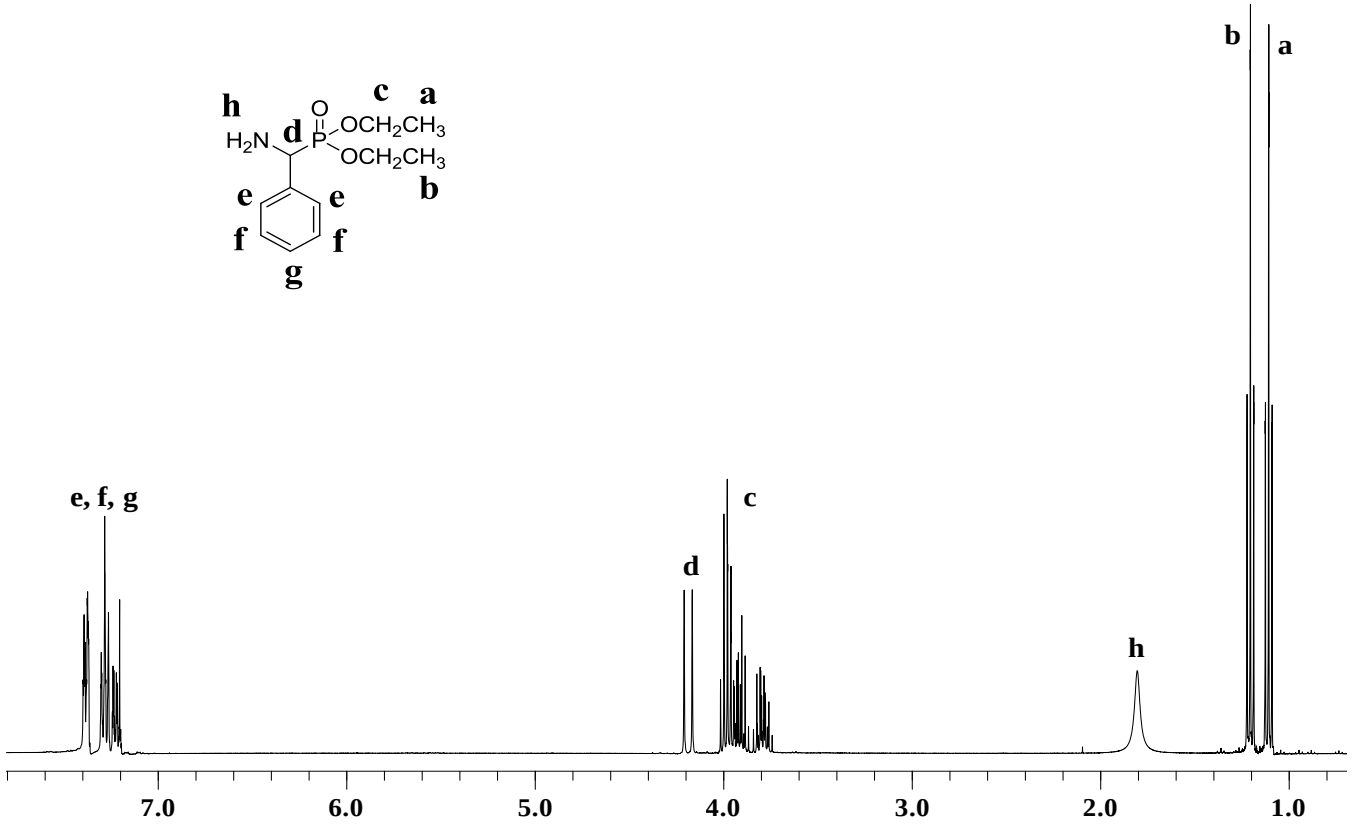


Figure A.1. ^{1}H-NMR spectrum of diethyl amino(phenyl)methylphosphonate in $CDCl_3$.

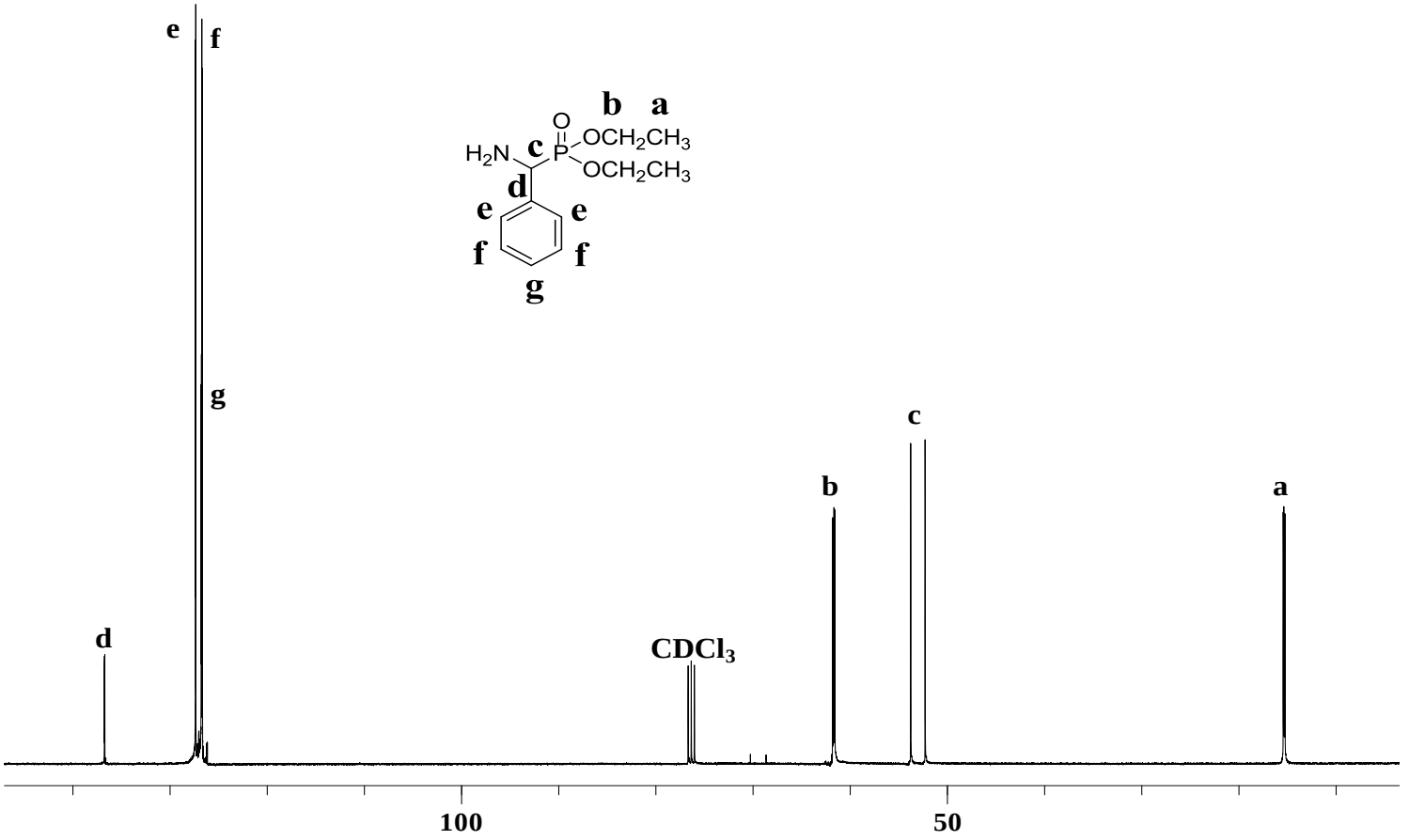


Figure A.2. ^{13}C-NMR spectrum of diethyl amino(phenyl)methylphosphonate in $CDCl_3$.

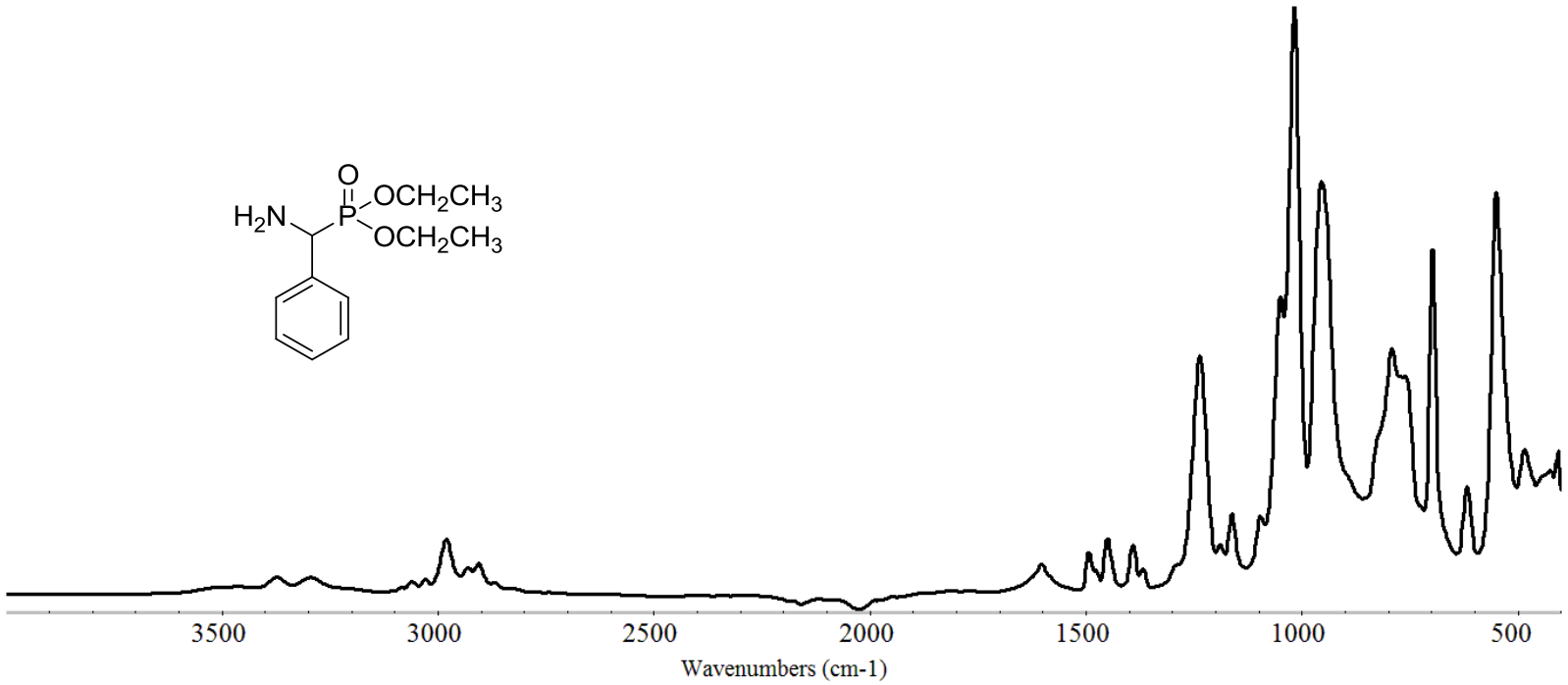


Figure A.3. FT-IR spectrum of diethyl amino(phenyl)methylphosphonate.

