DENDRITIC AND LINEAR POLYMERS FOR SEPARATIONS

A Dissertation

by

SERGIO OMAR GONZALEZ

Submitted to the Office of Graduate Studies of
Texas A&M University
in partial fulfillment of the requirements for the degree of

DOCTOR OF PHILOSOPHY

December 2004

Major Subject: Chemistry

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Approved as to style and content by:

Eric E. Simanek (Chair of Committee)	Stephen A. Miller (Member)
David E. Bergbreiter (Member)	Roger Morgan (Member)
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December 2004

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ABSTRACT

Dendritic and Linear Polymers for Separations.

(December 2004)

Sergio Omar Gonzalez, B.S., The University of Texas at San Antonio

Chair of Advisory Committee: Dr. Eric E. Simanek

Most new fields in chemistry usually began as a curiosity by the researchers, followed by an intrinsic interest in basic biological, physical and chemical properties of reactions, interactions, structural features, and response to external stimuli by chemical elements and/or chemical compounds. If the "curiosity" has appealing bio-physico-chemical properties this trend is followed by studies on the possible applications of such new fields. As a result, is it expected that these curiosities develop or give insights into new technologies. The development of the field of dendrimer chemistry is no different. In fact, dendrimer chemistry illustrates this trend fittingly.

The research in this dissertation follows a similar trend. First, the synthesis of a melamine-based dendrimer is achieved. The synthesis illustrates the concept of using triazines as building blocks in dendrimer synthesis. The characterization of this molecule was followed by a basic inquiry of the properties that were unique relative to its composition. This dendrimer is

compared against a small library of similar dendrimers in a structure-activity relationship (SAR) study.

From the basic concept of an SAR, we moved toward more applied studies of these molecules. The grafting of organic molecules onto inorganic supports has had influences in the fields of catalysis, separations, and sensors. We developed protocols for the grafting of melamine-based molecules onto hydroxyl rich surfaces. After extensive characterization using solution and surface analyses, we tested the sequestration abilities of these new materials toward the separation of molecules of environmental importance from water.

Following the data collected in these experiments, we moved toward a different type of applied technology. The use of linear polymers for separations instead of dendrimers is more attractive from an engineering perspective. We then used what was learned from the study of the separations performed by dendrimers and applied it to the design of linear polymers. We take advantage of a latent solid phase response to external stimuli to remove the herbicide atrazine from aqueous solution to the limit of detection.

DEDICATION

To the loving memory of Manuel Campos Lira (1924 - 2001) and Maria Reyes Valero de Campos (1929-2002). Loving grandparents whose departure left an immense emptiness.

ACKNOWLEDGMENTS

I thank God for all He's given me. I thank my advisor, my mentor, my friend Dr. Eric Simanek for his enormous patience, and recently, I thank him for his slight impatience. I also thank Dr. David Bergbreiter for his contributions to my achievements as a graduate student. I thank the rest of my advisory committee: Dr. Stephen Miller for accepting being a member before he arrived to Texas A&M, and Dr. Roger Morgan for his teachings and discussions on polymer science.

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Fernando, Brent, Chad, Mike, Jody, Cesar, Tara, Chunmei, Vicente, Schelter, the Juanes, and everybody else that made my stay in College Station a pleasant experience. I thank my parents for their unconditional support. I thank my siblings for their love and affection. I thank the rest of my family who are always there for me. I also thank Richard and Martha Landsman for supporting and believing the dreams of the immigrant kid who mowed their land. Finally, I thank my future wife LizaMar, whose encouragement and love these final months of my graduate career have been essential for success. De aquí en adelante corazón, sin miedo a nada.

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CHAPTER I

INTRODUCTION

Dendrimers: Branching Out of Polymer Chemistry. Dendrimers are highly branched, monodisperse polymers in which branching emanates from a central core.[1] Dendrimers are built in a step-wise manner. This laborious polymerization technique gives rise to synthetic macromolecules with defined molecular weight relative to other synthetic macrostructures. The well defined molecular weight, collectively with the branched architecture, gives the dendrimer its unique properties (Figure 1.1), including low viscosity and the absence of a glass transition temperature.[2] Because of its architecture and high molecular weight, we consider dendrimer chemistry as polymer chemistry branching out. Synthetic linear polymers, graft polymers, and network polymers, such as the well known and extensively used Nylon, Kevlar®, polyethylene, polystyrene, Rayon®, and Dacron® are now being joined by new classes of highly branched polymers. These novel branched structures included dendrimers and hyperbranched polymers. In this dissertation we will discuss phase separations of dendrimers, hyperbranched macromolecules, and linear polymers.

This dissertation follows the style and format of the Journal of Polymer Science, Part A: Polymer Chemistry.

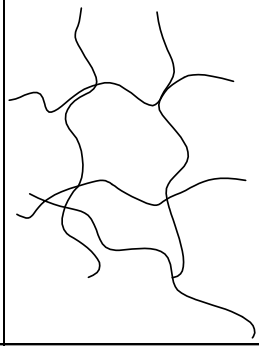
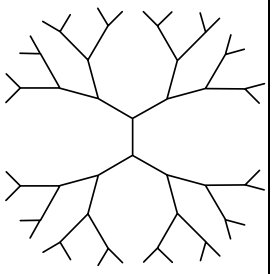
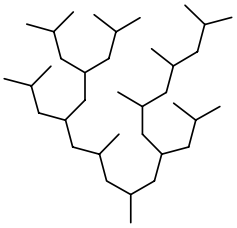
Linear Polymer	Graft Polymer	Network Polymer	Dendrimer	Hyperbranched Polymer
				
Polydisperse, no branching other than the end groups.	Polydisperse, branching due to monomer side reactions or a copolymerazation process.	Polydisperse, formed when linear and/or graft polymers are joined together, may also form from polyfuctional monomers.	Monodisperse, highly branched macromolecule, branching emanates from a central core.	Polydisperse, highly branched macromolecule exhibits dendritic branching without necessarily emanating from a central core.

Figure 1.1. Major classes of synthetic macromolecular architectures.

In the last two decades the chemistry literature has seen a rapid increase in the number of publications that communicate advances and applications of branched macromolecules (Figure 1.2). A Scifinder search from 1983 to 2004 using as the research topic “dendrimer, hyperbranched polymer” generates an excess of 11,000 hits.[3] Included in these hits are numerous reviews.[4-8] The term “dendrimer” is derived from the Greek word for “tree” (dendron) and the scientific suffix for “unit” (mer, as in poly*mer*). Because of its two dimensional structure these molecules have also been called arborols (from the Latin for tree), and cascade or starburst polymers.

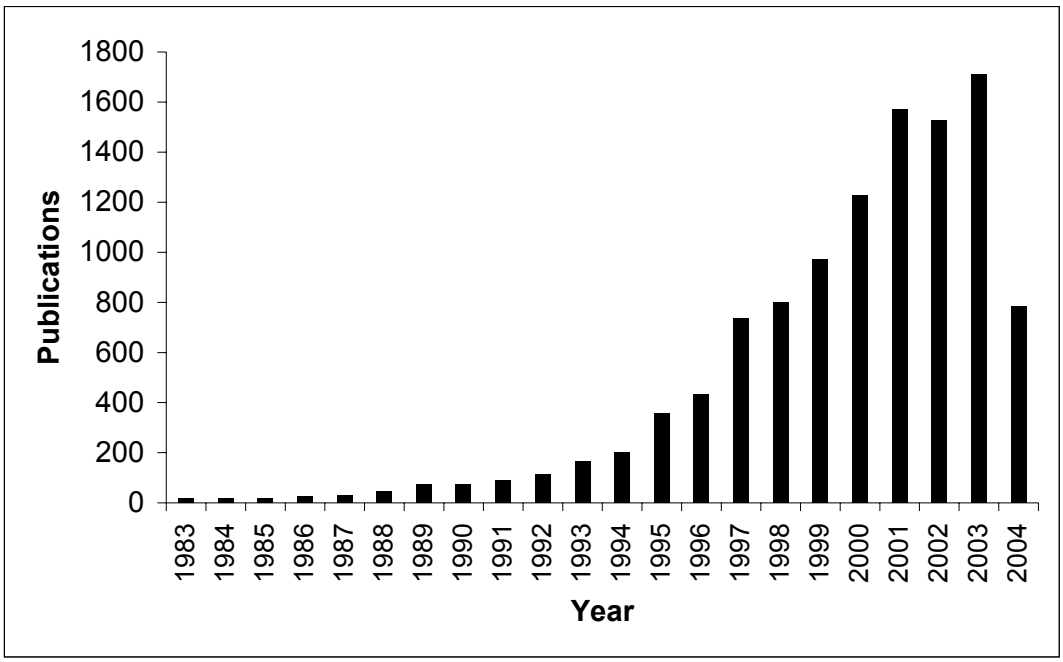


Figure 1.2. A search using the scientific search engine Scifinder; on the research topic "dendrimer, hyperbranched polymer". The results for 2004 are from January to June.[3]

Figure 1.3 shows a dendrimer (**1**) synthesized in our group.[9] Often, chemists like to draw similarities between molecules and everyday objects, such as "bucky balls",[10] "comb polymers",[11] and more recently "nanoputians".[12] The melamine-based dendrimer picture in Figure 1.3 is reminiscent of the mathematical idea of a fractal. No matter how much you magnify a fractal, it always looks the same (or at least similar). "Natural" fractals include ferns, snowflakes and trees. Chemists conjure their own terminology not only in naming these macrostructures but they also draw from nature, familiar structures, and common ideas to create an innovative nomenclature system.

The central unit of a dendrimer is called the "core". From the core, linking groups radiate or “branch” to the “periphery” or “surface” and are referred as "peripheral groups" or “surface groups”. The term “melamine-based” is drawn from the functionality at the branching points. Melamine, **2**, is a 1,3,5-triazine substituted with three amines. The synthesis and advantages of melamine-based dendrimers will be described later in this dissertation.

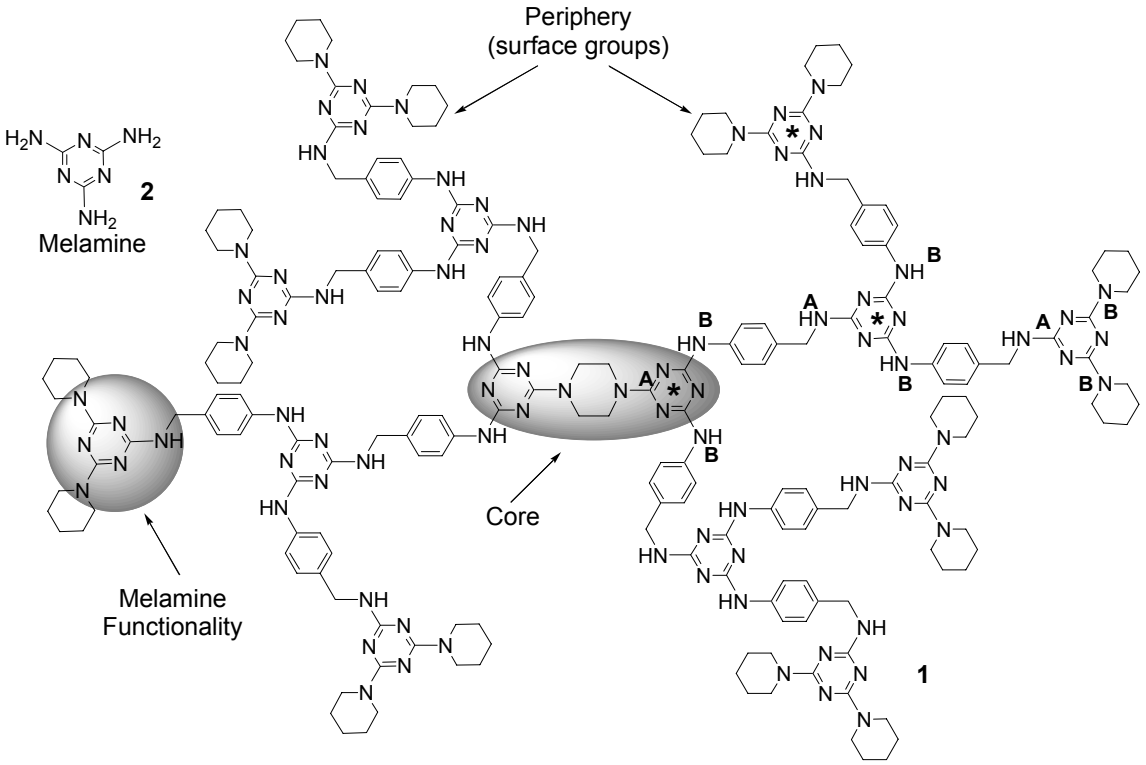


Figure 1.3. Melamine-based dendrimer prepared in the Simanek laboratory; it invokes the mathematical concept of a fractal, similar to patterns found in nature. We use an AB_2 monomer as the branching group (*) to prepare this generation 3 (g3) dendrimer. Melamine, **2**, is 1,3,5-triazine-2,4,6-triamine.

Description of the size of dendrimers has also developed its own nomenclature. Synthesizing monodisperse polymers such as dendrimers demands a high level of synthetic control which is achieved through stepwise reactions. That is to say, the dendrimer is put together one layer at the time or most commonly known as one “generation” at a time. The core is most often referred as "generation 0". Addition of a “mer” or repeating unit to the core arises in the next generation, "generation 1" or “g1”. Therefore, each addition of mer adds a generation to the dendrimer or dendron. It is important to mention that there are no sanctioned rules on dendrimer nomenclature. As a result, generation number may differ from dendrimer to dendrimer, and from research group to research group.

The g3 dendrimer, pictured in Figure 1.3, uses an AB_2 building block. This nomenclature is more straightforward than counting generations. The "A" refers to the number of bonds coming into a branching group (almost always 1) from the core; "B" refers to the number of bonds leaving a branching group toward the periphery (most commonly 2-5). In this case, we use the *sym*-triazines labeled with asterisks as the branching groups. We can see that one diamine linking group arrives from the core, and two diamine linking groups emanate toward the periphery, hence A_1B_2, or AB_2.

Due to their globular shape and molecular weight, dendrimers are considered nanostructures. The size of dendrimers lies between the upper limits of classical organic synthesis and the lower limits of material science.