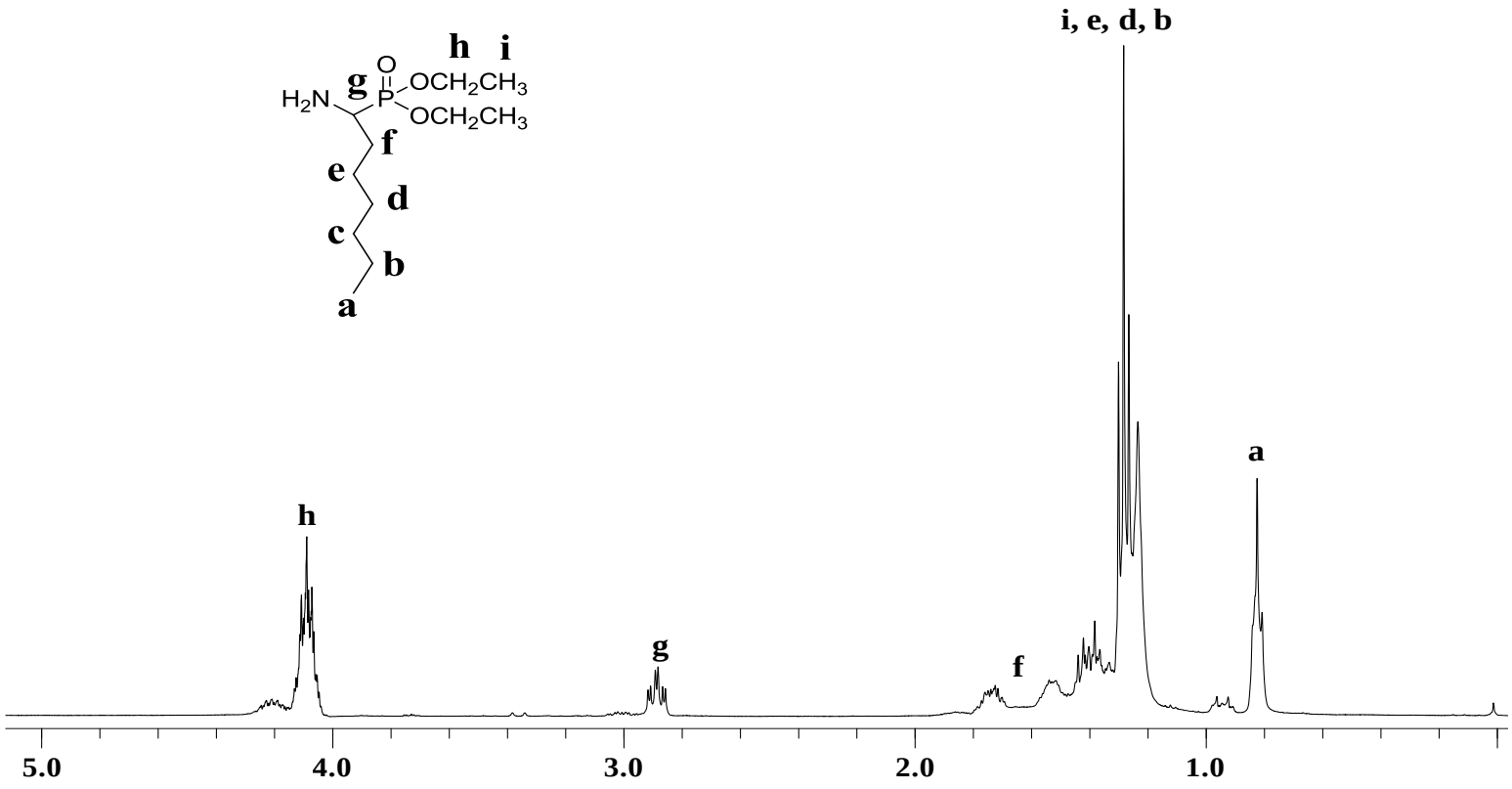


Figure A.4. ^{1}H-NMR spectrum of diethyl 1-aminoheptylphosphonate in $CDCl_3$.

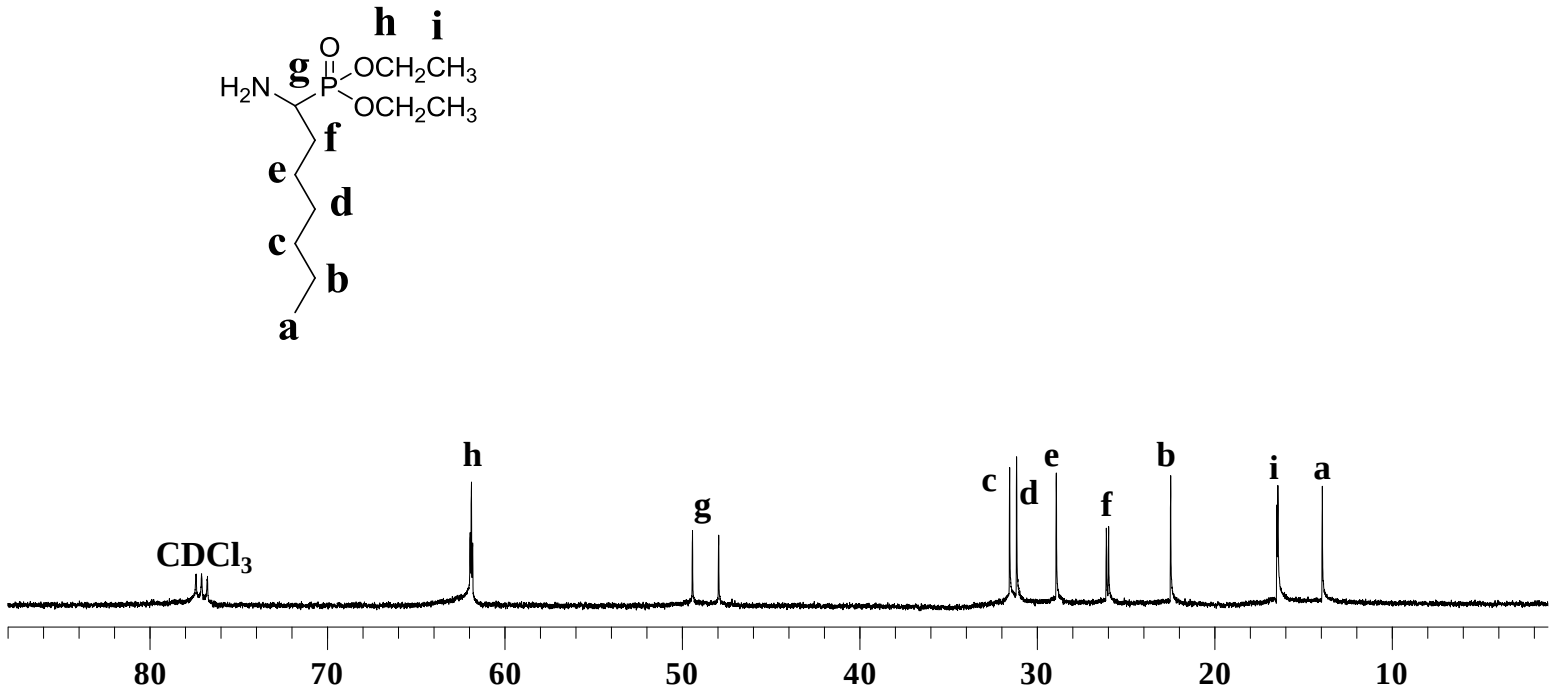


Figure A.5. ^{13}C-NMR spectrum of diethyl 1-aminoheptylphosphonate in $CDCl_3$.

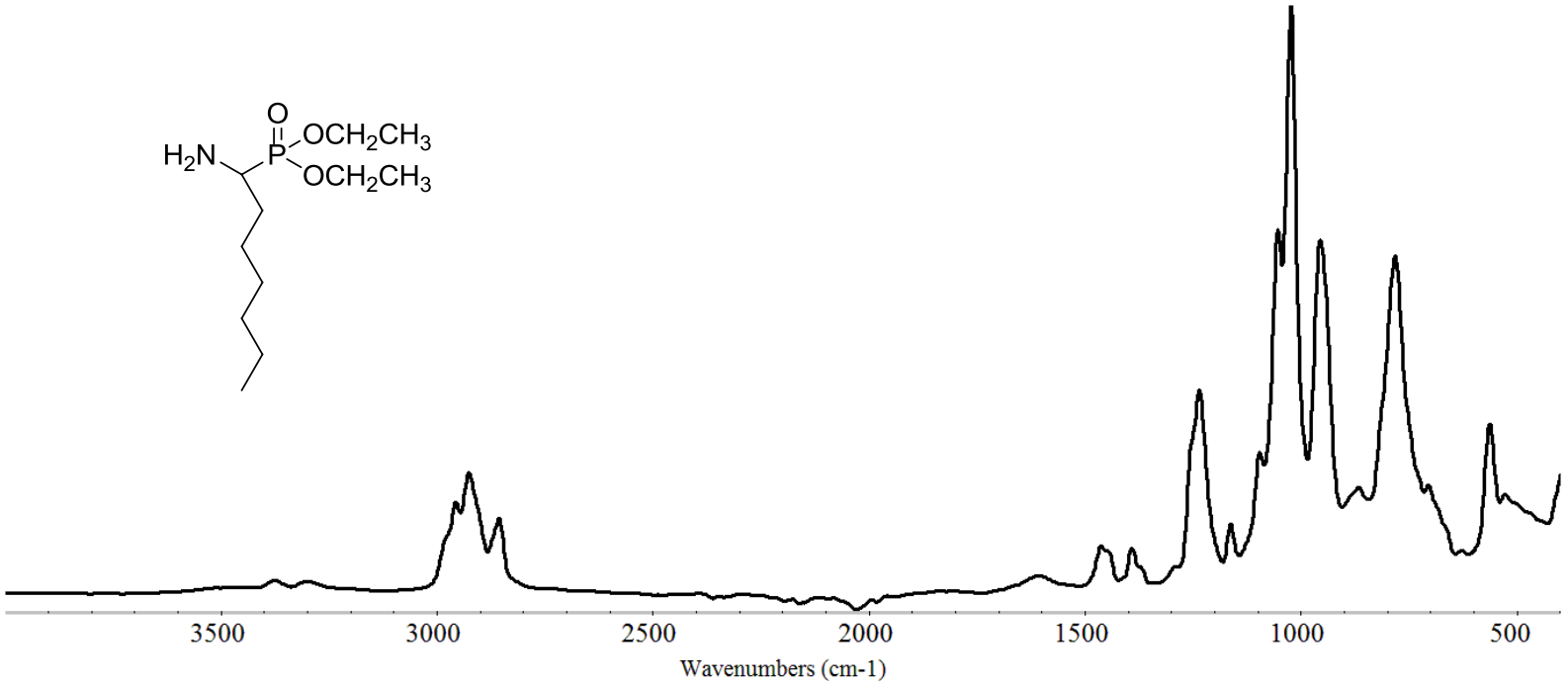


Figure A.6. FT-IR spectrum of diethyl 1-aminoheptylphosphonate.

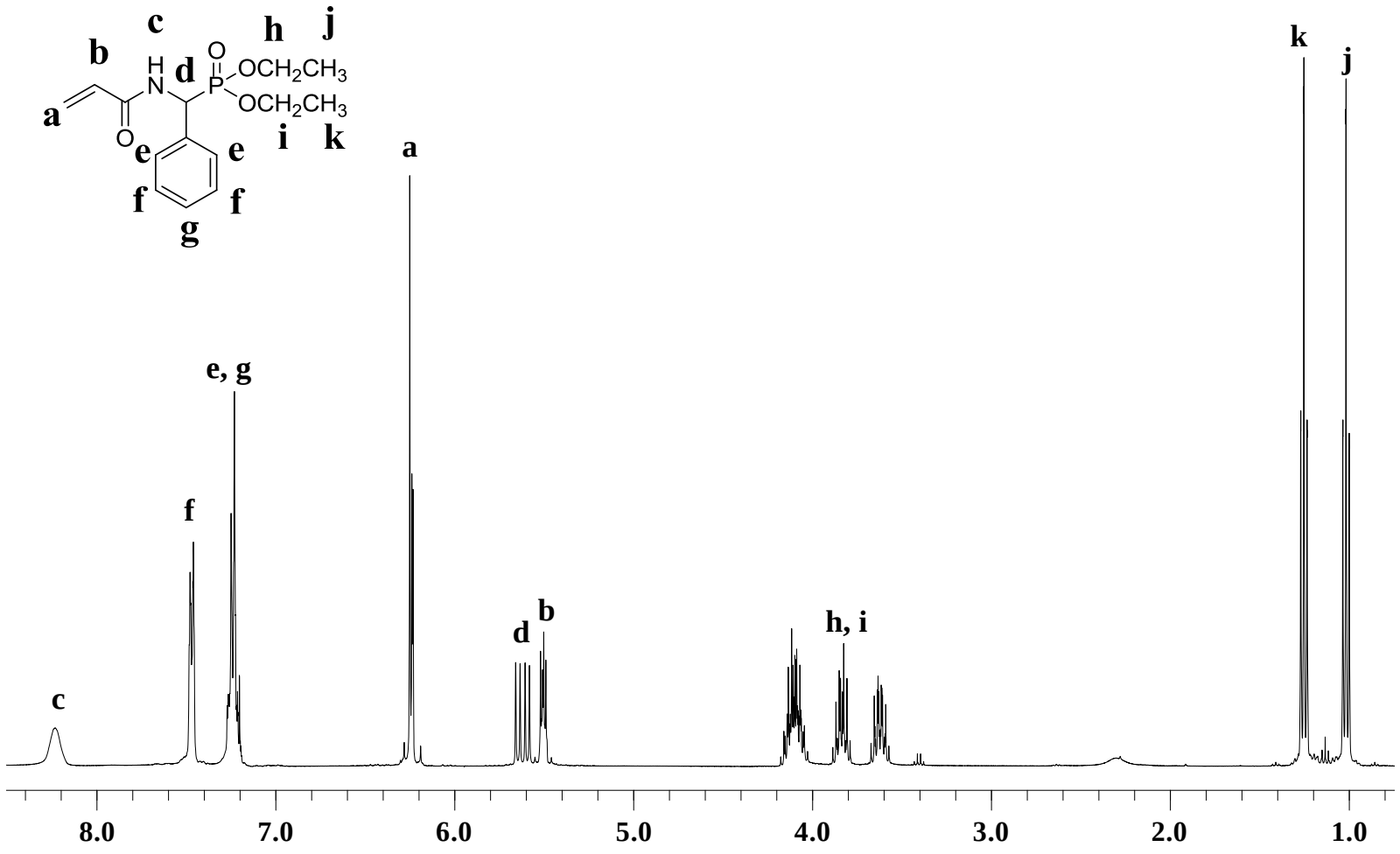


Figure A.7. ^{1}H-NMR spectrum of monomer 1 in $CDCl_3$.

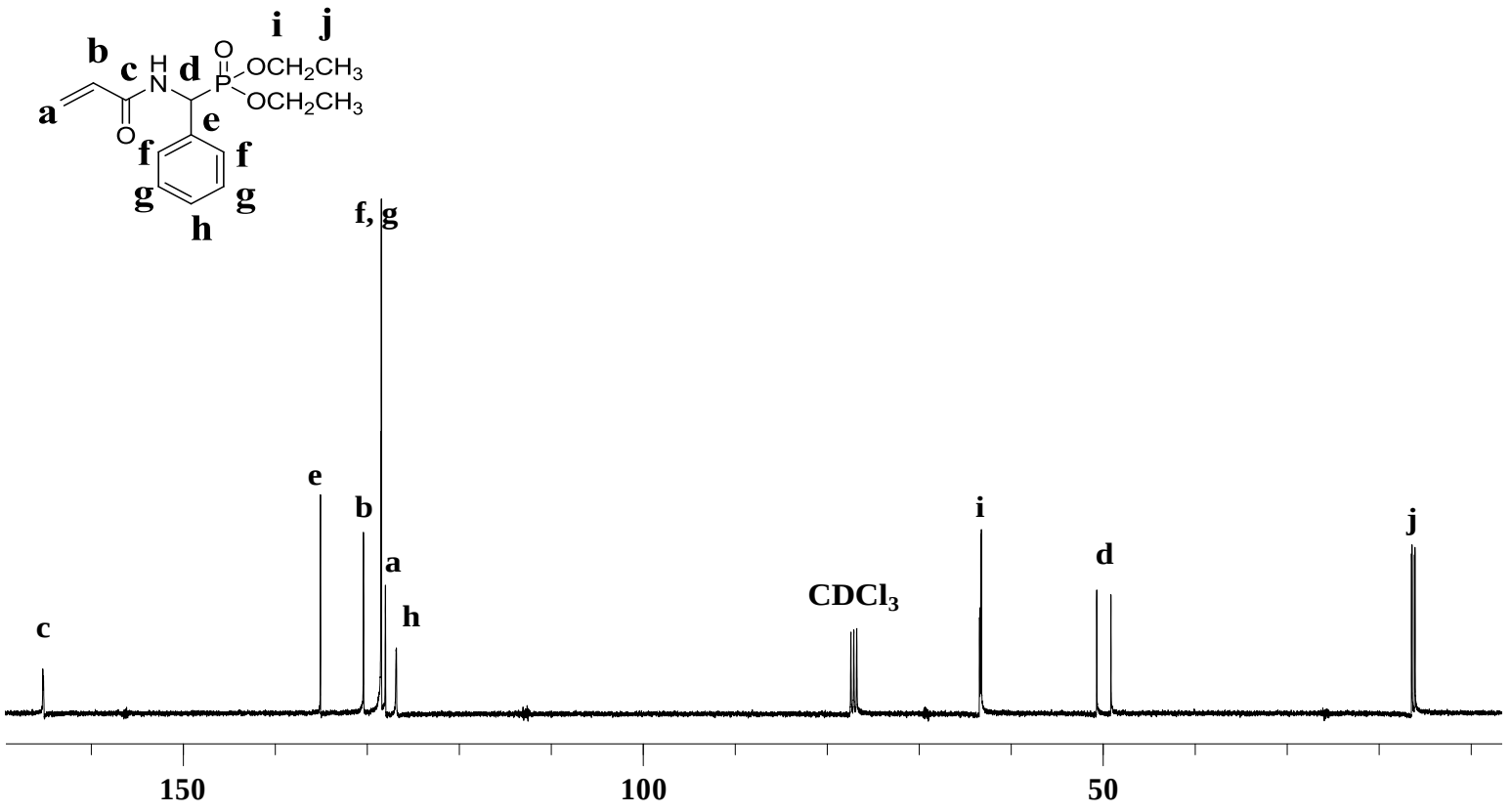


Figure A.8. ^{13}C-NMR spectrum of monomer 1 in $CDCl_3$.

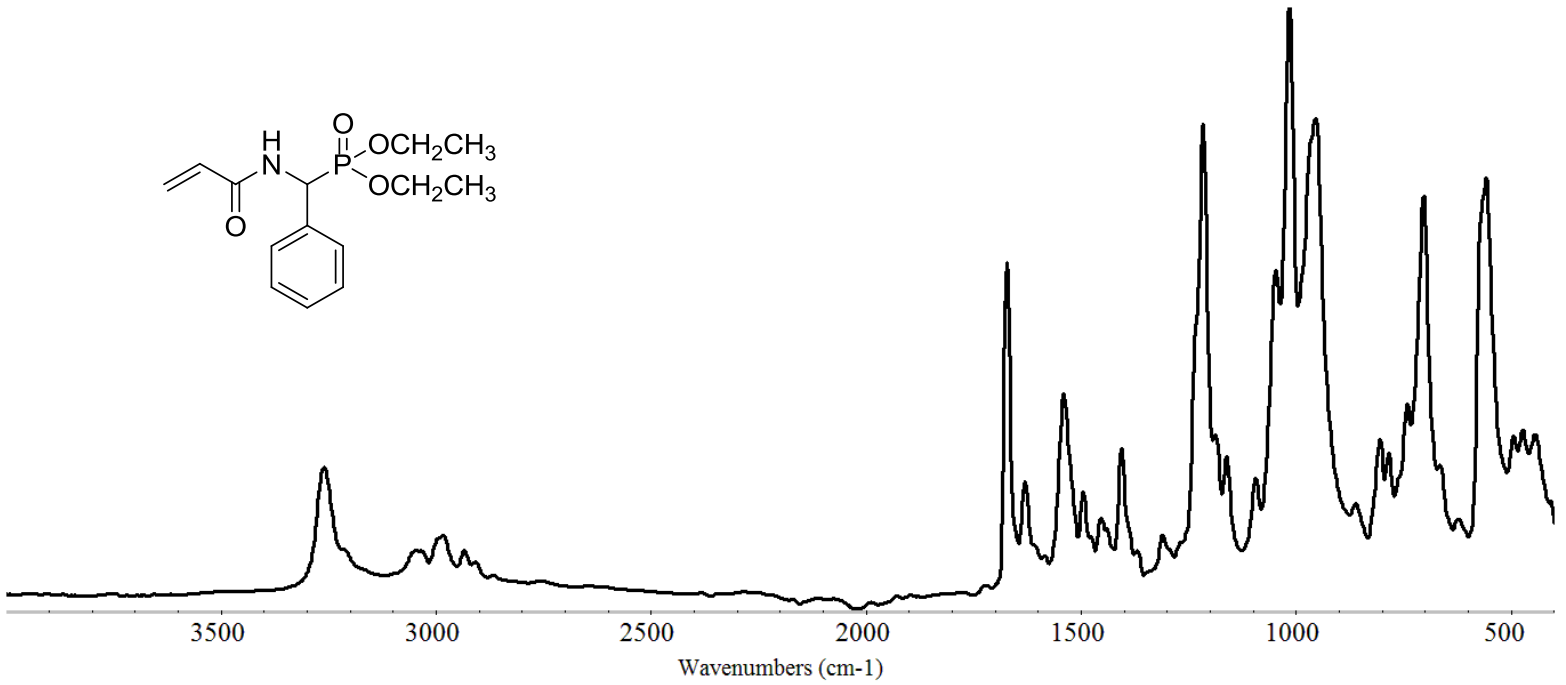


Figure A.9. FT-IR spectrum of monomer 1.