Therefore, dendrimers are measured in nanometers. A logarithmic scale bar relates the sizes of familiar objects to dendrimers (Figure 1.4). The size of a C—H bond is about 1 x 10^{-10} m, or 1 Å, a factor of 10 times smaller than the length of cholesterol and most prescription drugs. The C—H bond is smaller than a dendrimer by about a factor of 100. This means that dendrimers are approximately the size of proteins. This fact, added to the globular geometry of dendrimers, has caused significant attention in protein mimics.[13-15]

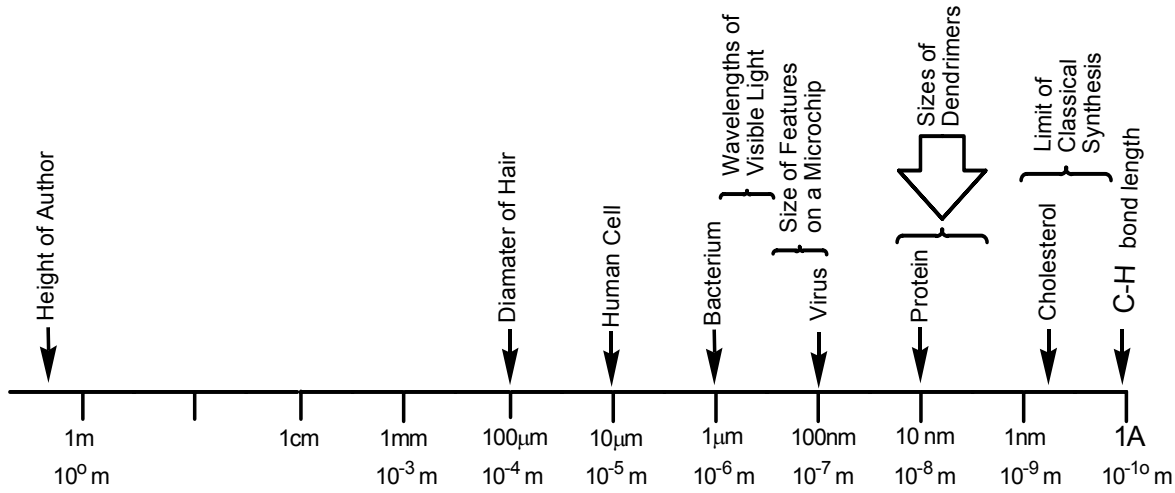
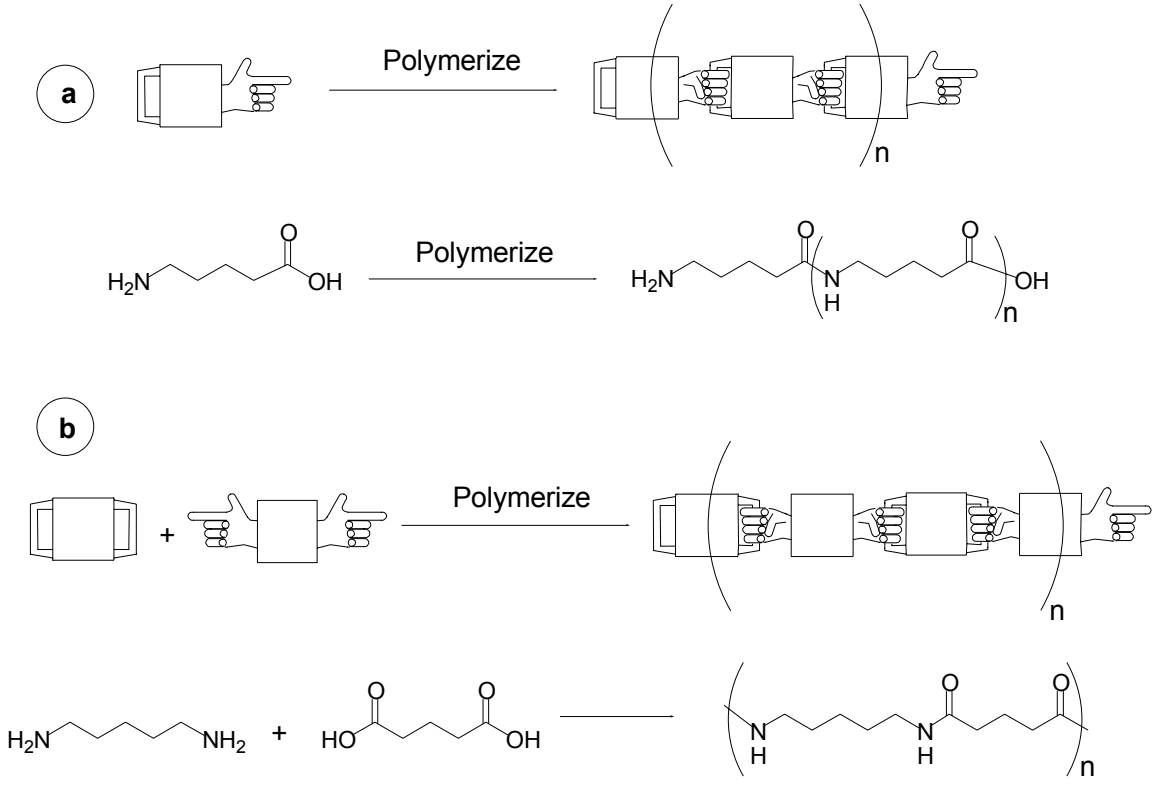


Figure 1.4. The sizes of dendrimers can be put into perspective using common objects related on a logarithmic scale bar.

Linear *versus* Branched Polymers. There are two main characteristics that both linear and dendritic polymers share. Both are considered macromolecules, and are built up from one or more repeating units. While they share these characteristics, their syntheses differ greatly. Repeating units of a

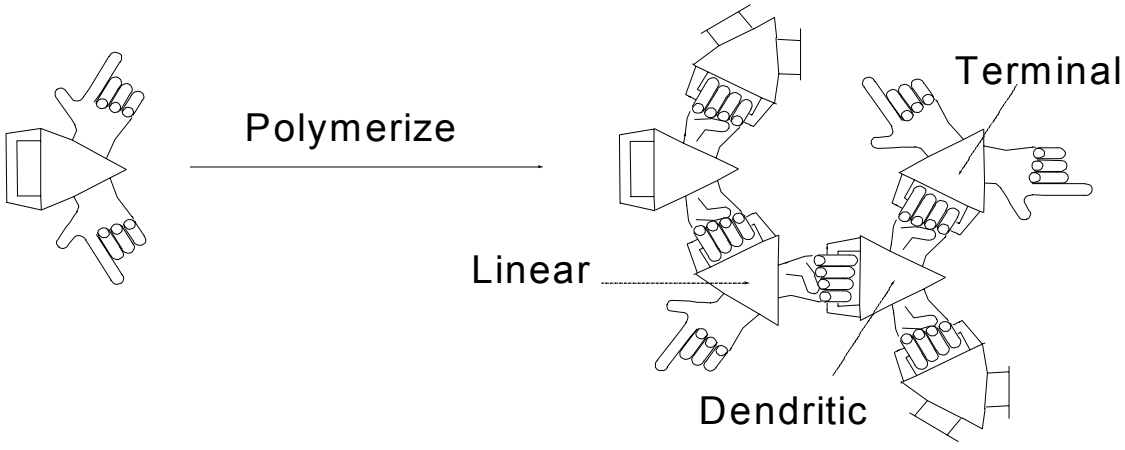
dendrimer or hyperbranched polymer have at least three sites for chemical manipulation. This requirement has implications on the type of polymerization technique. Linear polymers (Scheme 1) are prepared in one step by polymerizing difunctional monomers (a) or copolymerizing two suitable comonomers (b).



Scheme 1.1

Scheme 1.1a represents the polymerization to prepare Nylon 5, which is named for the number of carbons in the repeating unit. This monomer has both a nucleophile and an electrophile, represented by hands and handles. Under polymerization conditions, the hands react with the handles in a “head to tail”

manner. Explicitly, nucleophile adds to electrophile continuously. This technique produces primarily linear materials with high molecular weight (assuming hands can only grab handles). This technique is commonly referred to as a homopolymerization. A second technique to produce linear polymers is described in Scheme 1.1b. The copolymerization to make Nylon 5,5 which is a closely related polymer, can be obtained by mixing two different monomers. In this case, one molecule has two nucleophilic groups, while the other molecule (or comonomer) has two electrophiles. Again, the “hands” only grab handles, and a linear polymer is produced. In both cases, the only potential side-product results from cyclization of a polymer chain. This event usually creates low molecular weight materials since reactivity is terminated by the cyclization. This event is disfavored at high concentrations of reactants. Simply mixing monomers or co-monomers cannot be applied directly to dendrimer synthesis as illustrated in Scheme 1.2.



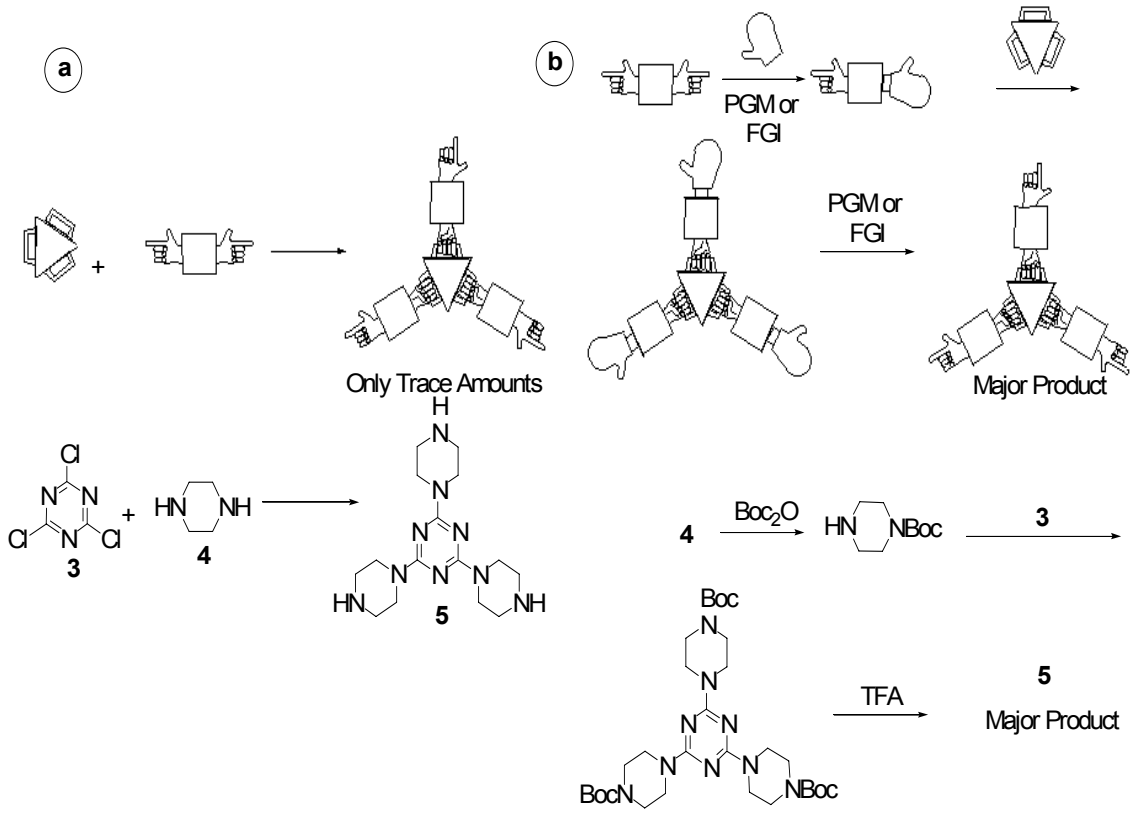
Scheme 1.2

Unlike the synthesis of dendrimers, polymerizing a multifunctional monomer leads to a distribution of branched products governed by statistics. This technique is usually employed to make network polymers or the closely related hyperbranched polymer. Dendrimers are monodisperse, highly branched macromolecules, where branching emanates from a central core. Hyperbranched polymers are polydiperse, highly branched macromolecules that exhibit dendritic branching without necessarily emanating from a central core. These polymers can display domains that are similar to dendrimers (labeled dendritic or terminal) and to linear polymers (labeled linear). Hyperbranched polymers offer a comparable degree of branching without the laborious synthetic steps involved in the preparation of dendrimers, but they lack the high order of dendrimers. This ease of synthesis, when coupled with the highly branched architecture, suggests that hyperbranched polymers could serve as an economical substitute for dendrimers. To prepare dendrimers alternative strategies have to be employed. Dendrimer synthesis requires significantly more attention because the synthetic chemist must exercise “control” over the reactions in order to avoid statistical mixtures of products to obtain a single product.

The Role of Protecting Groups and/or Functional Group Interconversions. There are two synthetic strategies that exercise control when carrying out the stepwise polymerization needed to prepare dendrimers.

They are protecting group manipulations (PGM) or functional group interconversions (FGI). Protecting groups are selectively and efficiently installed under mild conditions on the reactive group of interest, rendering it unreactive. The protecting group must survive subsequent chemical steps before it is selectively and efficiently removed under mild conditions. FGI converts the unreactive functional group to a reactive group through atom exchange.

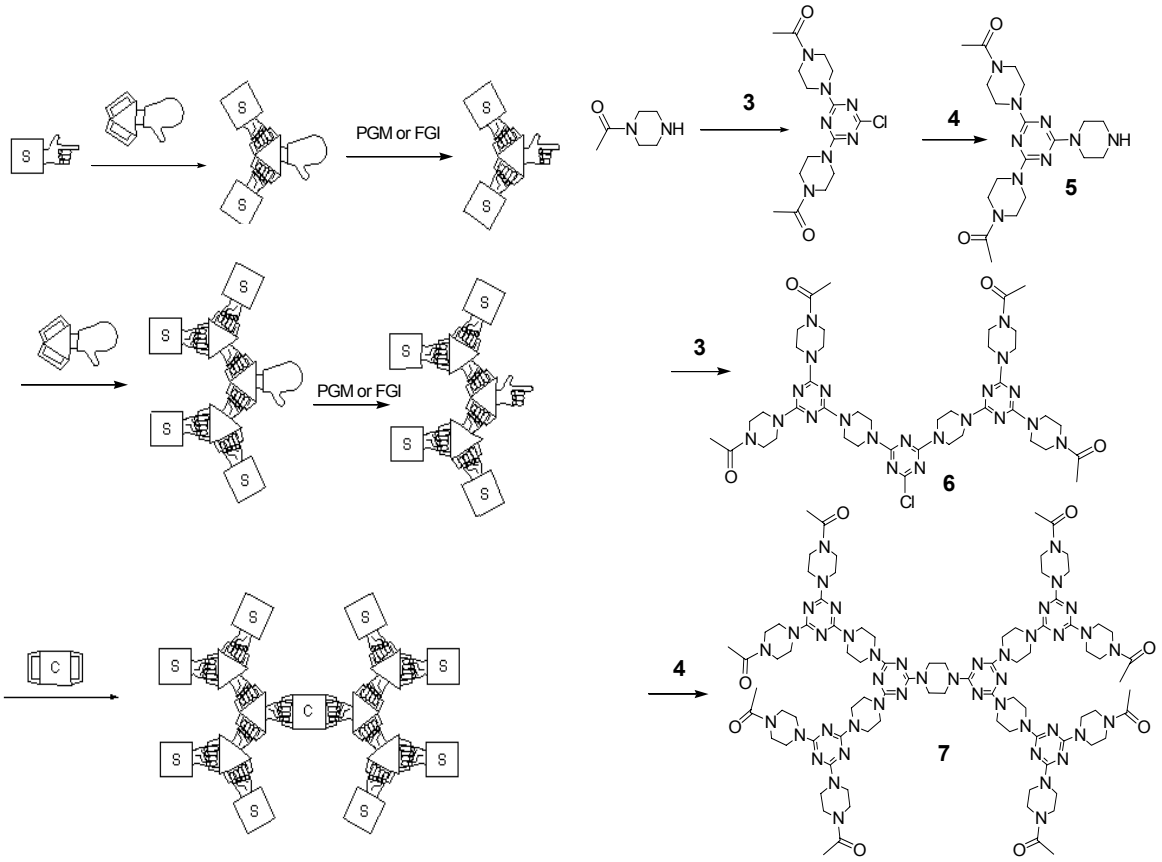
Both strategies are illustrated in Scheme 1.3, using a "mitten" as a protecting group (in this case BOC). In the absence of a “mitten", mixing the components in the appropriate ratio will lead only to trace amounts of the desired product. In fact, this is a common type of polymerization used to achieve materials like those illustrated in Scheme 1.2. Chemically, we can exemplify this process by the reaction of cyanuric chloride (**3**) with piperazine (**4**). This reaction forms large amounts of insoluble material. Instead of mixing the reactants directly, we can mask groups on one monomer, mix the components in a second step, and in a third step unmask the groups. Chemically, we can execute this by monoprotection of **4** with BOC-anhydride, followed by addition of cyanuric chloride, and acid deprotection (Scheme 1.3b).



Scheme 1.3

Convergent Approach. Two different approaches have been employed to synthesize dendrimers. The convergent approach developed, by Frechet,[16] is shown in Scheme 1.4. Synthesis begins with the surface groups, S. Branches are installed in an iterative fashion until the core is reached. That is, synthesis "converges" from the periphery to the core. This is illustrated chemically in Scheme 1.4 with the synthesis of a g2 melamine-based dendrimer. The surface acetylpiperidine groups are treated with cyanuric chloride before the interconversion of chlorine to an amine group by the addition of piperazine. The

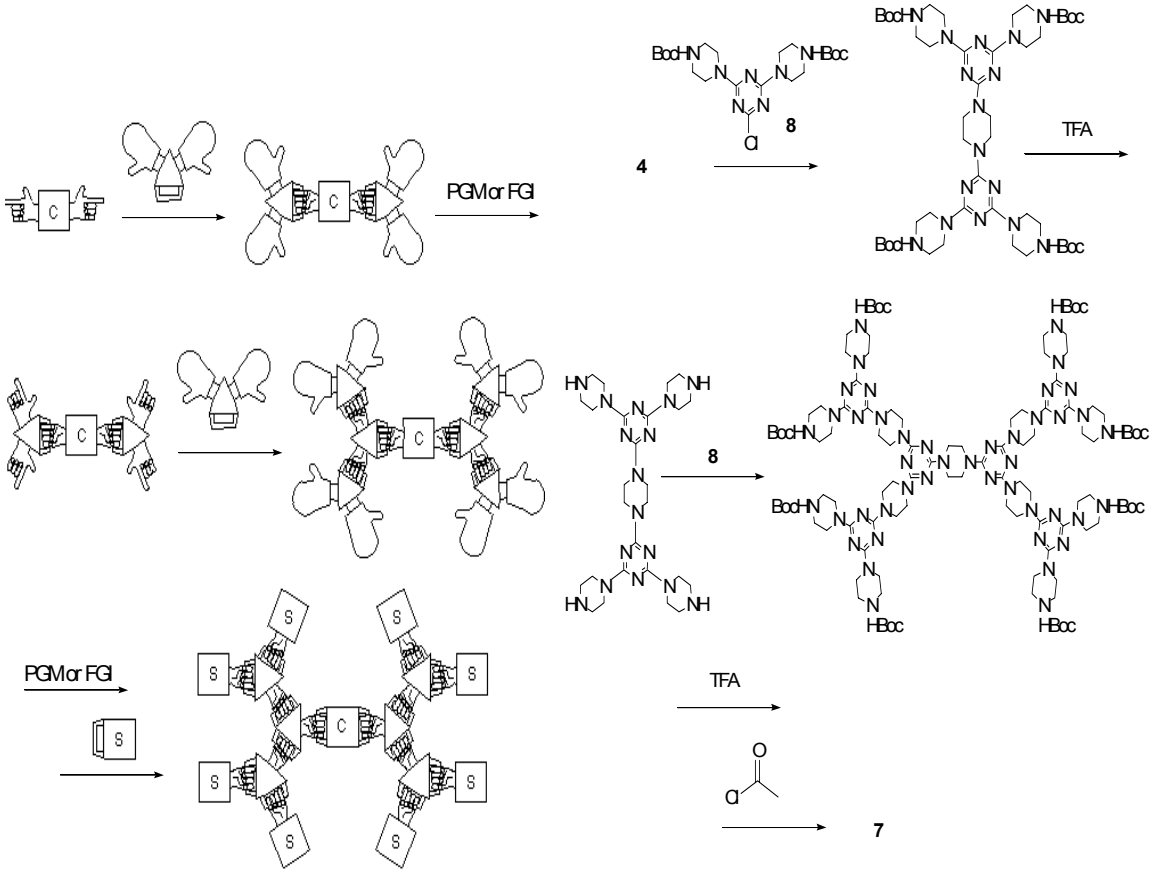
material is again reacted with cyanuric chloride to form a g2 dendron. This dendron is dimerized, by the addition of piperazine to form **7**.



Scheme 1.4

Divergent Approach. The second way is referred to as the divergent approach. Synthesis begins at the core, C, and branches are installed iteratively until the final step where the surface groups, S, are attached (Scheme 1.5).[17] That is to say, the synthesis "diverges" from the core to the periphery. This strategy is illustrated in Scheme 1.5. A monomer (**8**) unit (monochlorotriazine that has been previously protected with a BOC group) is dimerized with

pipererazine. This material is then deprotected with TFA, and the resulting material is again reacted with the same monomer unit **8**. This product is deprotected with TFA and acetyl chloride is added as a surface group.



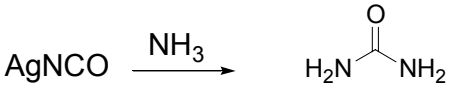
Scheme 1.5

The divergent approach to dendrimers was first reported by Vögtle and coworkers in the late 1970's.[18] He called these architectures cascade molecules, and to many, this was the beginning of dendrimer chemistry. The

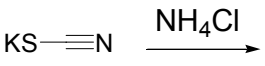
convergent approach was introduced by Frechet and coworkers in the early 1990's. Both strategies have advantages and disadvantagess. Covergent synthesis is usually more labor-intensive than the divergent approach, but at each stage only two molecules are required to react. In the divergent approach the numbers of molecules require to react increases by a factor of two at each generation. That is to say, for g0 to g1, 2^2 (4) molecules are needed to react. To go from g1 to g2, 2^3 (8) molecules are involved. The next generation, g3, 2^4 (16) molecules must react to form a perfectly branched molecule, and so on for higher generations. While this approach is usually easier to execute, the increased of numbers of reactions that must go to completion creates defects in the dendrimer structure due to incomplete reactions and/or crosslinking.

Melamine. Melamine, **2**, is an important molecule throughout this dissertation and is the basis for most of the chemistry presented here. It is the basic component we use to produce our dendrimers, and is very similar to molecules of environmental concern which will be presented later in this dissertation. Melamine is also commonly known as cyanuramide or triaminotriazine, and is a colorless, crystalline substance belonging to the family of heterocyclic organic compounds. Other, more systematic names given to melamine are 1,3,5-triazine-2,4,6-triamine, 2,4,6-triamino-1,3,5-triazine, and 2,4,6-triamino-*sym*-triazine. Melamine is used principally as a starting material for the manufacture of synthetic resins. The history of melamine is closely

connected with that of the first organic compound to be synthesized from inorganic starting materials. Urea was synthesized in 1828 by Friedrich Wöhler. Urea was found when Wöhler attempted to synthesized ammonium cyanate from silver cyanate by adding ammonia (Eq. 1.1), as a part of a study of cyanates which he had been carrying out for several years.

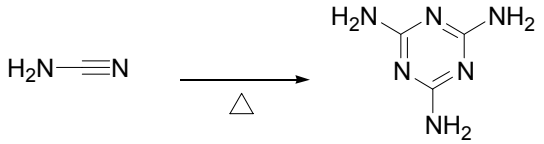


Eq. 1.1

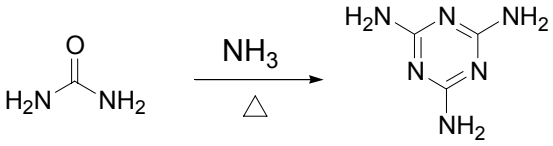


Melam **Eq. 1.2**

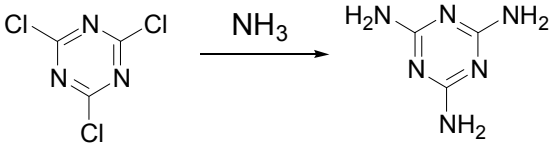
This event is attributed with the birth of organic chemistry. Within six years of this discovery, the German scientist Justus von Liebig first synthesized a compound by fusing potassium thiocyanate with twice its weight of ammonium chloride and called it melam)Eq. 1.2).[19] The compound synthesized was mostly melamine thiocyanate, with free melamine, and other byproducts. Improved synthetic techniques have been developed since Liebig's first reaction. They include heating of cyanamide (Eq. 1.3), heating of urea in the presence of ammonia (Eq. 1.4), and addition of ammonia to cyanuric chloride (Eq. 1.5), among a plethora of other syntheses.[20]



Eq. 1.3

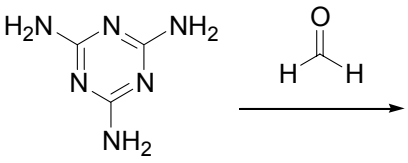


Eq. 1.4



Eq. 1.5

Cyanuric chloride and its chemistry will be discussed later in this dissertation. Almost 100 years have elapsed between Liebig's discovery in 1834 before a commercial process was developed. Melamine is primarily used for the production of melamine-formaldehyde resins (Eq. 1.6), which have much greater hardness and stain-resistance than urea-formaldehyde resins.



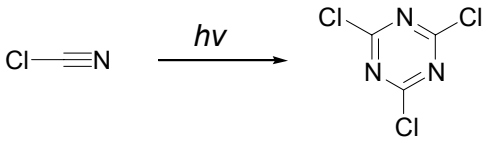
Melamine-formaldehyde resin **Eq.1. 6**

Melamine-Based Dendrimers. Dendrimers based on melamine were first reported by Zhang and Simanek in 2000.[21] The dendrimer was synthesized

using both convergent and divergent methods. It involved the use of *p*-aminobenzylamine as a linker molecule, and (4-amino-benzyl)-carbamic acid *tert*-butyl ester as the surface group. Shortly after the publication of this study, a group in Japan published the synthesis of a melamine-based dendrimer where 4-nitroaniline was used as the linker, followed by reduction of the nitro group to an amine.[22] Since then, a number of reports involving the syntheses, characterization, and applications of these macromolecules have been reported.[9,23-32] The starting point for all of the melamine-based chemistries described here is cyanuric chloride.

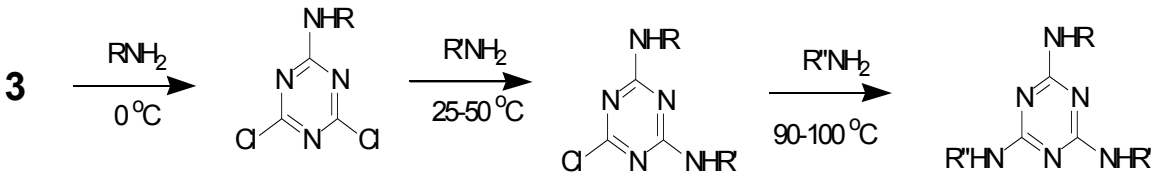
Cyanuric Chloride as a Building Block for Melamine-Based Dendrimers. Cyanuric chloride, **3**, is as old as organic synthesis. It has been known since the late 1820's, when it was considered by Liebig to be the trichloride of cyanogen. Serullas transformed cyanogen chloride (which is still the best source to prepare cyanuric chloride) into cyanuric chloride by the use of sunlight (Eq. 1.7). He assigned the resulting product to be an isomer of cyanogen chloride.[33] For some years there was confusion about the structure synthesized by Serullas, which was believed to be either cyanuric chloride or the trimer of cyanogen chloride. This trimer to monomer relationship was misunderstood for some time. By the time the infrared and ultraviolet spectra were published in 1947, there was little doubt about the structure of the

compound synthesized by Serullas. The spectra were consistent with the *s*-triazine structure that has *exo* chlorine atoms and first determined by Liebig.[34]



Eq. 1.7

Our interest in cyanuric chloride as a building block for dendrimer synthesis is based on two significant reaction properties that exhibits towards amines. First, cyanuric chloride reacts with primary amines, secondary amines, hydrazines, and related compounds in three steps. An oversimplified rule of thumb (Scheme 1.5), is that the first chlorine gets substituted at 0° C, the second at 25-50° C, and the last substitution occurs at 90-100° C.[35] This rule is usually true for unhindered primary amines. Constrained amines react at lower temperatures[36]. The choice of solvent, base, and concentration of reactants can also alter this rule.



Scheme 1.5

The second important reaction property is the difference in nuceophilicity of the amine to perform nucleophilic aromatic substitution of cyanuric chloride. This property can be used to generate control over the structure of the dendrimers as shown by Steffensen and Simanek.[28] As we can see from Figure 1.5, constrained cyclic amines react faster than primary amines, benzylic amines, anilines, alcohols or thiols.

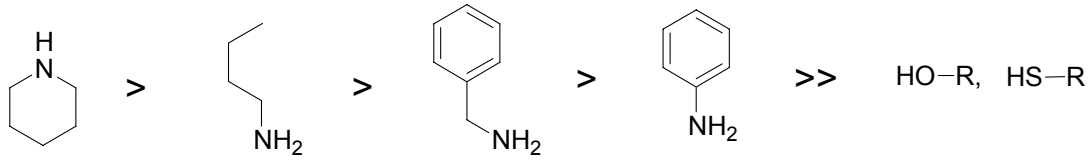
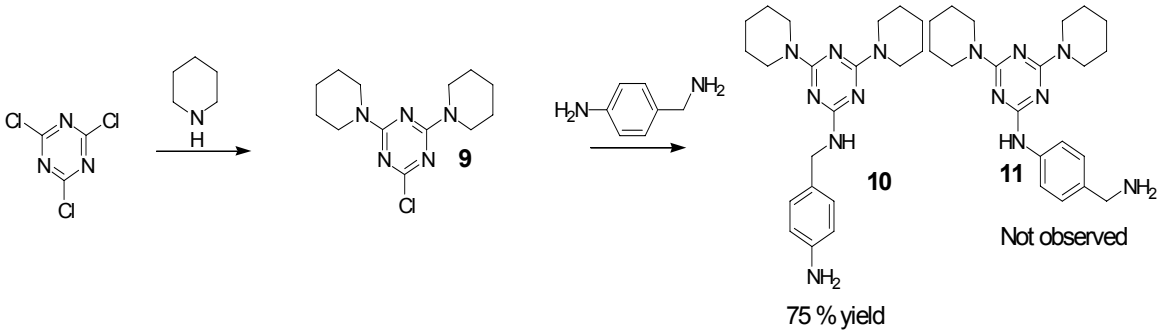


Figure 1.5. Difference in the nucleophilicity of several amines, alcohols, and thiols upon treatment with cyanuric chloride.

We have taken advantage of the differences in amine nucleophilicity when synthesizing our dendrimers. As illustrated in Scheme 1.6, we can take two equivalents of piperidine with one cyanuric chloride at room temperature to form the monochlorotriazine **9**. Molecule **9** selectively reacts with the benzylic amine of 4-aminomethylaniline to form compound **10**. Compound **11** was not formed in any detectable amounts.[9] By taking advantage of this property, we do not have to employ any protecting group methods for the aniline functionality. By using amines with different nucleophilicities, a number of steps in the synthesis of these macromolecules can be avoided.



Scheme 1.6

Gelation in Melamine-Based Dendrimers, a Structure-Activity Relationship in Macromolecules. In Chapter II, we will discuss gelation as a physical property that can be used to observe structure-activity relationships (SAR) in dendrimers. Examples of the use of gelation for SAR observations can be found in the literature.[37-41] There are also reports on SAR studies in dendrimers.[42-44] In Chapter II we will discuss the SAR of a small library of dendrimers and the structural changes that lead to, or preclude gelation. Melamine-based dendrimers offer many benefits over other dendritic structures, and can be used in SAR studies of macromolecules. The ease of synthesis, coupled with the plethora of amines that can be purchased or synthesized makes these molecules a good alternative over other dendrimers.

Dendrimers in Solid Supports. Chapter III will introduce the grafting of melamine-based dendrimers and dendritic structures onto solid inorganic supports. Reports of dendrimer-grafted solid supports are abundant in the

literature. Some of these supports include gold,[45-47] glass,[48,49] silica gel,[30,50] and clays.[31,51] Application of these hybrids include catalysis,[52,53] separation technologies,[30,54] and microarrays.[55,56] To carry out the grafting of these macromolecules, we decided to use hydroxyl rich surfaces, such as glass, silica gel, and alumina. This task is accomplished by activating the surface; first, with amine-terminated silane, and then with cyanuric chloride. We decided to use glass as a model system; first small organic molecules were installed and characterized to establish an effective protocol. The additions of dendrimers followed the model studies. Figure 1.6 shows a schematic representation of our method to immobilize small molecules and dendrimers onto hydroxy rich surfaces. A second model system was also tested on silica gel.