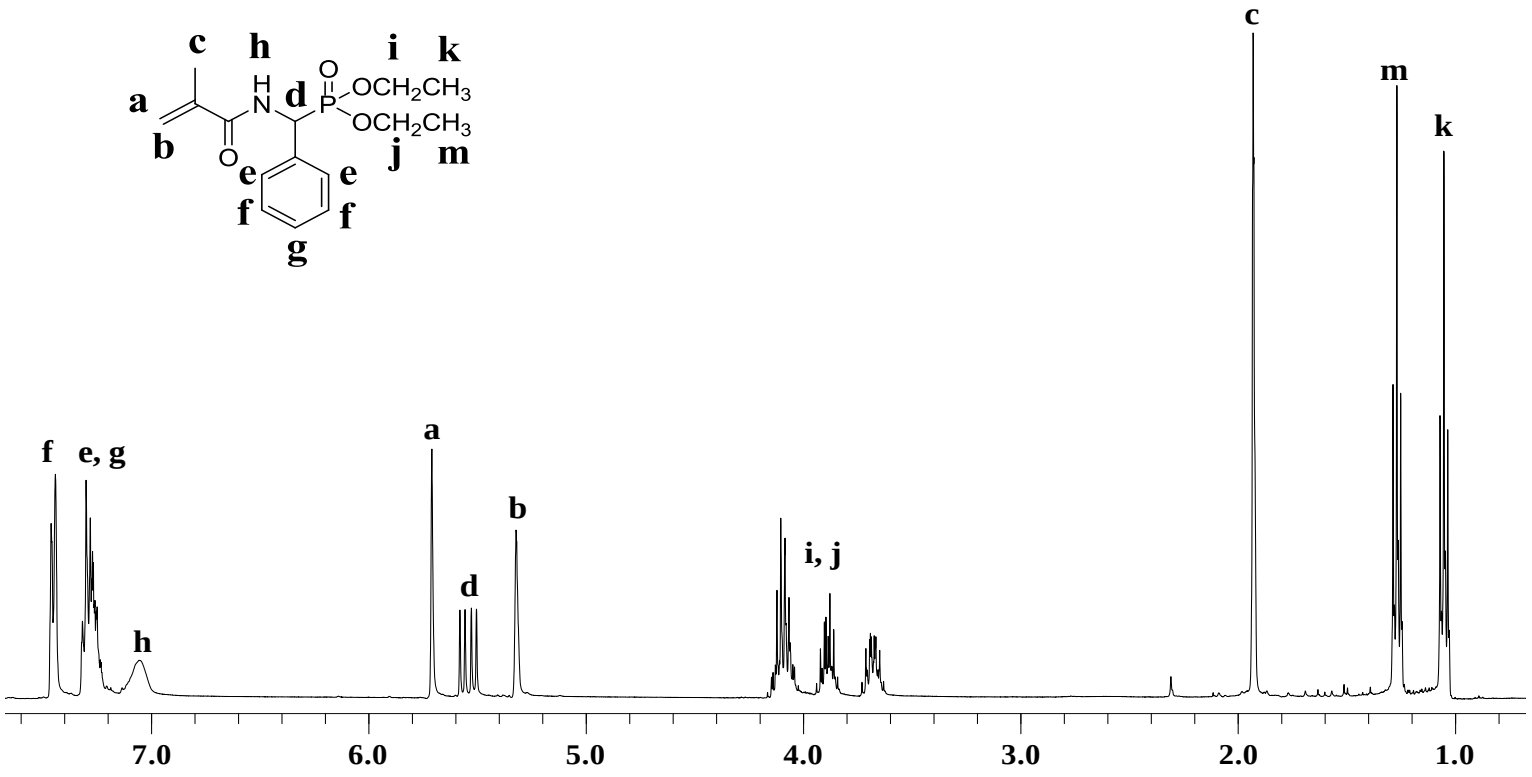


Figure A.10. ^{1}H-NMR spectrum of monomer 2 in $CDCl_3$.

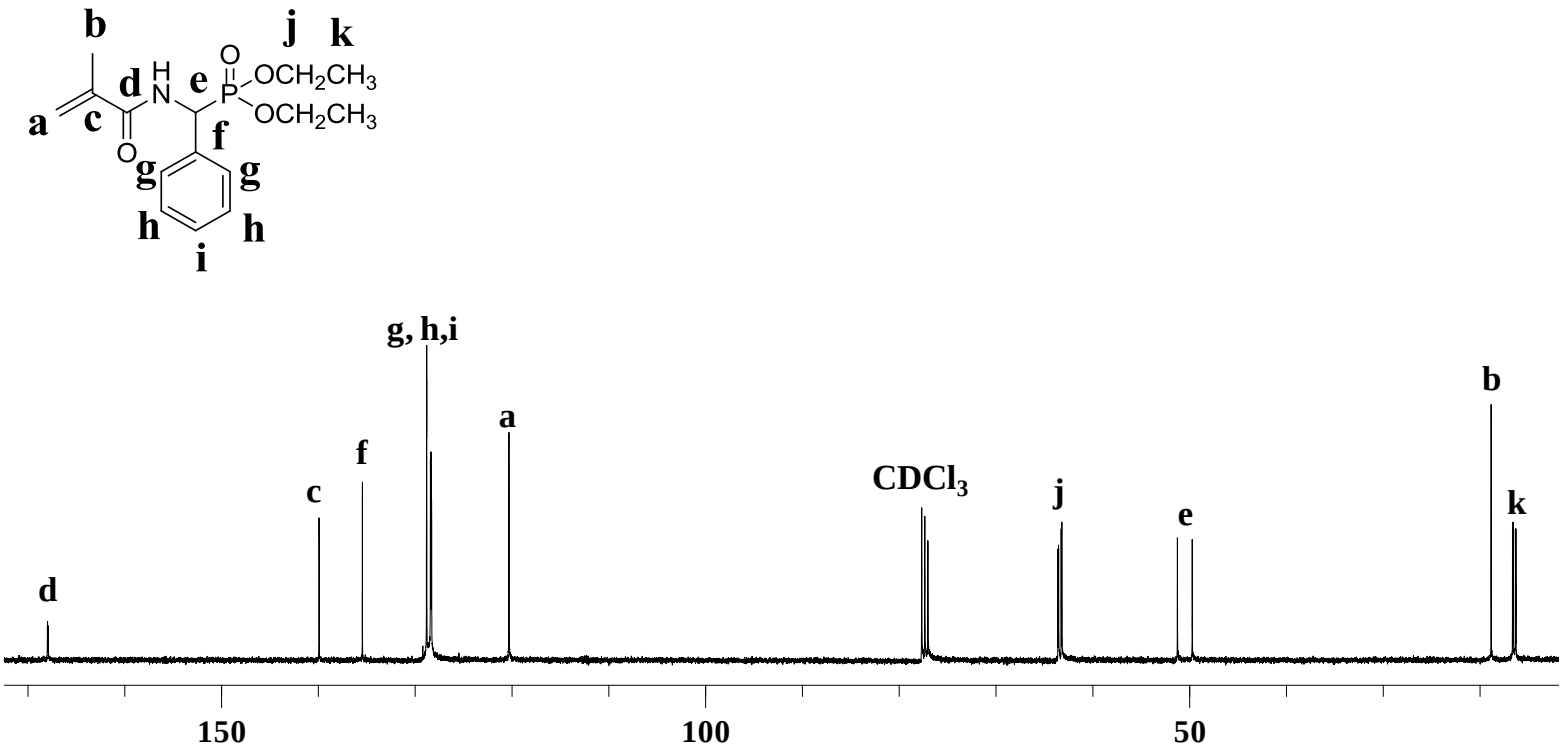


Figure A.11. ^{13}C-NMR spectrum of monomer 2 in $CDCl_3$.

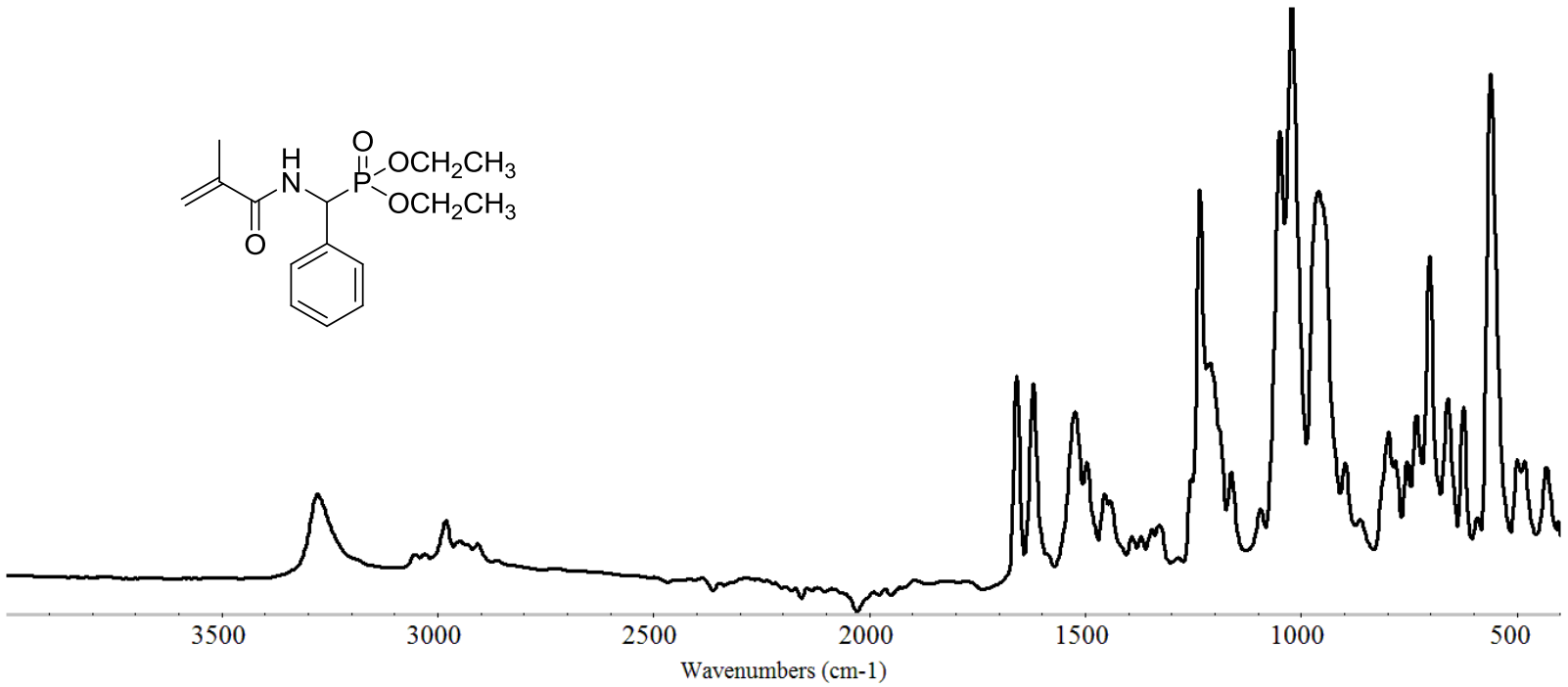


Figure A.12. FT-IR spectrum of monomer 2.

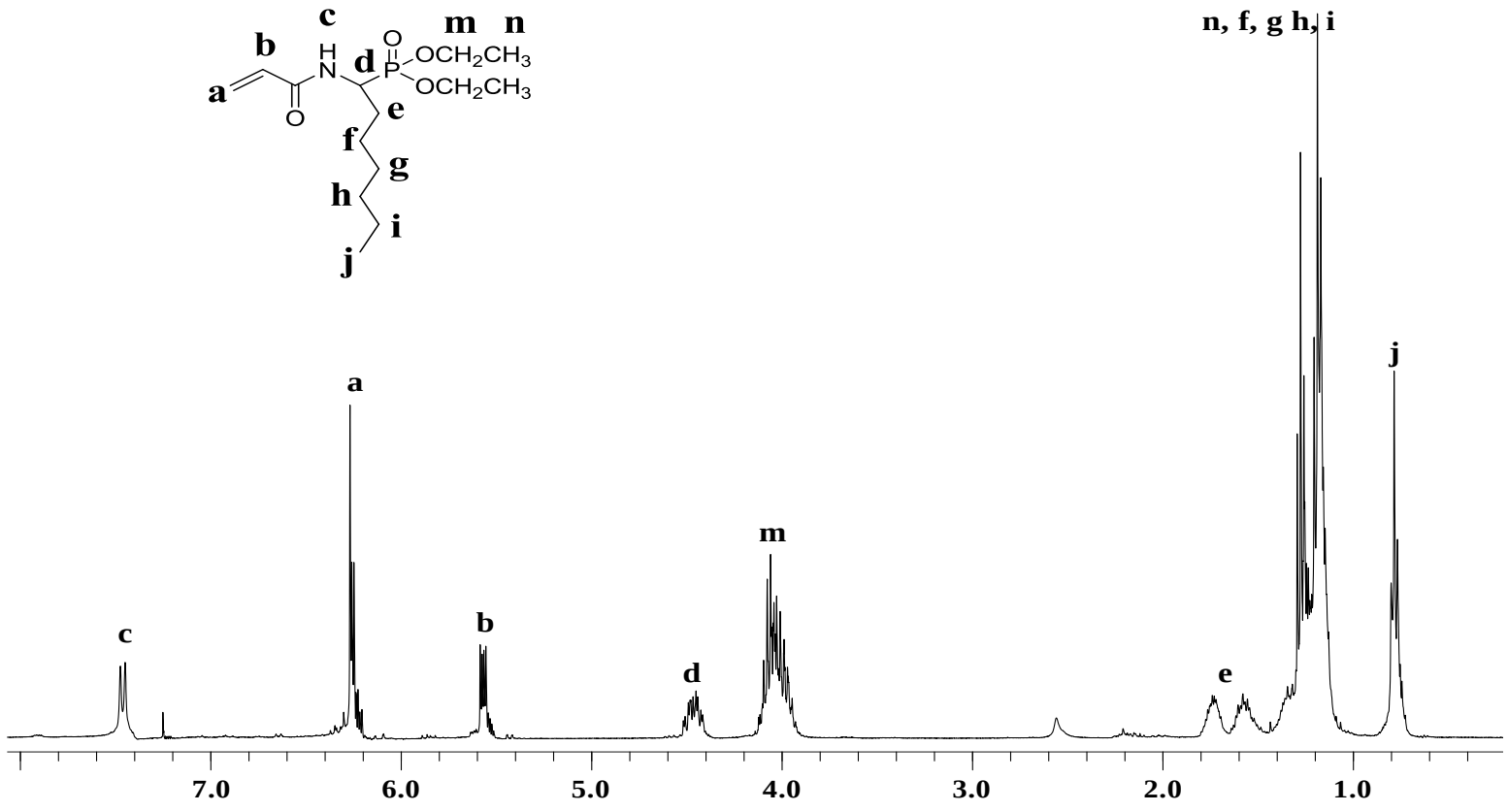


Figure A.13. ^{1}H-NMR spectrum of monomer 3 in $CDCl_3$.

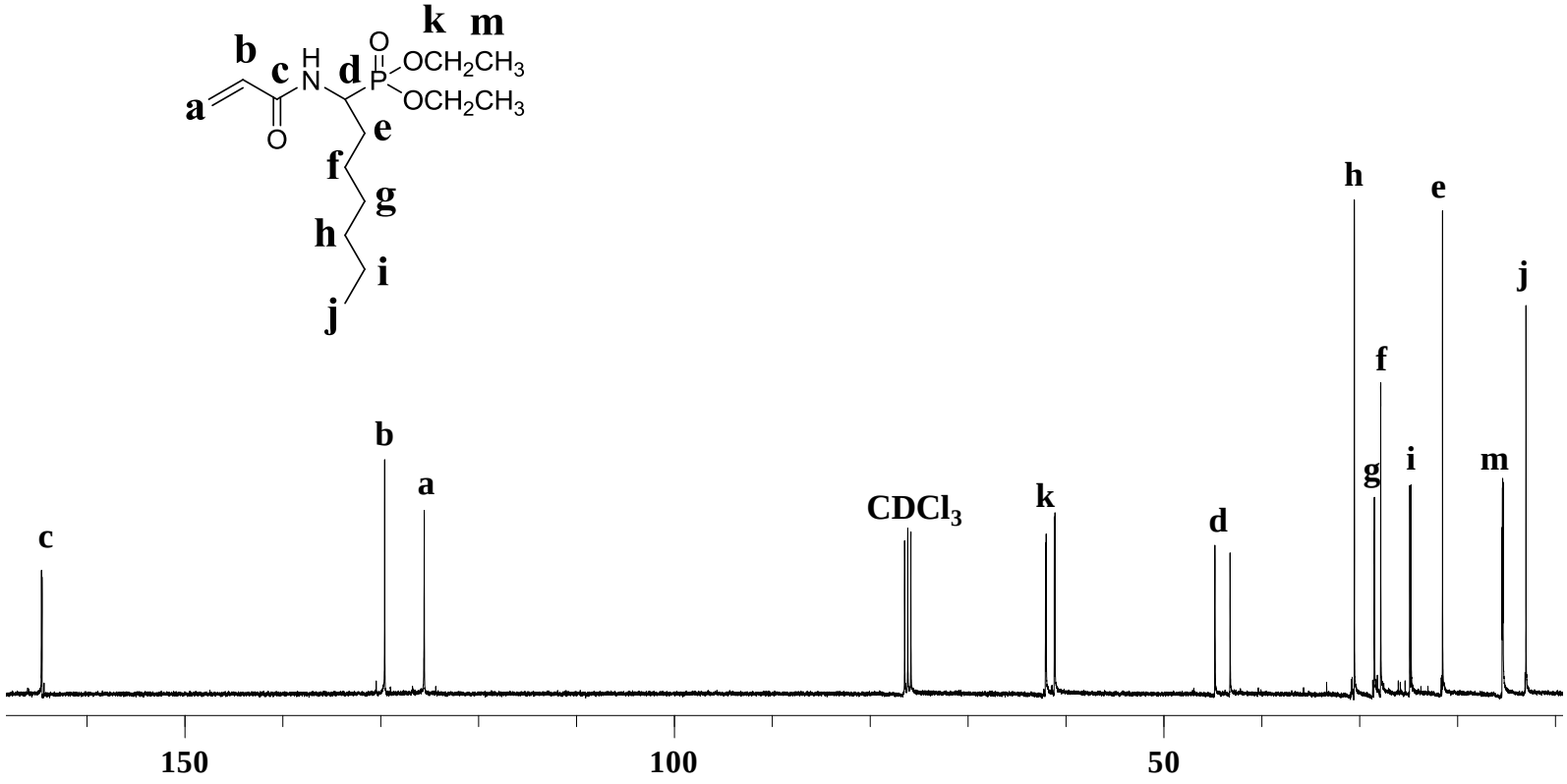


Figure A.14. ^{13}C-NMR spectrum of monomer 3 in $CDCl_3$.

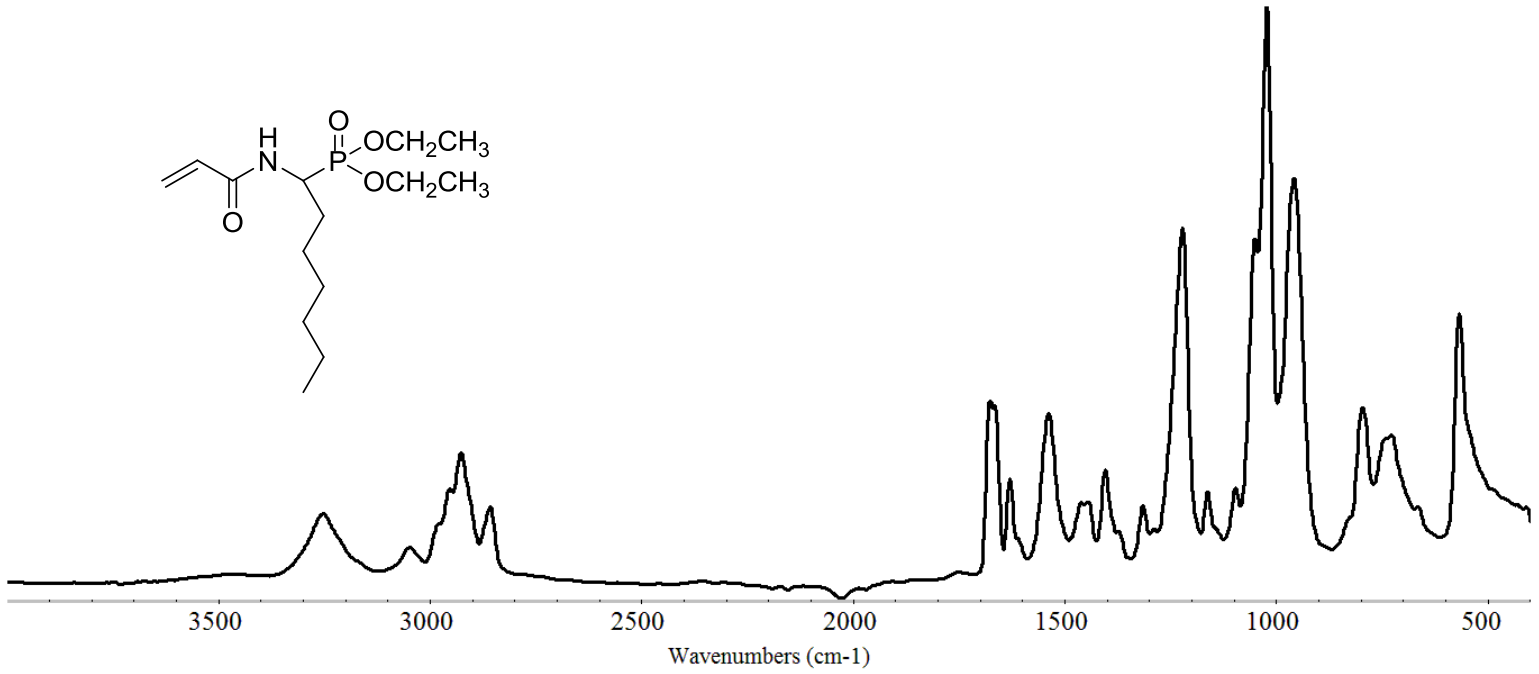


Figure A.15. FT-IR spectrum of monomer 3.