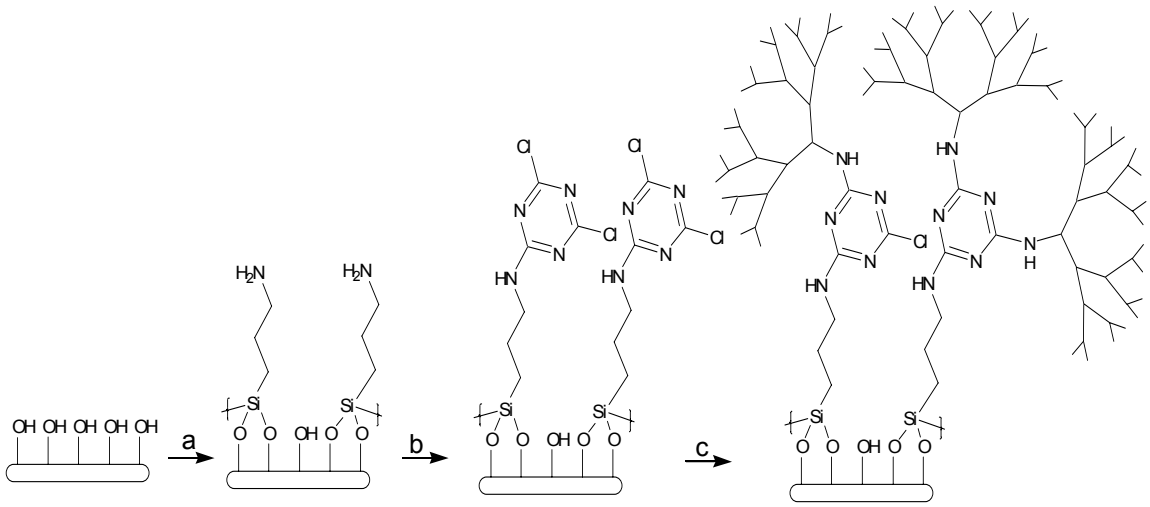


Figure 1.6. Schematic representation of our method to immobilize small molecules and dendrimers onto hydroxy rich surfaces. a) Treatment with aminopropyl-triethoxysilane (AMPS), b) treatment with cyanuric chloride, c) treatment with amine molecule.

Once we established a protocol for grafting on surfaces, we decided to move into materials that can be used in separation technologies. Silica gel is an excellent candidate for such a purpose. Silica gel is inexpensive, it has a hydroxyl rich surface, and it is one of the most common materials used in separations. We developed two strategies (Figure 1.7) for the grafting of these melamine-based macromolecules onto the inorganic support. We began with a commercially-available, amine-functionalized silica gel. Using the convergent approach, dendritic molecules were prepared in solution and then grafted onto the silica gel. Using the divergent approach, the molecules were grafted into the silica gel one monomer at a time. There are advantages and disadvantages to both strategies. The convergent approach is a more labor intensive synthesis than the divergent approach. These are more pronounced in purification steps. The convergent approach relies on recrystallization and column chromatography of most or all synthetic intermediates. The divergent approach relies on simple solvent washes. We presume that perfectly branched structures are formed when using the convergent approach, since the dendrimers were prepared before grafting. Due to incomplete reactions at the surface, the divergent approach creates more of a hyperbranched molecule than a dendrimer. By adding a new layer of amine at every other step of the synthesis in the divergent approach, more material is grafted by using this approach. The sequestration properties of these materials toward the removal of the herbicide atrazine were also tested.

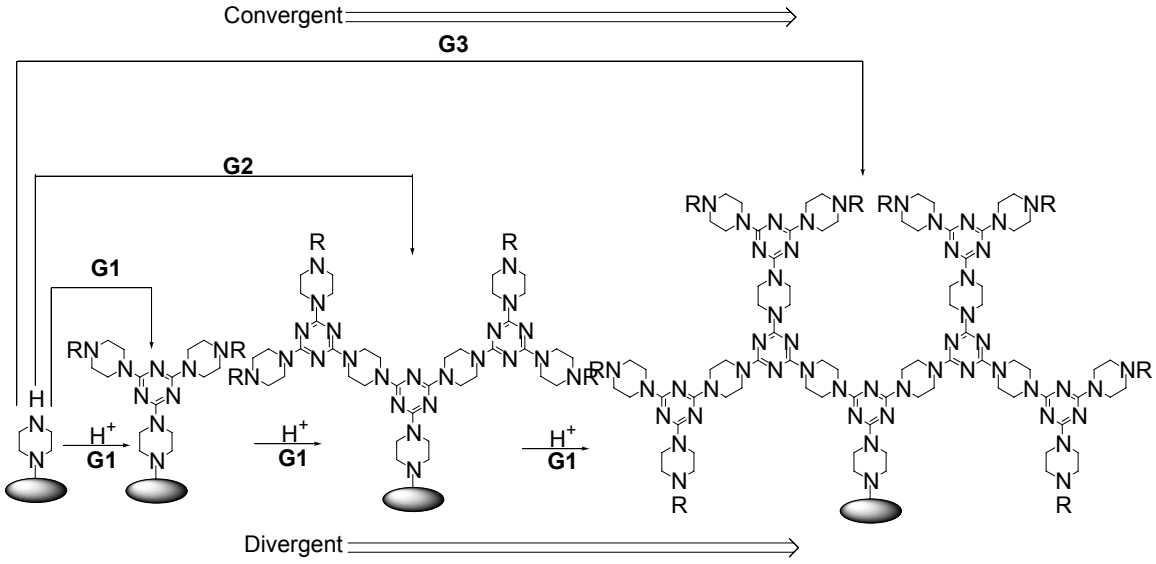
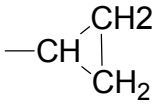
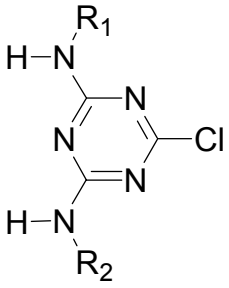


Figure 1.7. Schematic representation of both the convergent and divergent approaches of grafting dendritic molecules onto silica gel.

The Atrazine Problem. Atrazine is an *s*-triazine herbicide (Table 1.1), very similar in structure to melamine. Atrazine is the most important member of the family of herbicides based on monochlorotriazines. As a selective herbicide, atrazine inhibits photosynthesis in certain plants.[57] Atrazine is primarily used on corn for the selective control of broadleaf weeds, such as pigweed, cocklebur, and velvetleaf, and certain grass weeds. Annual atrazine sales average between 80-90 million pounds per year. According to recent water quality studies, atrazine is found 10 to 20 times more frequently than the next most detected pesticide.[58]

Table 1.1. Common monochloro-*s*-triazine herbicides with side groups labeled as R_1 and R_2, respectively.

Compound	R_1	R_2
Atrazine	—$CH(CH_3)_2$	—CH_2CH_3
Simazine	—CH_2CH_3	—CH_2CH_3
Cyanazine		—CH_2CH_3
Terbutylazine	—$C(CH_3)_3$	—CH_2CH_3
Eglinazine	—CH_2COOH	—CH_2CH_3
Proglinazine	—CH_2COOH	—$CH(CH_3)_2$
Propazine	—$CH(CH_3)_2$	—$CH(CH_3)_2$



High dose animal oral exposure showed adverse effects to the lungs, liver, kidney, spleen, adrenal glands, and the brain. The EPA has officially classified atrazine as possible human carcinogen (class C). In recent changes to the Safe Drinking Water Act, the "safe" concentration of atrazine has been set to 3 ppb. Atrazine concentrations in the Midwest are often as high as 33 ppb.[59] The best available technology for removal of herbicides is "granulated activated carbon" (GAC). Studies have shown that high doses of GAC are needed when atrazine concentrations exceed 15 ppb.[58] This treatment technology is somewhat efficient in places were atrazine concentrations are low, but the equipment needed for this treatment is expensive. Other techniques like ozone,

advanced oxidation, reverse osmosis, photocatalytic reactions,[60] and synthetic resins such as molecularly imprinted polymers show promise, but require additional study.[61] The necessity of an efficient system for the removal of atrazine from water is an on-going problem.

Alumina Membranes in Gas Separations. The grafting and use of alumina membranes are also investigated in Chapter III. Gas separations are important in the chemical industry.[62] Examples include the separation of oxygen from air, and the separation of volatile organics from effluent streams. The use of membranes for separations has gained attention over the past 20 years.[63]

Separations by porous membranes are controlled by permeability. Permeability results from solubility and diffusivity. While diffusivity is a function of particle size, solubility is a function of both structural and chemical composition. While most membrane separations are based on diffusivity, solubility is frequently preferred to separate hydrophobic particles from water. By adding melamine-based molecules to the pores of membranes, it is presumed that hydrophobic molecules such as propane will be absorbed on the membranes on basis of solubility, rather than at the hydrophilic nitrogen. In other words, we will have a higher selectivity of propane over nitrogen. As we can see from Figure 1.8, the modified membrane can act as both a size exclusion membrane (diffusion) as well as a structure-exclusion membrane (solubility) for maximum permeability. Membranes are advantageous over filters

because the unwanted materials are removed into a separate compartment where they can be removed and destroyed.

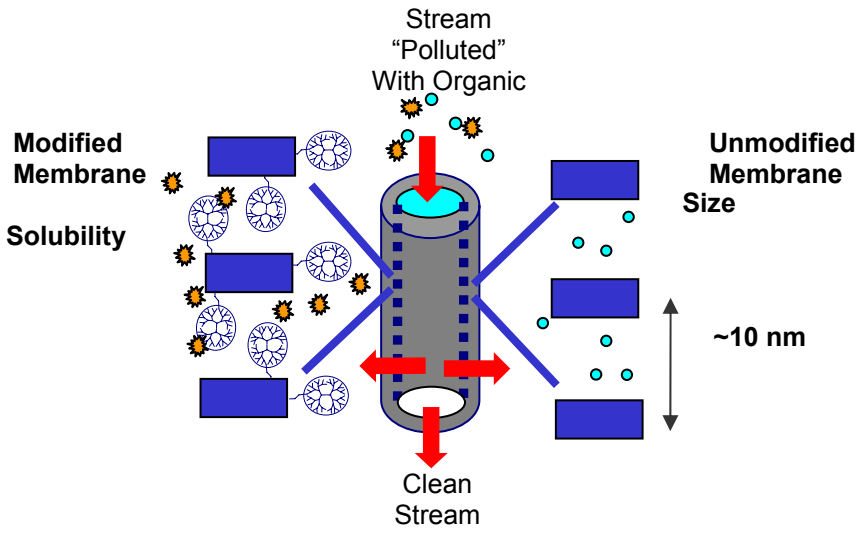


Figure 1.8. Schematic representation of melamine-based molecules coated membranes for separations based on selective solubility.

Thermoresponsive Polymers in Phase Separation. In our efforts to find a separation technology, we decided to investigate a class of linear polymers that shows solubility that is inversely temperature dependent (Figure 1.9). While we have used insoluble inorganic supports to accomplish separations, it is ironic that the property that makes them an excellent technique in separation will also be their greatest drawback. The fact that these particles are insoluble creates problems in characterization, incomplete reactions, and more importantly concentration of reagents. Usually longer times and more

intense mechanical agitation are needed to make the reagents in solution react with or approach those grafted on the surface of a particle. A latent solid phase separation strategy offers the advantages of separation of insoluble supports coupled with the efficiency of soluble reagents. There are a number of ways of inducing a latent solid phase, including salt addition,[64,65] change in pH,[66,67] addition of solvent,[68,69] and change of temperature[70,71] Polymers of *iso*propylacrylamide can precipitate by any of the methods discussed. The point at which this precipitation/dissolution property takes place is known as a lower critical solution temperature (LCST). For a homopolymer of *iso*propylacrylamide the LCST is 32 °C.

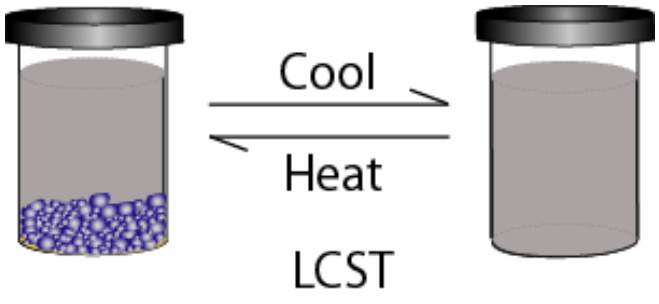


Figure 1.9. Inverse temperature dependent solubility, the polymer has a LCST at which it precipitates if the temperature is increased or dissolves if temperature is decreased.

The use of soluble thermoresponsive polymers to sequester or scavenge hydrophobic guest molecules from dilute aqueous solutions upon heating is described in Chapter IV. In these studies, a homopolymer of *N-iso*propylacrylamide and a copolymer of poly(*N-iso*propylacrylamide)-co-poly(*N*-4-(acrylamidomethyl)piperidine) were used. The sequestration properties of these materials for the herbicide atrazine were investigated. In addition two dye-labeled monochlorotriazine guests were synthesized. In one case, an atrazine analog was designed so as to contain a dansyl group for fluorescence analysis. In the second case, an atrazine analog was labeled with a methyl red group to facilitate visual and spectrophotometric analysis. The homopolymer has no active sites for covalent attachment, and is presumed to performed nonconvalent sequestration of the hydrophobic guest. The copolymer has reactive piperidine groups, and presumably, will scavenge triazines from solution by covalent bond formation. This is accomplished by nucleophilic aromatic substitution of the chlorine of the monochlorotriazines by the piperidine nucleophile on the copolymer.

Conclusion. This dissertation ends with a summary and conclusion of the chemistries presented in the previous chapters. It will draw parallels with the evolution of dendrimer chemistry. It will open a discussion on the work done and the work that can still be done to transform some of these early results into working technologies.

CHAPTER II

SYNTHESIS AND STRUCTURE-ACTIVITY RELATIONSHIPS OF A DENDRIMER BASED ON TRIAZINES COMPARED AGAINST A SMALL LIBRARY OF SIMILAR DENDRIMERS: GELATION DEPENDS ON CHOICE OF LINKING AND SURFACE GROUPS *

Structure-Activity Relationships of Melamine Dendrimers. During our investigations of the synthesis, characterization, and properties of melamine based dendrimers,[21,24,25] we became aware of the ability of some of these molecules to form gels at low concentration in acidic chloroform.[9] Then, we determined that molecules **1** and **2** (Scheme 2.1) form gels in organic solvents such as chloroform, dichromethane, and benzene at concentrations as low as 2 mM. The ease of synthesis and the abundance of commercially available and synthetically accessible amines, which can be used as surface and linking groups,[28] provides an opportunity to investigate a small library of macromolecules to probe the molecular basis for gelation.

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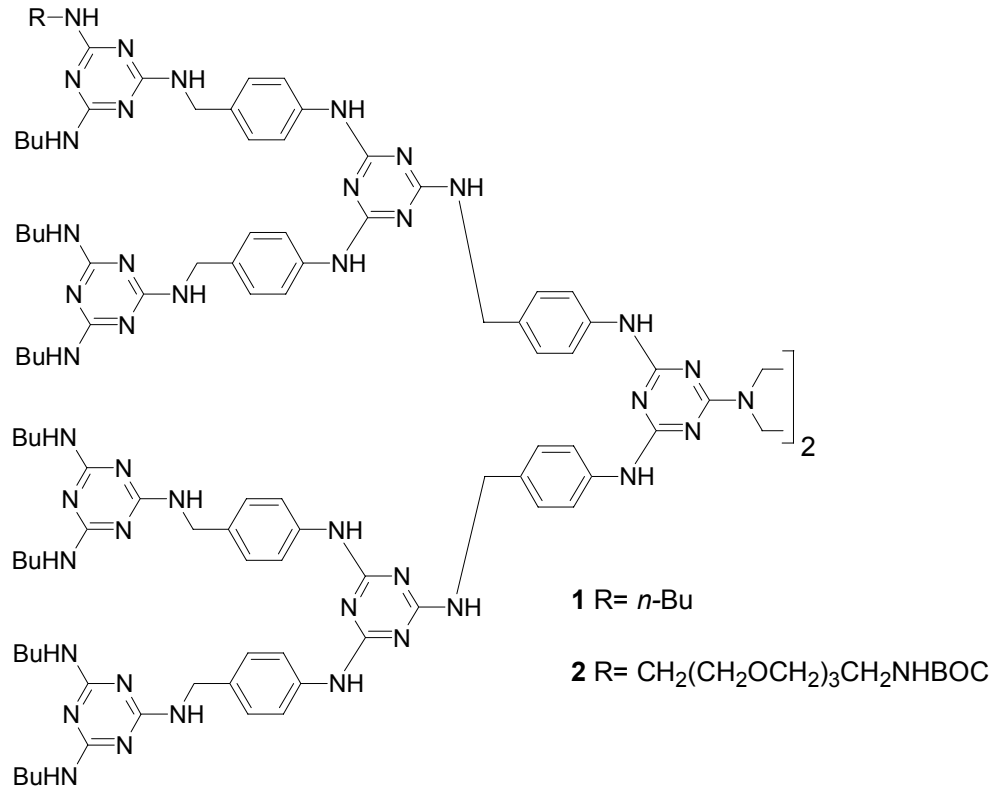


Scheme 2.1

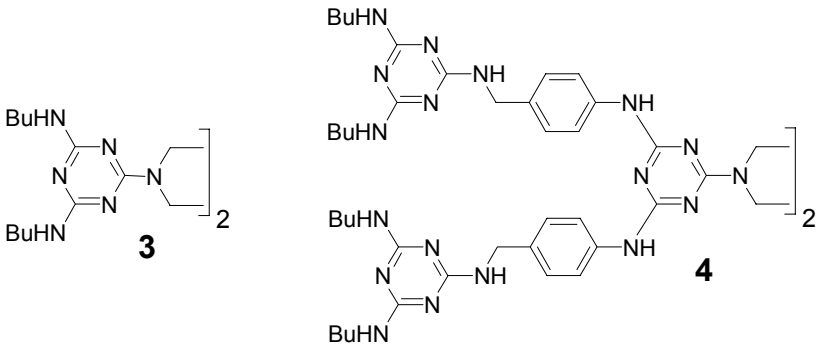
The number of reports of branched macromolecules that form a gel is very limited. An organogel molecule that incorporates a first-generation dendritic building block into a three domain molecule was reported by Stupp and co-workers.[72] A gel of dipeptides functionalized with poly(benzyl ether) dendrons has also been reported.[73] Newkome and Jorgensen have synthesize *bis*-arborols which are described as "dumbell" shaped, second generation dendrimers which form columnar fibers.[74,75] Phosphazine dendrimers that gel aqueous solutions have also been described.[76] The rate of gelation is increased in the presence of various small molecules. Gelation of poly(lysine) dendrimers

in the presence of aliphatic diamines is also known.[77] It is worth noting that Shirai and Shinkai have reported a two-component, melamine-based system with complementary hydrogen-bonds that gels.[78]

Hydrogen-Bonding of Melamine-Based Dendrimers. Both molecule **1** and **2** have an abundance of hydrogen-bond donors and acceptors. In order to assess the contribution that hydrogen-bonds might have on formation of gels in melamine-based dendrimers, a library of molecules was prepared. The library varied in size, the choice of internal linking groups and the choice of surface groups. The triazine dendrimers investigated here are prepared from two components: a triazine core from which branches radiate and diamine branches. We have chosen diamines which once incorporated into the macromolecule can have or lack the ability to donate hydrogen for hydrogen bonding. In the literature, there are numerous examples of the role that hydrogen bonding plays in the formation of low molecular weight organogels.[78-87]

One of the many advantages of using dendrimers as models in structure-activity relationships studies is the dendritic effect. The dendritic effect is often definied as the generation-dependent differences in physical and chemical behavior of dendrimers. Numerous studies have researched this phenomenon; they include solubility studies,[7] exchange and release studies,[23,88,89] catalysis,[90,91] molecular recognition of small molecules,[92,93] molecular recognition of transition metals,[24,94] and other applications[6,8] such as molecular

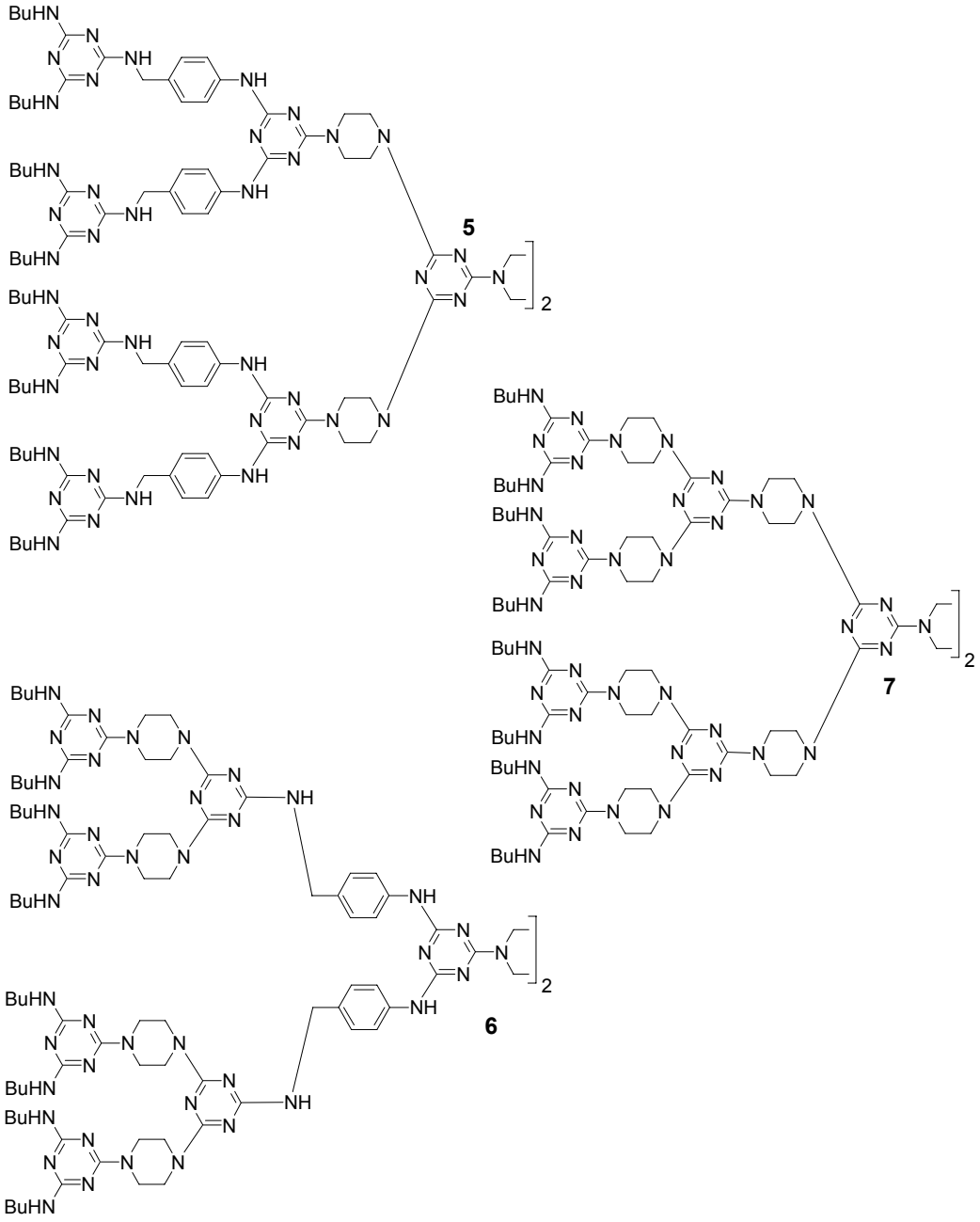
antennas and scavengers of small organic molecules. The difference in behavior of these macromolecules is presumed to be in direct correlation with the overall molecular shape, or conformation.[2] Our curiosity of the effect that size has in the gelation of melamine-based dendrimers led to the synthesis of molecules **3** and **4** (Scheme 2.2). Molecule **3** is a generation 1 dendrimer, while molecule **4** is a generation 2 dendrimer.



Scheme 2.2

The difference between molecules **1** and **2** and molecules **5** to **7** (Scheme 2.3) is the choice of the diamine linking group. Once *p*-aminobenzylamine (PABA) is incorporated in the dendrimer, it contains both hydrogen-bond donors and acceptors. Alternatively, piperazine has only secondary amines. After piperazine is used as linking group, it lost its ability to be a hydrogen-bond donor. In dendrimer **5**, the inner layer (closest to the core) of the PABA linking groups were replaced with piperazine. In molecule **6** the outer (closest to the

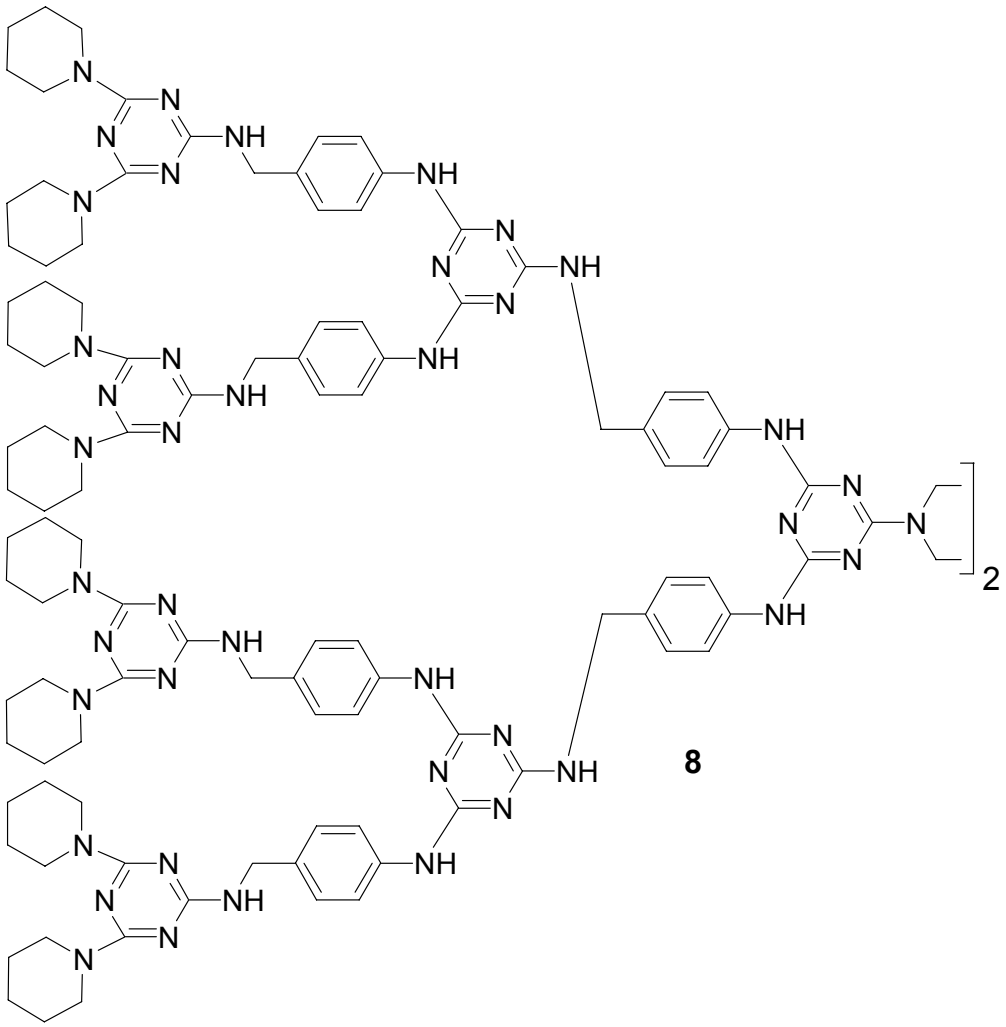
surface) layer of linking groups was modified from *p*-aminobenzylamine to piperazine. In molecule **7**, both layers were modified to piperazine.



Scheme 2.3

As mentioned previously, the chemical literature is rich with examples of dendritric (size) effects, but reports on the how composition affects the physical and chemical properties are scarce.[95,96] These seven molecules show that the size and choice of linking groups have an effect on the gelation properties. The recognized importance of hydrogen-bonding networks in gel formation is well recognized.[97,98]

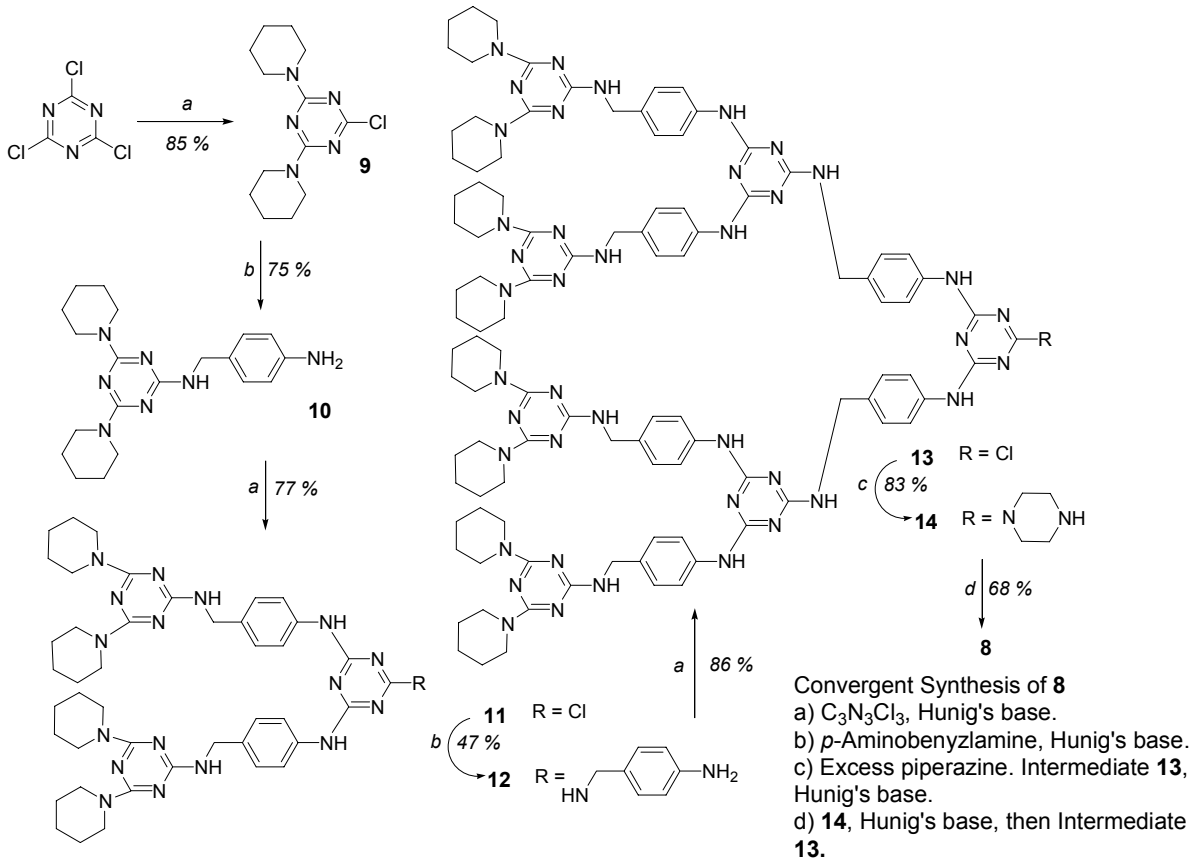
To help corroborate the structure-activity trend it was fundamental to design and synthesize a molecule that lacked hydrogen-bond donors on the surface. The same strategy of using secondary cyclic amines to install chemical groups that lack hydrogen-bond donors was used. Scheme 2.4 shows molecule **8**, a generation 3 dendrimer that is rich is hydrogen-bond donors in its interior (linking branches), however its exterior (surface groups) has no hydrogen-bond donors. As shown in Scheme 2.4, in this dendrimer, the *n*-butylamine surface groups of **1** and **2** were replaced by the secondary cyclic amine, piperidine. Here, we report a detailed synthesis of molecule **8**. We also describe the gelation properties of molecules **1** to **8**. It is our objective to establish that triazine-based dendrimers are readily amenable for structure-activity investigations based on inherent characteristics of their chemistry.