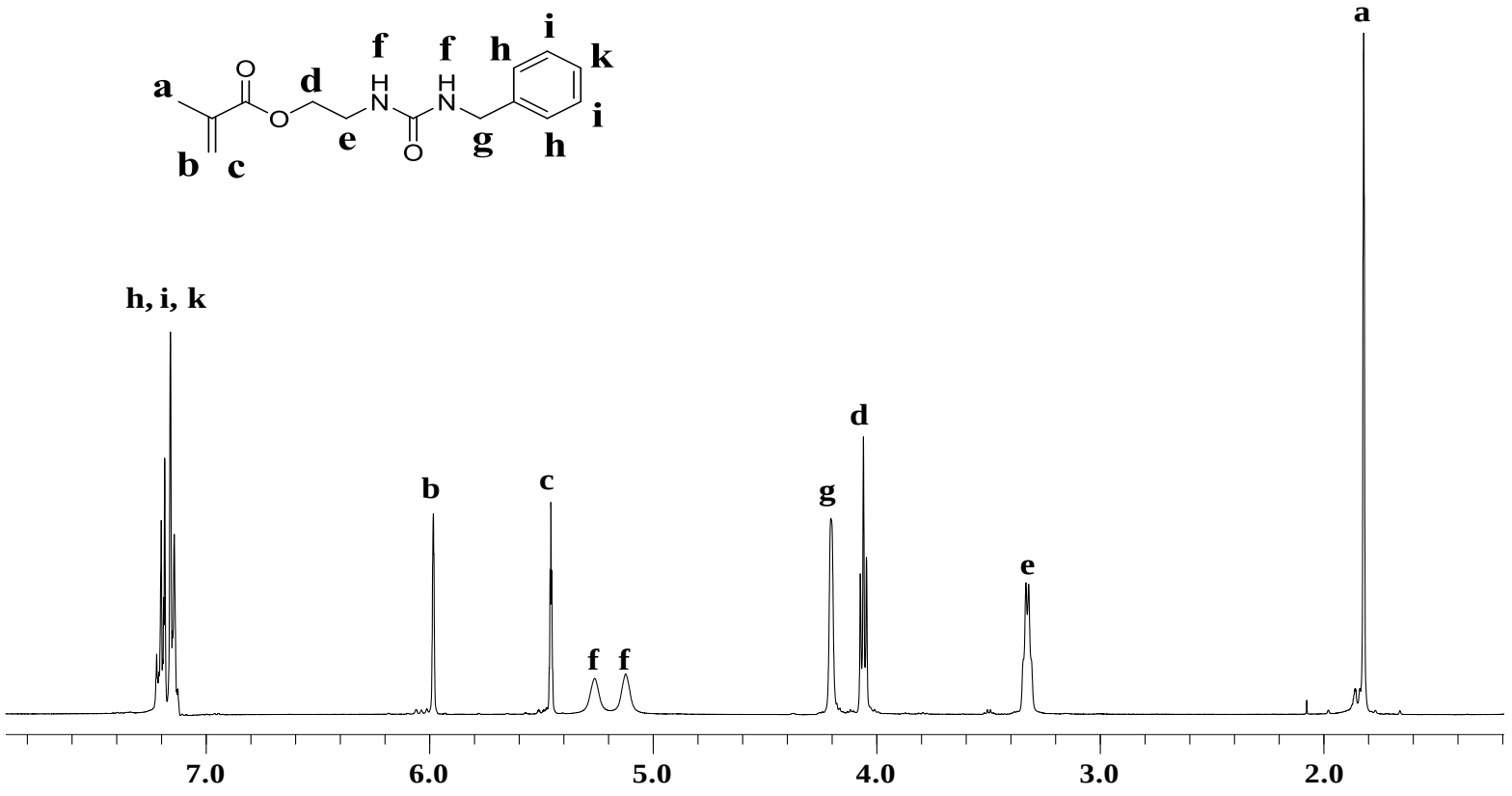


Figure A.16. ^{1}H-NMR spectrum of monomer 4 in $CDCl_3$.

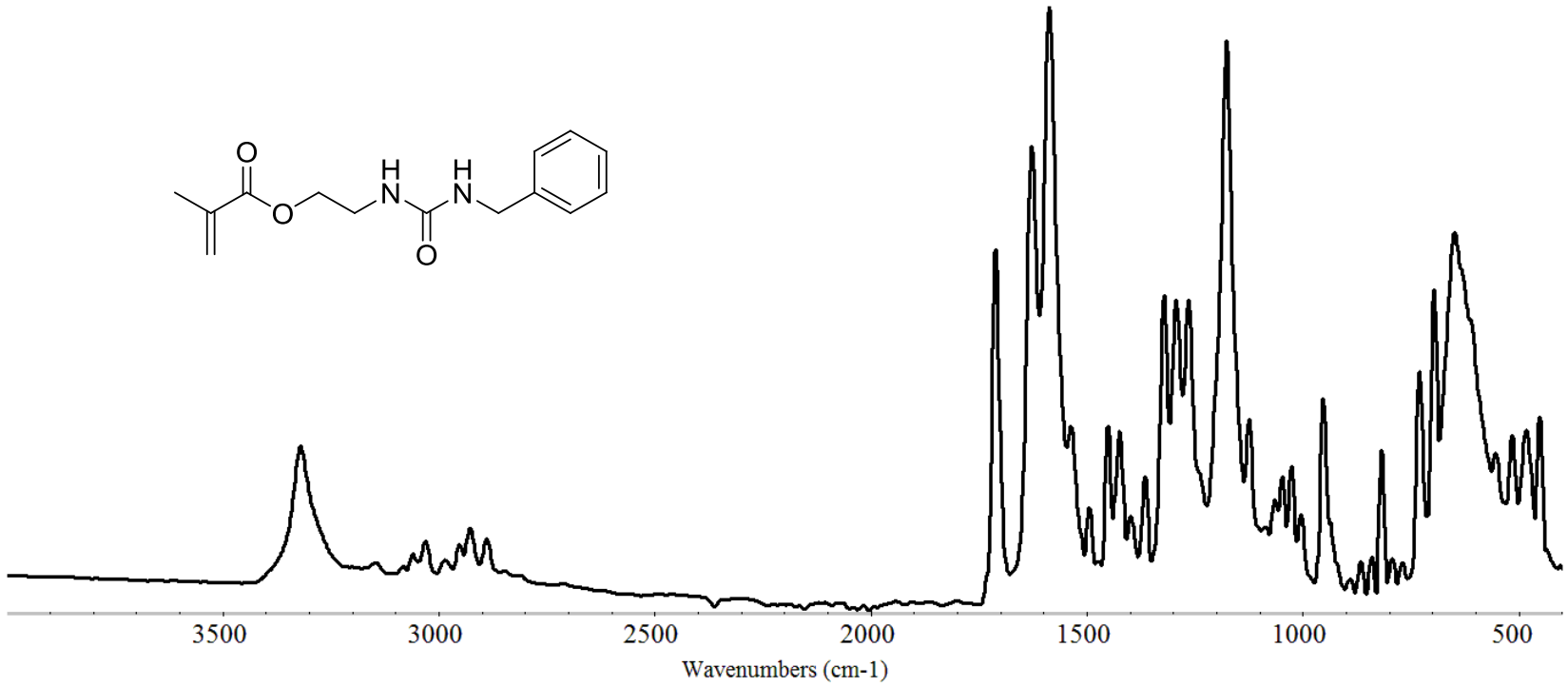


Figure A.17. FT-IR spectrum of monomer 4.

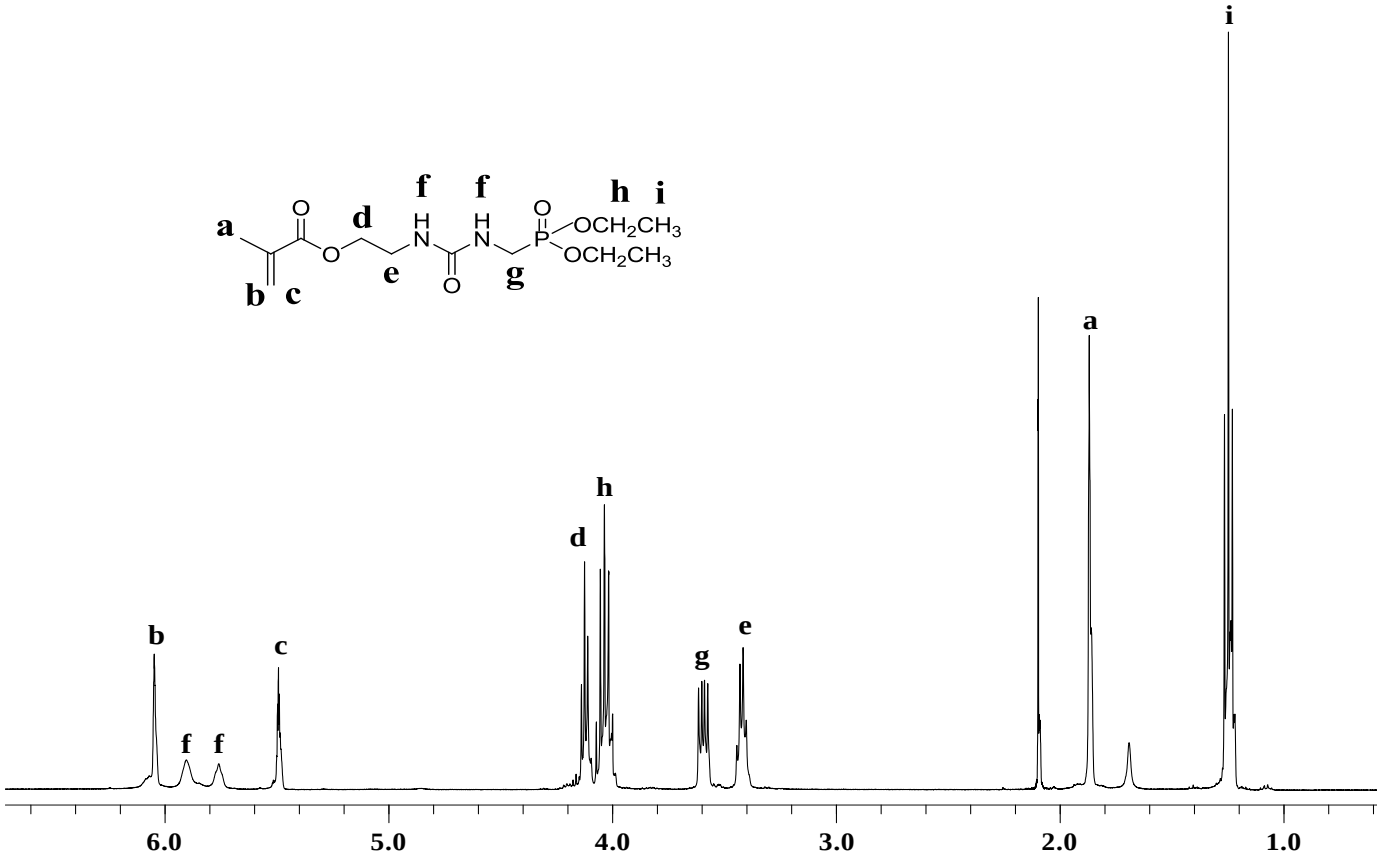


Figure A.18. ^{1}H-NMR spectrum of monomer 5 in $CDCl_3$.