Scheme 2.4

Synthesis. The final target, **8**, was prepared in seven linear steps with an unoptimized, overall yield of 12% and a purity of 97% (Scheme 2.5). The synthesis proceeded from the surface to the core, using the convergent approach. From our experience the convergent approach remains the best strategy for the preparation of melamine-based dendrimers. Throughout the

syntheses of these architectures, the reactions can be monitored readily by thin-layer chromatography; most reactions proceed spot-to-spot. We began the synthesis with the addition of two equivalents of piperidine to one equivalent of cyanuric chloride to create the surface groups. These surface groups were then transformed to reactive amine branching units by the addition of a diamine linker. In case of dendrimer **8,** the benzylic amine functionality of the *p*-aminobenzylamine reacted almost exclusively with the triazine under the conditions used.[21,28] After functional group interconversion to form intermediate **10,** this amine was treated with half an equivalent of cyanuric chloride to form the monochlorotriazine **11**. Intermediate **11** was treated with an excess of *p*-aminobenzylamine to provide **12**. This amine functionalized dendron was added to cyanuric chloride to yield intermediate **13**. The dimerization of this dendron was accomplished by functionalizing **13** with an excess of the piperazine to form intermediate **14**. This amine was reacted with **13** to generate dendrimer **8**.



Convergent Synthesis of **8**
a) $C_3N_3Cl_3$, Hunig's base.
b) *p*-Aminobenyzlamine, Hunig's base.
c) Excess piperazine. Intermediate **13**, Hunig's base.
d) **14**, Hunig's base, then Intermediate **13.**

Scheme 2.5

Gelation. Gelation of dendrimer **1** was first observed when solutions were prepared in $CDCl_3$ for NMR analysis. Further investigations showed that at concentrations as low as 2 mM of **1**, a transparent gel was obtained within minutes. This gel is stable to temperatures exceeding 70 °C. We have observed that larger generation dendrons (third or greater) based on *p*-aminobenzylamine aggregate. This aggregation takes place through the formation of networks of

hydrogen bonds between the nitrogen atoms of the triazine and the melamine N*H* group.[24] When we attended to repeat the gelation experiment using stock chloroform, it was discovered that the solution failed to form a gel. We discovered that the presence of acid was important for a gelation event. $CDCl_3$ showed acid content on performing an acidity test.[99] Dendrimer **1** gelled when gaseous HCl was added to anhydrous $CHCl_3$ that had no EtOH added as a stabilizing agent. Neutral organic solvents did not provide gels. Characterization by NMR spectroscopy and MS spectrometry of **1** before gelation and of recovered material after gelation showed no noticeable change.

In our investigations of the gelation phenomenon, the importance of hydrogen bonding was corroborated with the observation that addition of as little as 1% EtOH to solutions of deuterated acidic chloroform prevented the gelation from occurring. Other solvents that may be involved in hydrogen-bonding such methanol, 2-propanol, and DMSO also did not result in the formation of a gel to concentrations just below the solubility limit of **1**.

From our investigations we determined that three factors influence gelation of melamine-based dendrimers. First, the pH dependence of gelation is important yet not unique.[100,101] Second, gelation with smaller generation dendrimers **3**, **4** did not occur using the same protocol of acidifying organic solvents. Dendrimer **3** formed a precipitate upon standing, while **4** form a turbid solution in acidic chloroform. Thirdly, and most significantly, small changes in composition of these macromolecules greatly affected gelation.

Higher concentrations of dendrimer were needed for gelation when the hydrogen bond donating groups of *p*-aminobenzylamine were replaced with piperazines at different layers in the dendrimer. That is to say, molecule **5,** where the inside linker groups are piperazines, failed to produce a gel at 2 mM in acidic chloroform. The same trend was observed for **6**, where the outside linking groups are piperazines. Once incorporated into a macromolecule the piperazine group lacks hydrogen bond donors. Accordingly, solutions of **5** and **6** must have higher concentrations than solutions of **1** and **2** (about a factor of 15) in order to form a gel. Molecule **7** has no *p*-aminobenzylamine group, therefore does not gel.

After establishing the importance of size and the composition of the interior of the dendrimers with respect to gelation, we examined the importance of surface groups. We replaced the surface butylamines with piperidine groups to obtain **8**. Under the gelation conditions outlined above, molecule **8** fails to produce a gel to its limit of solubility of 100 mM in the range of organic solvents used in the gelation protocol.

In order to further comprehend the gelation phenomenon, we sought evidence of aggregation. Transmission electron micrographs (TEM) of gels of **1** were obtained after exposure of the gel-coated EM grids to vapors of OsO_4. These micrographs revealed the typical network morphology, with fiber dimensions of approximately 50 nm (Figure 2.1). No fine structure in these

fibrils could be seen, precluding us from proposing a model for structure of the gel.

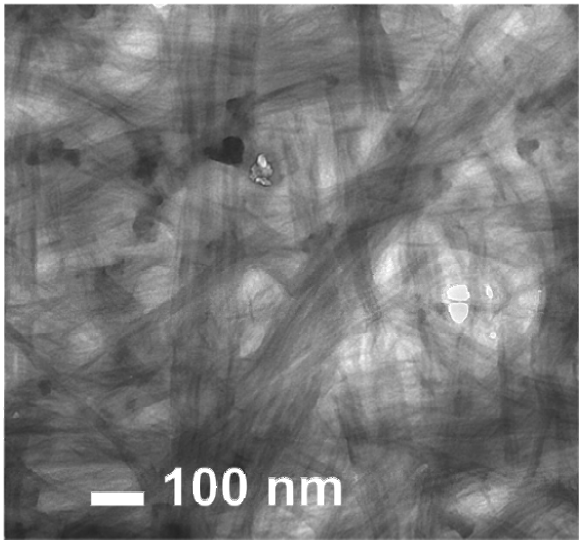


Figure 2.1. TEM image of the gel. The scale bar represents 100 nm.

Other techniques failed to provide evidence of aggregation. The IR spectra of **1** in neutral and acidified chloroform showed no difference. Light-scattering experiments at a lower concentration than that needed to form gels could not be execute. No reliable data could be produced due to the turbidity of solutions of **1** at the concentrations needed for light-scattering analysis. Gas-phase computational models of **1, 2, 7,** and **8** did not show dramatic differences in the shapes and sizes of these molecules (Figure 2.2). Globular structures resulted for all targets due to low energetic barriers between piperazine conformers.

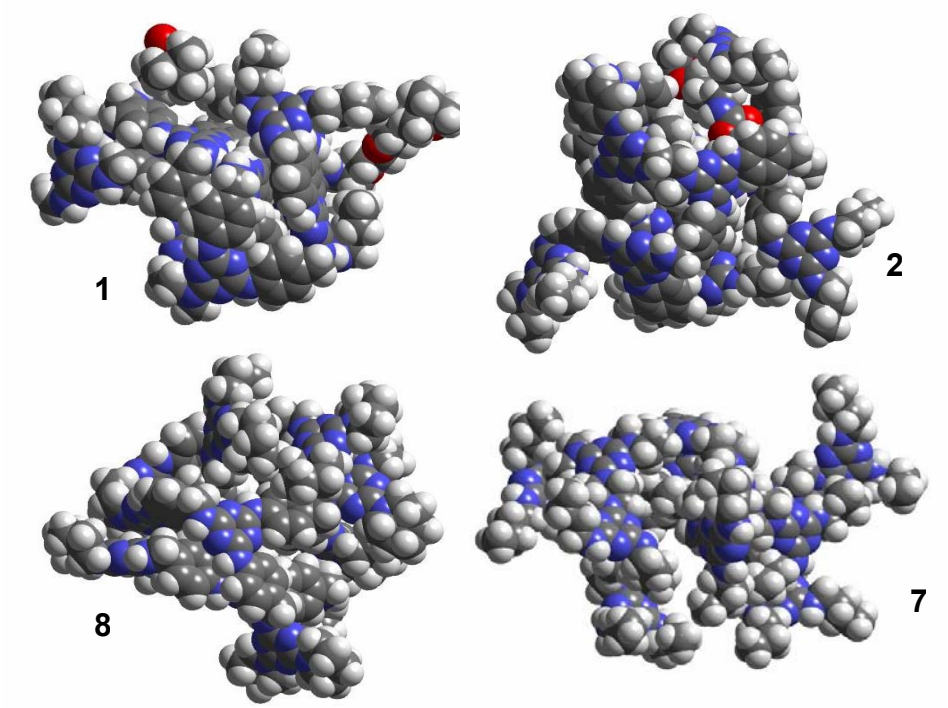


Figure 2.2. Computational models of **1**, **2**, **7**, and **8** beginning in the upper left corner moving clockwise.

Gel permeation chromatography (GPC) of all the molecules provided interesting data (Figure 2.3). When the samples are prepared in acidified *versus* neutral chloroform (the GPC mobile phase is THF), the retention time for dendrimers that form gels is significantly different. Acidified samples elute before the neutral sample. In GPC this observation is consistent with a higher molecular weight species in solution. As would be expected, this trend is most pronounced in molecules **1** and **2**, which form gels at the lowest concentrations.[102] Smaller differences in retention times are seen when

dendrimers **5** and **6** are injected into the GPC. We attribute these differences in retention times to the higher concentrations that are required of molecules **5** and **6** to form gels. There was a small difference in the retention times of the smaller generation molecules **3** and **4**. As for dendrimers **7** and **8**, which did not form gels up to 100 mM, the peaks elute at very similar times.

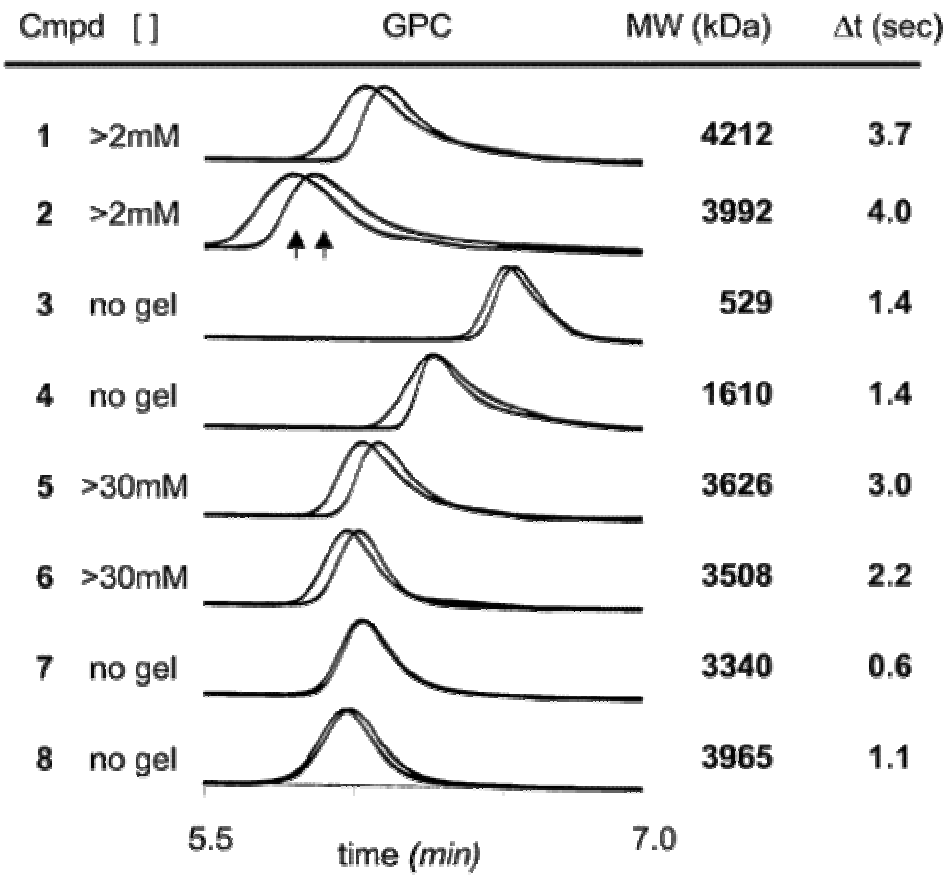


Figure 2.3 Concentrations required for the gelation of dendrimers **1**-**8**; an overlay of the GPC traces of the dendrimers derived from acidified and neutral chloroform (toluene standard); their molecular weights from mass spectrometry; and the difference in retention time (indicated with arrows for **2**) when constituted in acidified *versus* neutral solvents.[102] The acidified sample always eluted before the neutral sample.

Conclusion. The synthesis of dendrimer **8** was accomplished using a convergent approach. The gelation properties of this molecule were compared to a small library of compounds (**1**-**7**). It was established from this research that melamine-based dendrimers offer the opportunity to execute structure-activity studies by changing the diamine component and the surface amine component of this two-component dendrimer system. While we report gelation, we suggest that these architectures are an excellent scaffold for phenomonological inquiries in a range of areas. We have shown that we can have same kind of influence concerning the range of concentrations at which these molecules gel and can stop the gelation event entirely. We have shown the pH dependence of gelation. This phenomenon is due to the protonated state, which has been attributed to hydrogen bonding or ionic interactions,[101] or a destabilizing electrostatic repulsion that precludes gelation.[100] The acidic conditions required for gelation of the macromolecules do not significantly affect the structure of the molecule. In fact, the noticeable change, other than gelation, is the aggregation suggested by gel permeation chromatography.

Materials. All reagents and solvents were obtained from commercial sources and used without further purification unless specified. ^{1}H NMR spectra were obtained on Varian Inova 300, Mercury 300, or Inova 500 spectrometers at 300 or 500 MHz. ^{13}C NMR spectra were obtained on Varian Inova 300, Mercury 300, or Inova 500 spectrometers at 75 or 125 MHz. ^{1}H and ^{13}C chemical shifts

are reported in ppm referenced to tetramethylsilane or residual solvent peaks, respectively.

MALDI Mass Spectrometry. Dry drop preparation was performed with 2,4,6-trihydroxyacetophenone (THAP) as a matrix. A 1:1 overlayer mixture of 1 μM aqueous analyte and 10 mg/mL THAP matrix in methanol was spotted in 1 μL aliquots on a Teflon coated plate. MALDI-TOF mass spectra were acquired in positive ion mode on a Voyager-DE STR mass spectrometer (Applied Biosystems, Framingham, MA), equipped with a pulsed nitrogen laser emitting at 337 nm. Samples were analyzed in linear mode using a delayed extraction time of ~500 ns and an accelerating voltage of 20 kV. Laser strength was adjusted to provide optimal signal-to-noise ratio. All spectra were recorded as an average of 50-100 laser shots.

Gel Permeation Chromatography. Traces were obtained on a Waters 600 chromatograph system at room temperature by monitoring at λ= 254 nm with a Waters 2487 dual absorbance detector using a Waters Styragel HR 5E column (MW range 10^3-10^6). THF was used as the carrier solvent at a flow rate of 0.6 mL/min. All dendrimers were analyzed at 0.06 mM using an injection volume of 10 μL.

TEM Imaging. A portion of gel was smeared across a TEM grid and then placed in a sealed chamber with an open vessel containing aqueous OsO_4 overnight. The grids were examined using a Ziess 10C instrument (80 kV).

Dendrimer 8. Intermediate **13** (15 mg, 0.008 mmol) was dissolved in 1.5 mL of THF, and *N,N*-diisopropylethylamine (0.25 mL, 1.4 mmol) was added to the reaction mixture. Intermediate **14** (15 mg, 0.008 mmol) was added, and the reaction was stirred for 24 h at 80 °C. After removal of the solvent, column chromatography (40:1 DCM:MeOH) provided a white solid (68%). ^{1}H NMR (DMSO-d_6) δ 1.49-1.87 (br, 96H), 3.59 (br, 64H), 3.77 (br, 8H), 4.30 (br, 16H), 4.43 (br, 8H), 7.19 (br, 24H), 7.64 (br, 24H). ^{13}C NMR (DMSO-d_6) δ 25.02, 26.01, 43.86, 44.21, 79.18, 79.63, 120.43, 134.56, 128.15, 139.36, 164.71, 166.40. MS (ESI): calcd, for $C_{210}H_{264}N_{84}$: 3964.91; found 3965.34 $(M + H)^+$.

Intermediate 9. Cyanuric chloride (2.00 g, 10.87 mmol) was dissolved in 100 mL of THF. The solution was cooled in an ice/water bath. Two equivalents of *N,N*-diisopropylethylamine (2.81g, 21.73 mmol) were added to the cooled solution. Piperidine (1.87 g, 21.73 mmol) was dissolved in 15 mL of the THF and added dropwise (over 1 h) to the cooled solution of cyanuric chloride. After the reaction mixture was stirred at room temperature for 24 h, the precipitate was removed by filtration, and the solvent was evaporated under reduced pressure. The crude product was dissolved in 150 mL of CH_2Cl_2 and extracted

twice with 100 mL of water, once with 100 mL of saturated sodium bicarbonate and once with 100 mL of brine. The solute was dried over sodium sulfate. The sodium sulfate was removed by filtration and the solvent was removed under reduced pressure. Recrystallization from 150 mL of ethanol yielded a white solid (85%). Mp: 117-119 °C. ^{1}H NMR ($CDCl_3$) δ 1.52-1.67 (m, 12 H), 3.71 (t, *J* = 5 Hz, 8H). ^{13}C NMR ($CDCl_3$) δ 25.03, 26.05, 44.76, 164.22, 169.57. MS (ESI) calcd for $C_{13}H_{20}ClN_5$: 281.78; found 282.14 $(M + H)^+$.

Intermediate 10. Intermediate **9** (2.00 g, 7.10 mmol) was dissolved in 100 mL of THF, and 4-aminobenzylamine (3.47 g, 28.4 mmol) was added. The solution was stirred at 80 °C for 12 h. Upon cooling, the precipitate was removed by filtration and the solvent was evaporated. Column chromatography (9:1 DCM:MeOH) provided a yellow solid (75%). Mp: 120-123 °C. ^{1}H NMR ($CDCl_3$) δ 1.55-1.64 (m, 12 H), 3.71 (br, 8H), 4.45 (d, *J* = 5.7 Hz, 2H), 6.61 (d, *J* = 8.4 Hz, 2H), 7.71 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR ($CDCl_3$) δ 25.41, 26.21, 44.36, 44.75, 1115.26, 129.24, 130.11, 145.50, 165.26, 166.48. MS (ESI) calcd, for $C_{20}H_{29}N_7$: 367.49; found 368.24 $(M + H)^+$.

Intermediate 11. Cyanuric chloride (0.405 g, 2.20 mmol) was dissolved in 20 mL of THF. The solution was cooled in an ice bath. Two equivalents of *N,N*-diisopropylethylamine (0.57 g, 4.40 mmol) were added to the cooled solution. Intermediate **10** (1.85 g, 5.03 mmol) was added to the reaction

mixture. The reaction was warmed to room temperature and stirred for 16 h. The solvent was evaporated under pressure. The crude product was washed three times with 150 mL portions of saturated sodium bicarbonate. The mixture was dissolved in about 35 ml of hot THF, and 1 g of silica gel was added. The solvent was removed under reduced pressure. The silica was loaded onto a column. After column chromatography (9:1 DCM:MeOH), a yellow solid was recovered (77 %). ^{1}H NMR ($CDCl_3$) δ 1.44-1.74 (m, 24 H), 3.69-3.77 (m, 16H), 4.56-4.58 (b, 4H), 7.23-7.42 (m, 8H); ^{13}C NMR ($CDCl_3$) δ 25.35, 26.10, 26.18, 44.39, 121.75, 128.43, 136.18, 137.19, 163.85, 165.15, 166.45. MS (ESI) calcd. for $C_{43}H_{56}N_{17}Cl$: 846.47; found 846.47 $(M + H)^+$.

Intermediate 12. Intermediate **11** (1.3 g, 1.54 mmol) was dissolved in 100 mL of THF. To the solution, five equivalents of 4-aminobenzylamine (0.75 g, 6.14 mmol) was added. The solution was heated to 80 °C and it was stirred for 12 h. The solvent was evaporated under reduced pressure. The solid recovered was dissolved in ~ 25 mL of THF, and 1 g of silica gel was added. The solvent was removed under reduced pressure. After column chromatography (9:1 DCM:MeOH), a solid was recovered (47 %). ^{1}H NMR ($CDCl_3$) δ 1.44-1.91 (m, 24H), 3.71-3.77 (b, 16H), 4.43-4.49 (m, 6H), 6.56 (d, *J* = 0.028 ppm, 2H), 7.06-7.31 (b, 10H); ^{13}C NMR ($CDCl_3$) δ 25.38, 25.99, 26.20, 44.37, 44.85, 115.39, 120.38, 120.79, 128.35, 128.86, 128.96, 134.38, 137.95,

145.79, 165.22, 166.51. MS (ESI) calcd. for $C_{50}H_{65}N_{19}$: 932.18; found 932.57 $(M + H)^+$.

Intermediate 13. Cyanuric chloride (1.74 g, 9.46 mmol) was dissolved in 30 mL of THF to make a 0.32 M solution. From this solution, 0.75 mL (0.24 mmol of cyanuric chloride) was drawn out and placed in a round bottom flask. After addition of 2 mL of THF, *N,N'*-diisopropylethylamine (0.1 g, 0.77 mmol) was added. Intermediate **12** (0.44 g, 0.47 mmol) was added to the reaction mixture, and the reaction was stirred for 24 h. The solvent was removed under reduced pressure. After column chromatography (40:1 DCM:MeOH), a white solid was recovered (86 %). ^{1}H NMR ($CDCl_3$) δ 1.50-1.88 (b, 48H), 3.73 (b, 32H), 4.44 (b, 12H), 7.12-7.32 (b, 24H); ^{13}C NMR (DMSO) δ 25.02, 26.008, 43.86, 44.22, 120.65, 128.19, 134.62, 139.39, 140.21, 164.65, 164.82. MS (MALDI), calcd. for $C_{103}H_{128}ClN_{41}$ 1975.10; found 1976.01 $(M + H)^+$.

Intermediate 14. Intermediate **13** (20 mg, 0.010 mmol) was dissolved in 3 mL of THF. To this solution, 5 equivalents of piperazine (0.04 g, 0.51 mmol) were added. The reaction was stirred for 16 h. The solvent was removed under reduced pressure. The product was isolated after column chromatography (40:1 DCM:MeOH). A white power was isolated (83 %). ^{1}H NMR ($CDCl_3$) δ 1.50-1.80 (b, 48 H), 2.77 (b, 4H), 4.42 (b, 12H), 7.10 (b, 12H), 7.32 (b, 12H); ^{13}C NMR (DMSO) δ 21.87, 25.25, 26.20, 31.22, 35.18, 44.139, 120.38, 125.54, 128.07,

128.69, 134.74, 139.15, 139.85, 152.05, 164.52, 165.01, 166.35. MS (MALDI), calcd. for $C_{107}H_{137}ClN_{43}$ 2025.20; found 2025.77 $(M + H)^+$.

CHAPTER III

MELAMINE-BASED MOLECULES ON INORGANIC SUPPORTS *

Dendrimers on Surfaces. In Chapter II, a dendrimer was synthesized. Its physical properties were compared against a small library of dendrimers based on their structural features. The elegance of a stepwise polymerization was illustrated and basic questions on how size and composition affect triazine dendrimers were answered. The logical continuation of this research is work toward an application. From basic research, we learned that these molecules do molecular recognition. Molecular recognition is important in the science of separations.[103,104] We decided to evaluate the use of melamine-based molecules in separations.

The use of a solid phase is an important concept in separations. Techniques of solid phase separation include silica gel modification,[105,106] molecularly imprinted polymers,[105,106] and ionic polymers.[107] There are advantages of solid phase-based separation over solution phase. Among these advantages are ease of manipulation of substrates, lesser amounts of solvent required, no problem with the miscibility of solvents, ease of adaptability for very selective extractions, ease of automatization, prevention of incomplete phase separations, and no emulsion formation as encountered in liquid-liquid extractions.

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Characterization of Surfaces. Since these molecules are grafted on insoluble surfaces, we had to rely solely on surface analysis techniques for characterization, including contact angle, x-ray photoelectron spectroscopy (XPS), and attenuated total reflectance infrared spectroscopy (ATR-IR) (Figure 3.1). Contact angle measurements give information on the first 5 Å of the surface and distinguishes between hydrophobic and hydrophilic surfaces. X-ray photoelectron spectroscopy (XPS) is the most common surface-sensitive analytical tool, giving information between 10 to 100 Å. XPS employs soft X-rays to remove electrons from surface atoms and the ejected electrons have characteristic binding energies that allow for the identification of the source atom. Attenuated total reflectance infrared spectroscopy is used for deeper surfaces and gives information up to several μm deep; ATR-IR uses absorption of energy to reveal different functional groups. Other surface-sensitive analytical techniques that can be employed include surface-enhanced Raman spectroscopy, ion-surface interactions, and ion analysis of the surface such as Cf-desorption mass spectroscopy and ion scattering spectroscopy.[108]

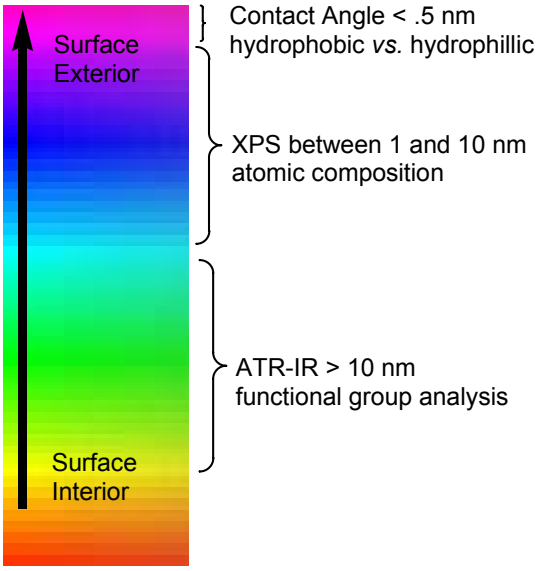
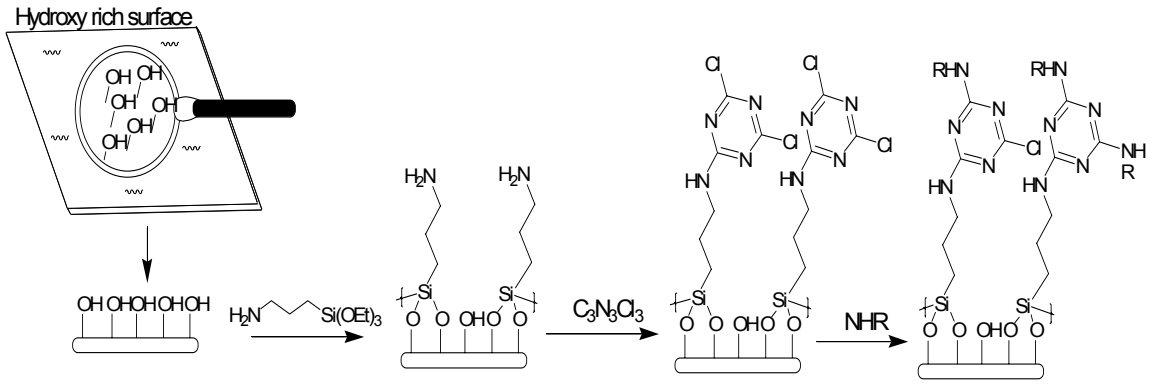


Figure 3.1. Common tools used for surface characterization.

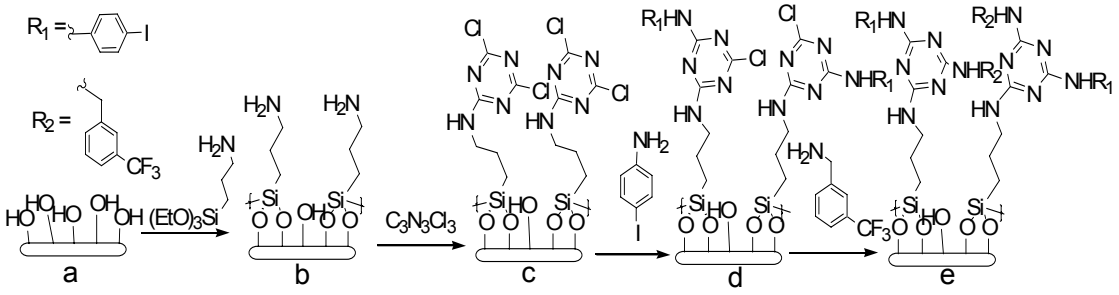
Glass as a Model System. Our strategy was to use glass as a model and then move towards other solids supports. The idea was to functionalize the surface with cyanuric chloride, and untimely immobilize melamine-based molecules on these supports. Our choice of activation with cyanuric chloride is not only based on the familiarity with the molecule's chemistry but also on the great selectivity it exhibits toward nucleophilic aromatic substitution. As illustrated in Scheme 3.1, the surface is cleaned by the RCA-method then is activated by treatment with 3-aminopropyltriethoxysilane (AMPS). The next step of the treatment is the addition of cyanuric chloride. The installation of the triazine allows for branching on the surface. The surface is then capped with an amine-terminated molecule.



Scheme 3.1

Characterization of Glass Surfaces. XPS can be used to characterize the surface at each step of the reaction because we introduce a new element at each step (Figure 3.2). The clean glass slide shows evidence for oxygen at around 550 eV for the 1s electron. There is also evidence for the expected 2p and 2s peaks of silicon at 150 and 100 eV, respectively. The addition of 3-aminopropyltriethoxysilane (AMPS) introduces carbon and nitrogen to the glass surface. Carbon is found at 277 eV and nitrogen is found at 400 eV. The introduction of chloride with $C_3N_3Cl_3$ is reflected by the appearance of two new peaks. XPS data at 200 eV for chloride's 2p electron and at 265 eV the 2s electron of the chloride were observed. There is also a considerable percentage increase of the intensity of the nitrogen region of the spectrum due to the addition of the triazine molecule. Substitutions on the dichlorotriazine surface sequentially with 4-iodoaniline and 3-triflouromethylbenzylamine show the appropriate peaks by XPS. The glass slide was submerged in a solution of 4-iodoaniline for two days at room temperature. The 4d electron peak appears at

about 620 eV. This slide was then treated with 3-trifluoromethylbenzylamine at 80 °C for two days. Substitution of the 3-trifluoromethylbenzylamine was confirmed by the appearance of the 1s fluorine peak at 700 eV.