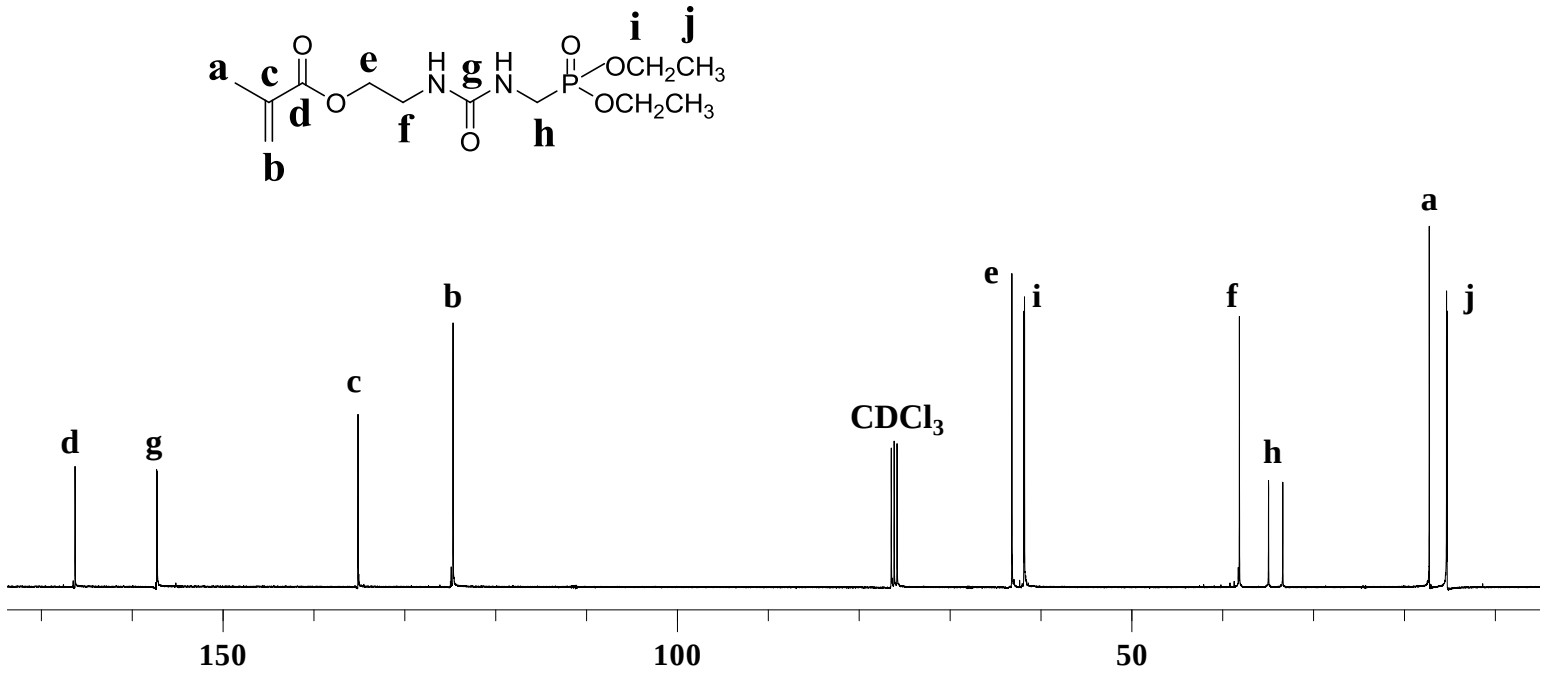


Figure A.19. ^{13}C-NMR spectrum of monomer 5 in $CDCl_3$.

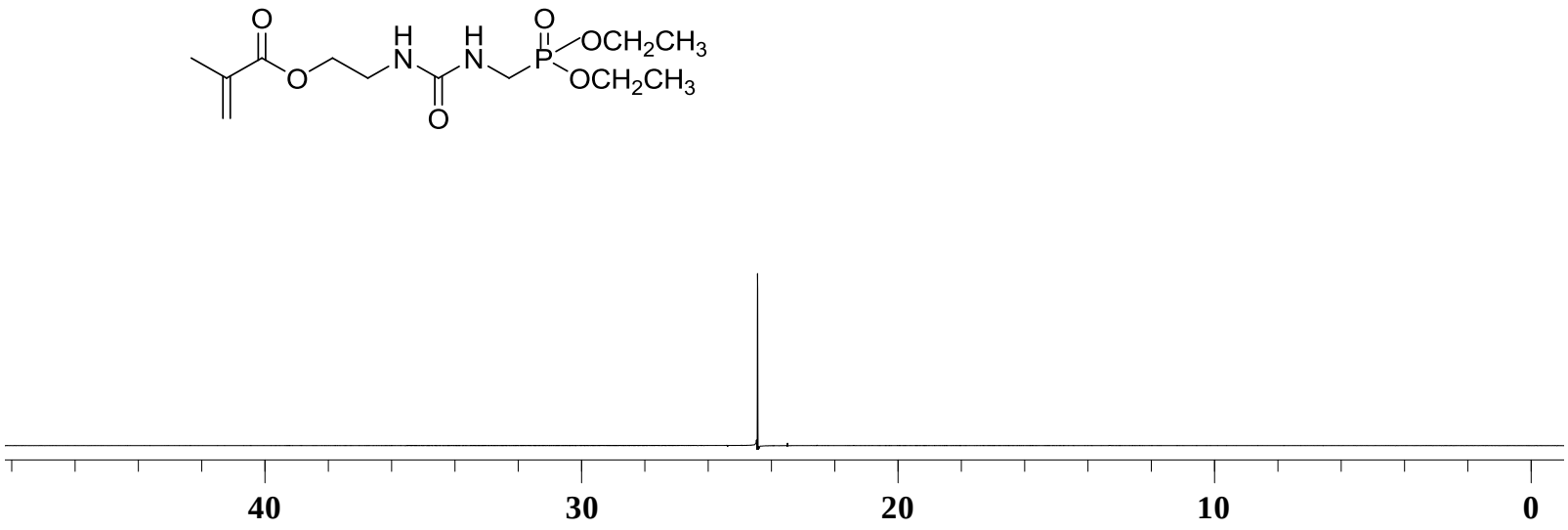


Figure A.20. ^{31}P-NMR spectrum of monomer 5 in $CDCl_3$.

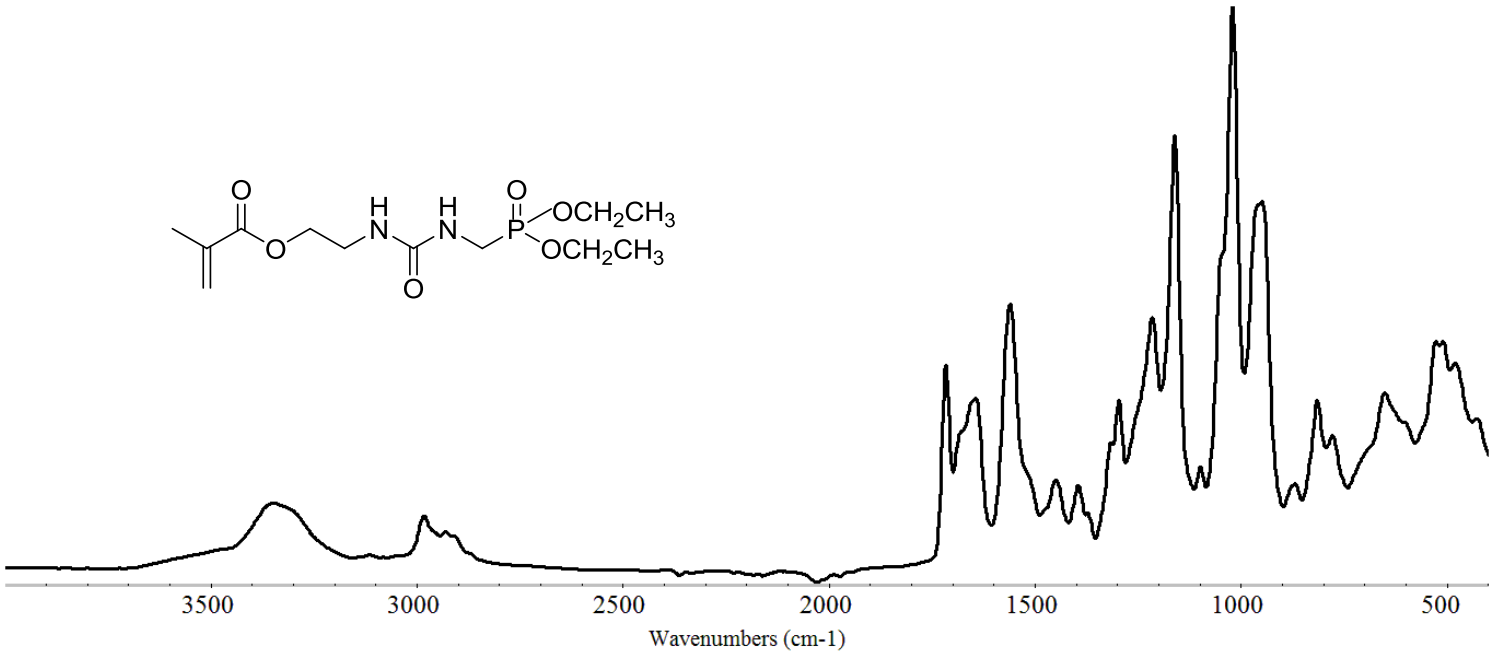


Figure A.21. FT-IR spectrum of monomer 5.

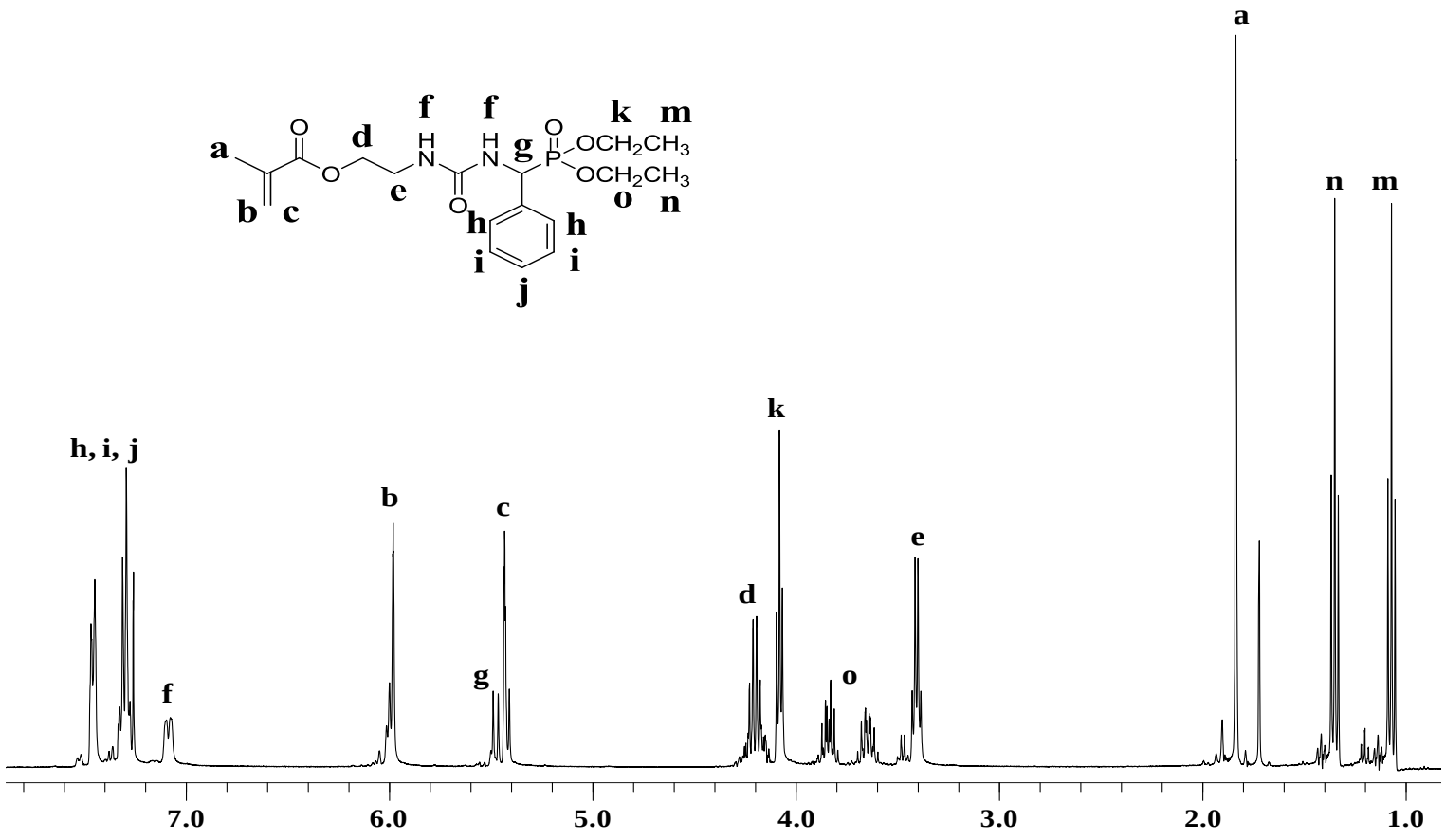


Figure A.22. ^{1}H-NMR spectrum of monomer 6 in $CDCl_3$.

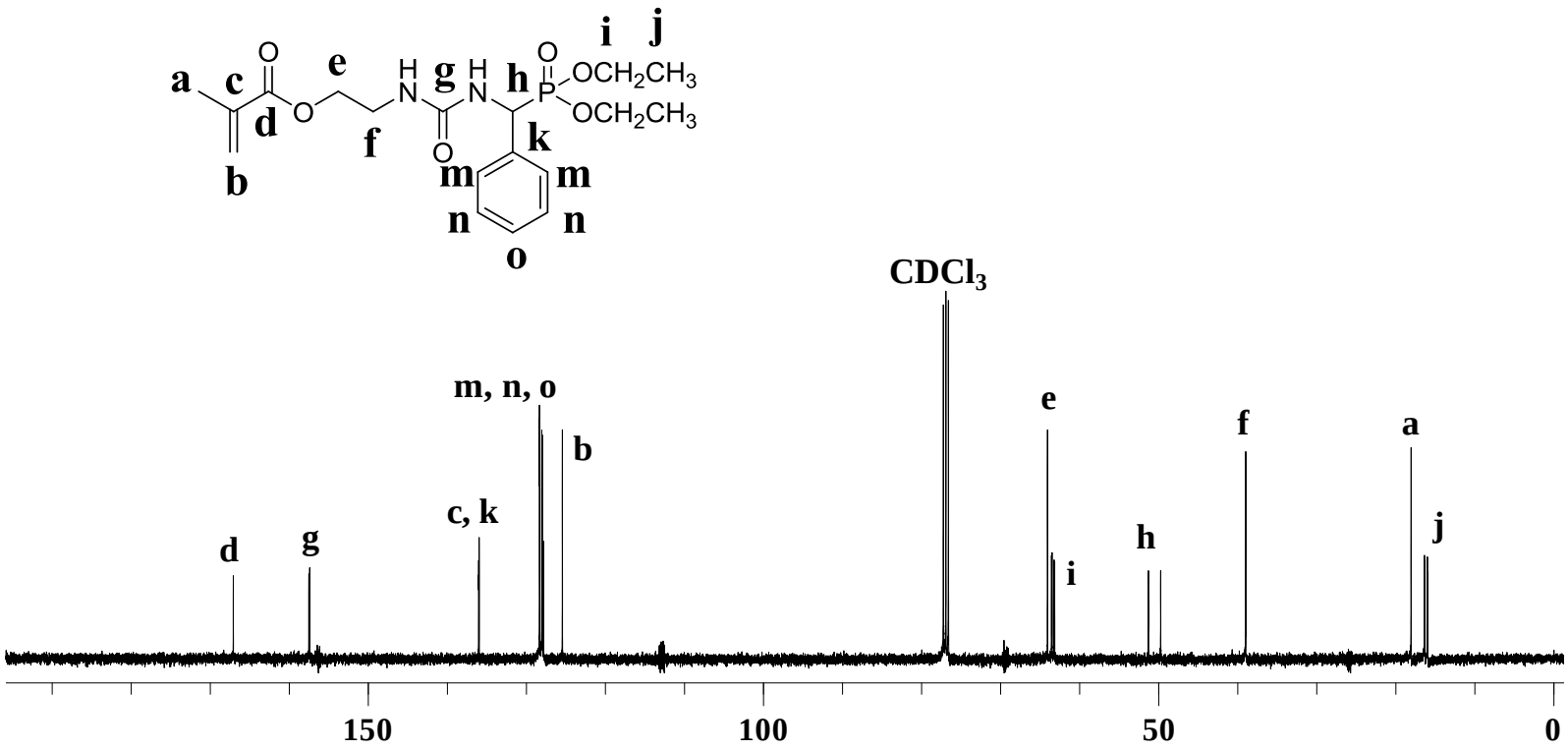


Figure A.23. ^{13}C-NMR spectrum of monomer 6 in $CDCl_3$.

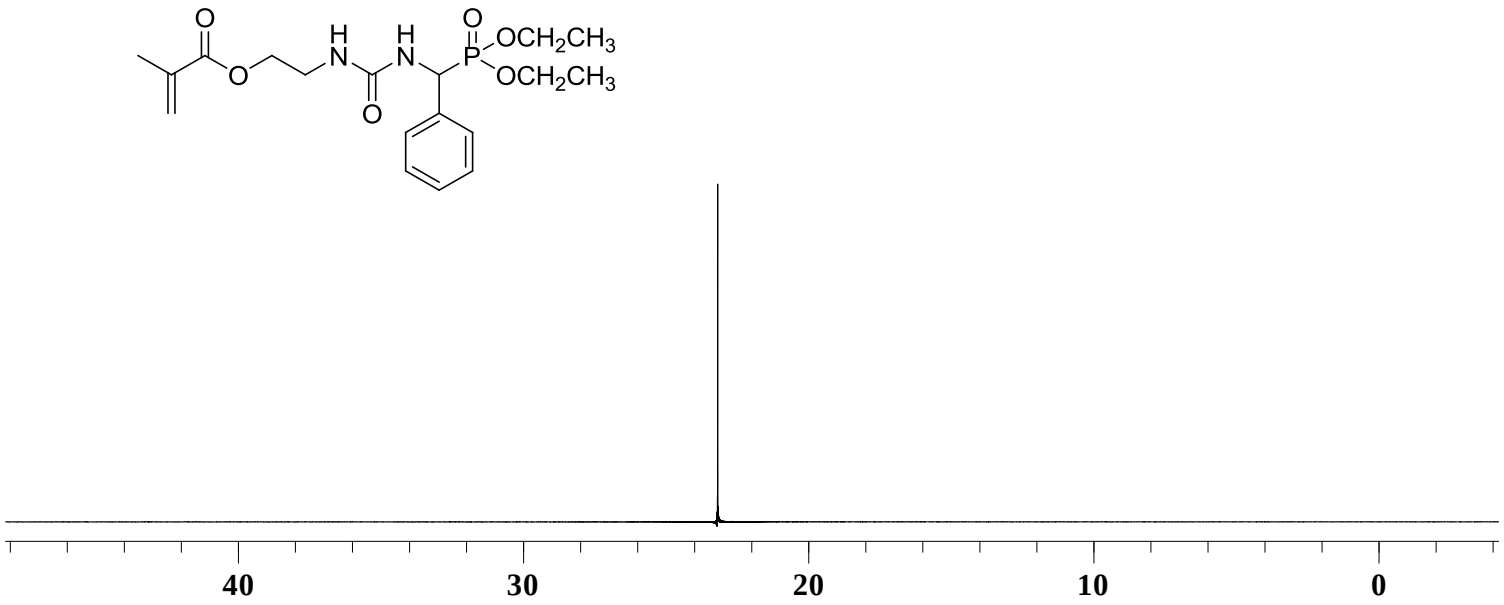


Figure A.24. ^{31}P-NMR spectrum of monomer 6 in $CDCl_3$.

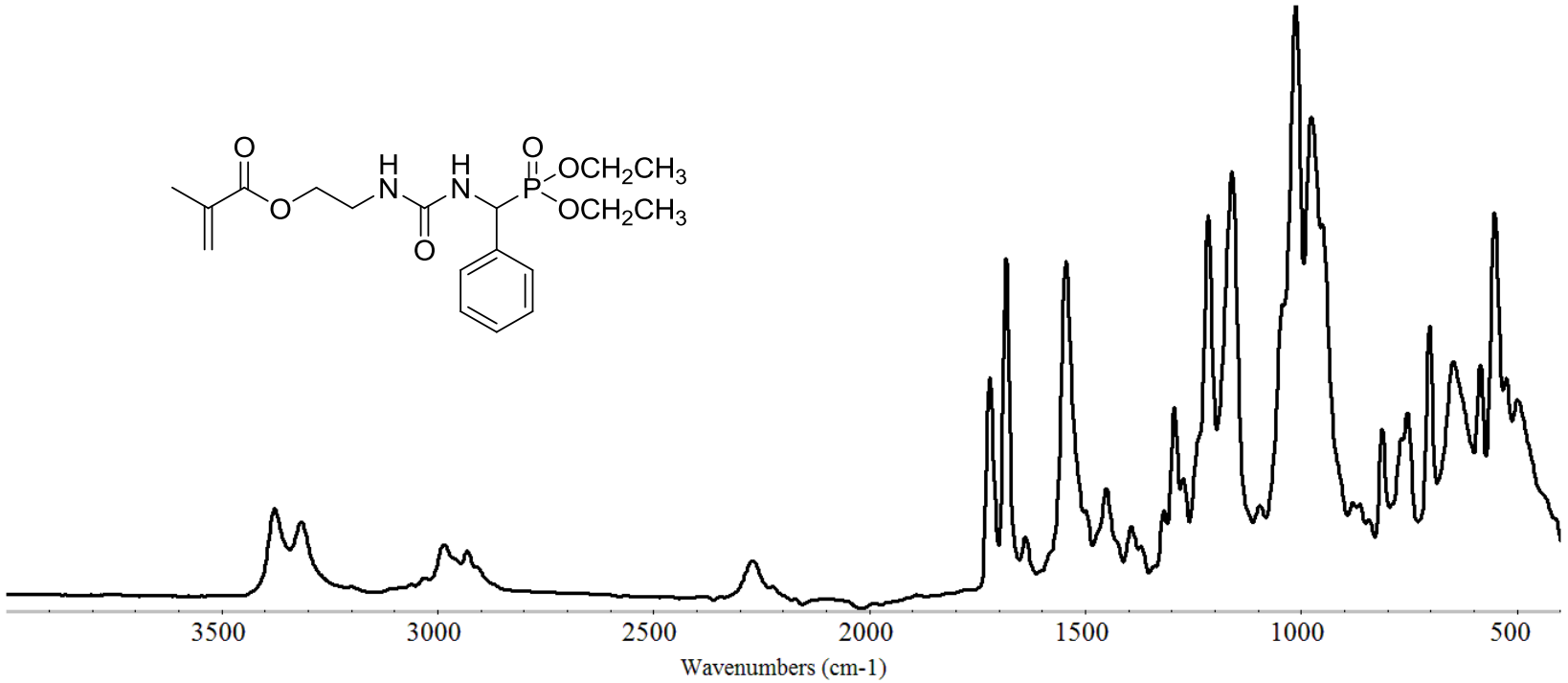


Figure A.25. FT-IR spectrum of monomer 6 in $CDCl_3$.

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