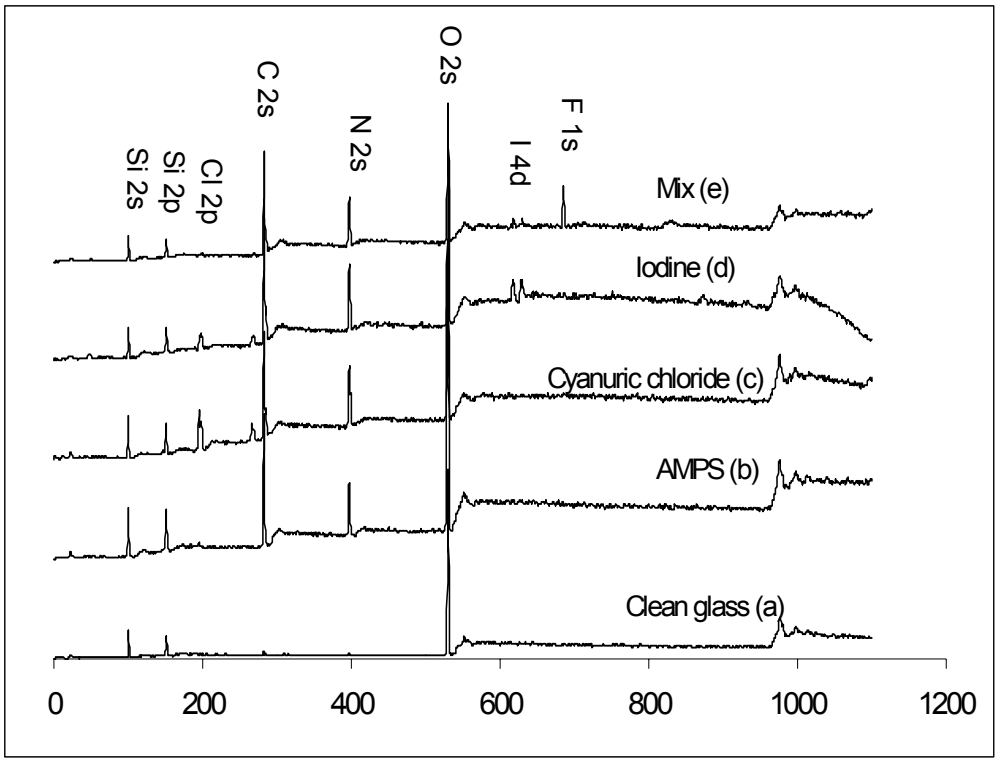


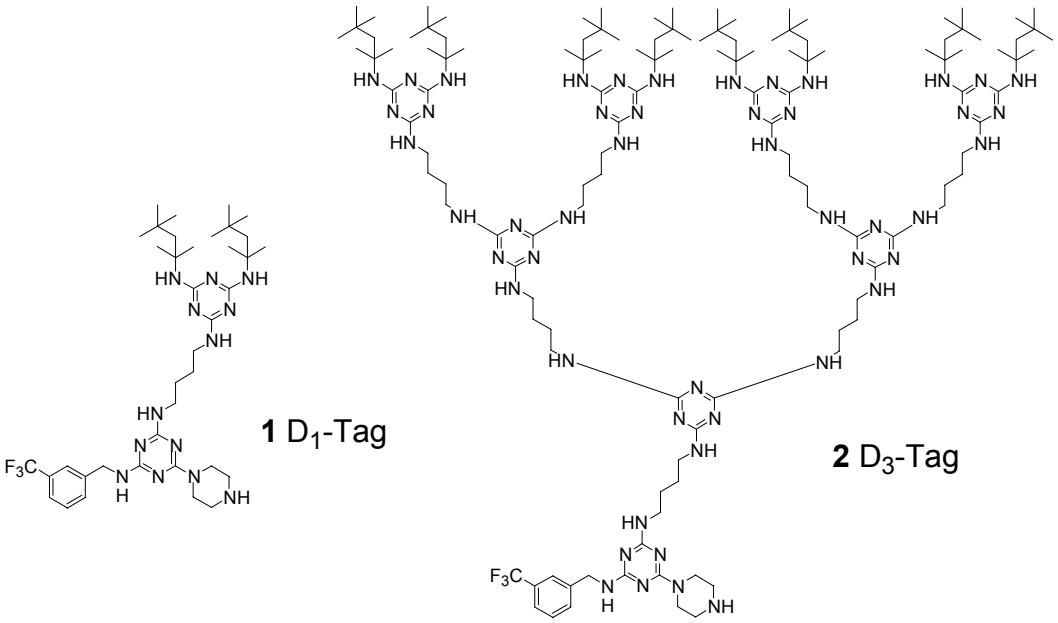
Figure 3.2. XPS of the clean glass slide (a) addition of the amine (b) cyanuric chloride addition (c) to the cyanuric chloride glass slide a molecule with an iodine tag can be added (d) to this same glass slide a fluorine tag molecule is added (e).

XPS not only gives information on the type of element, but also on mass concentration of the last 5 nm of the surface. For slides a-e, this information is presented in Table 3.1. As expected, the clean slide only had oxygen and silicon with small traces of carbon. Upon addition of AMPS, there is a significant increase in the amount of carbon in the surface; this is clearly shown by comparing the ratio of carbon *versus* silicon. There is a new peak for nitrogen. The attachment of the triazine molecule increases the surface nitrogen as shown by comparing ratios; this step also introduces chlorine to the surface. As expected, the chlorine is reduced significantly following the addition of iodoaniline, and there is a new peak belonging to the newly introduced element, iodine. After the addition of 3-trifluoromethylbenzylamine, there is only a small trace of chlorine left on the surface, while new peak belonging to surface fluorine emerges.

Table 3.1. Mass concentrations of elements on glass slides (a-f).

	O	Si	C	N	Cl	I	F	C/Si	N/Si
Clean (a)	65.5	30.7	3.8	0	0	0	0	0.12	
AMPS (b)	26.2	27.6	48.2	10.1	0	0	0	1.75	0.37
Cyanuric (c)	20	11.4	45.4	15.7	7.5	0	0	3.99	1.38
Iodo (d)	19	9.9	53.3	14	3.4	0.5	0	5.38	1.41
Fluorine (e)	16.9	10.1	53.8	14.6	0.4	0.2	3.9	5.33	1.45

Dendrimers on Glass. Once we proved that our technique for addition of amines to a surface was tractable, we synthesized dendrimers in order to graft them onto glass. Since glass was still our model system, it was important to be sure that the dendrons were being grafted on the surface. To accomplish this task we synthesized dendrons with fluorine labels. In collaboration with Erick Acosta, tag molecules **1** and **2** were synthesized using the convergent method (Scheme 3.2). A small dendron (**1**) and a large dendron (**2**) were prepared to provide evidence that these molecules could go onto the surface, regardless of their size.



Scheme 3.2

Results from the grafting of **1** and **2** dendrons on glass show that our model system is feasible for the grafting of amine-terminated molecules (Figure 3.3). The XPS data showed the expected fluorine peak at 700 eV in each case. There is also a significant increase of the carbon and nitrogen signal, and a substantial decrease in the oxygen and silicon signal, thus establishing the existence of a thin film on the glass surface.

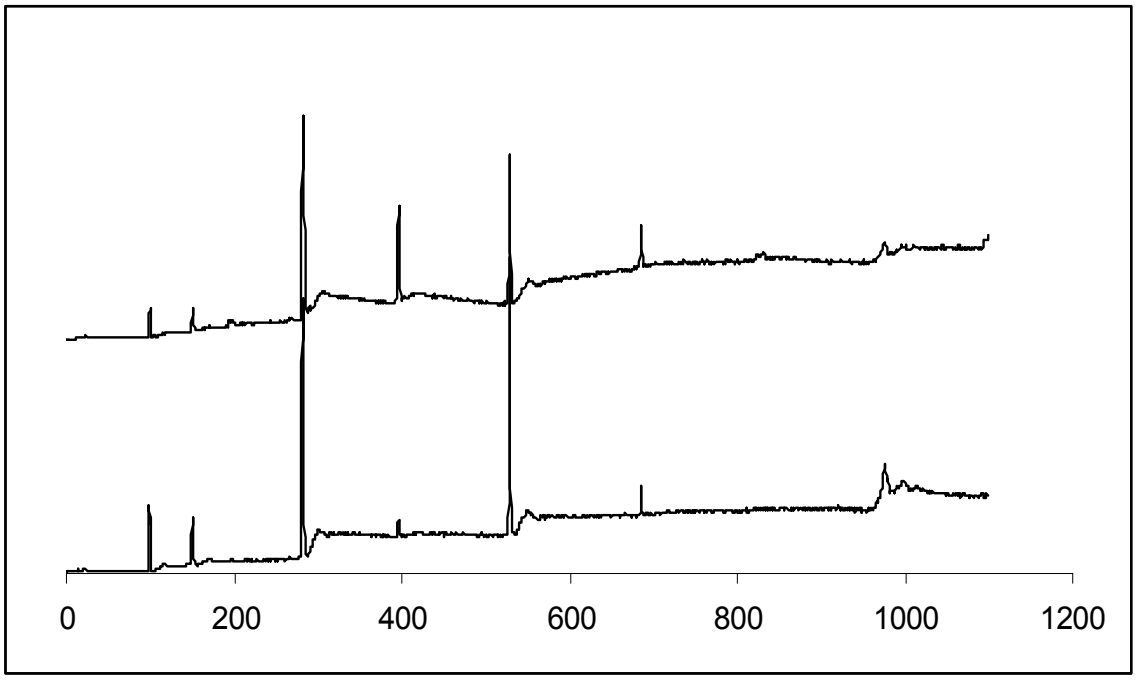


Figure 3.3. XPS of glass slides after grafting of **1** and **2**. The mass concentration was measured and compared to the theoretical values.

Dendrons on Silica Gel. Once the model studies established a working protocol for the grafting of dendrons on hydroxy surfaces, we moved to a more practical inorganic support, silica gel. The chemistry of silica gel allows us to use the techniques we developed for the glass surfaces. Silica gel also offers opportunities to use solid phase separations to characterize the sequestration properties of our systems. The silica gel is activated in the same way as the glass surface, namely by installing AMPS on clean silica gel. XPS is used to characterize the support, using the fluorine-tagged dendrons **1** and **2**. Figure 3.4 shows the XPS data following this procedure. A sharp decrease in the chlorine intensity is presumably due to the substitution of the amine-terminated molecule onto the triazine ring. The expected peak for fluorine is observed.

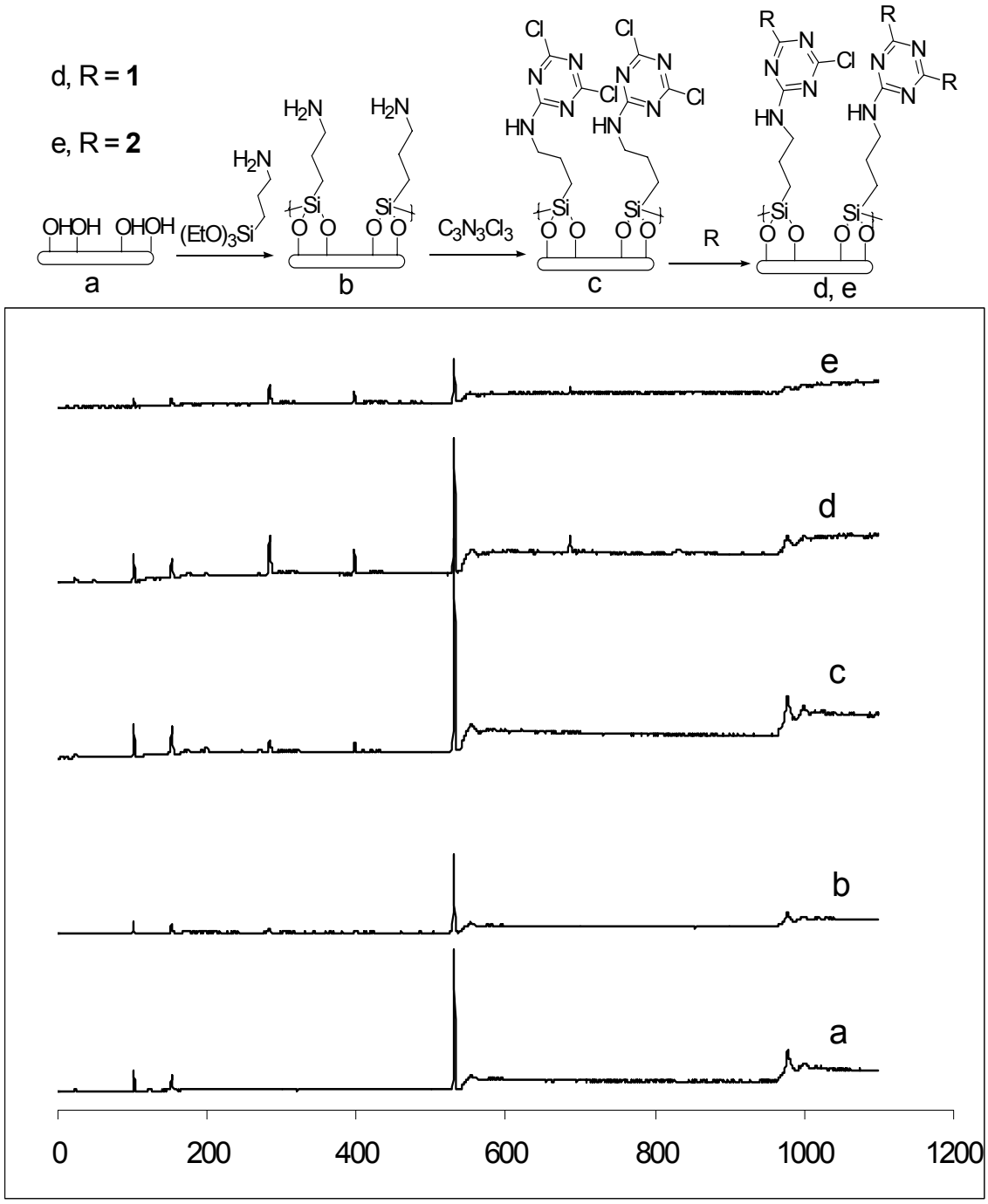
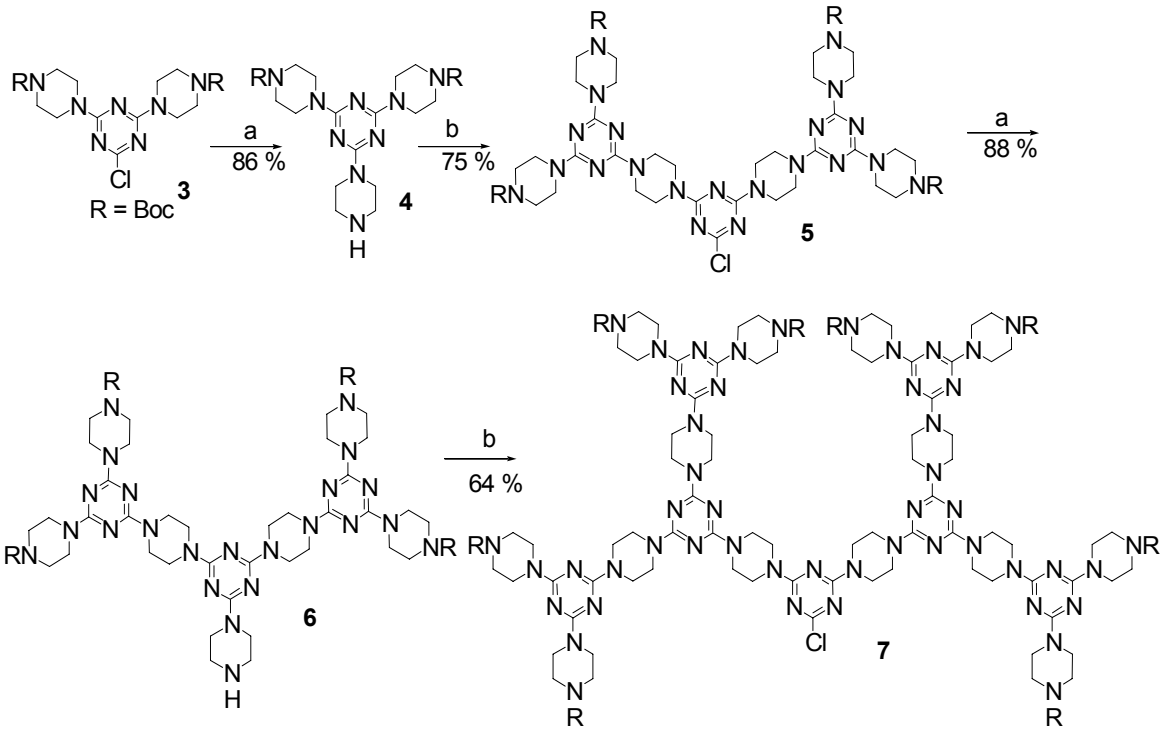


Figure 3.4. XPS data of synthetic modification of silica gel. The spectra is that of the unmodified silica (g), addition of AMPS (h), addition of cyanuric chloride (i), addition of **1** (j), and addition of **2** (k).

Convergent and Divergent Strategies for Dendrimers on Silica Gel. The experiments described earlier serve as a model for the grafting and characterization of melamine-based molecules onto silica gel. From this early data, it was decided to build dendritic architectures onto silica gel by two different approaches, using a convergent or divergent strategy. In the convergent approach, the dendrimers are first synthesized in solution (Scheme 3.3), and then incorporated onto the solid support. The divergent approach relies on iterative synthetic manipulations of the solid-supported organic material. These materials were characterized by Fourier transform infrared spectroscopy, thermal gravimetric analysis, and X-ray photoelectron spectroscopy. The organic molecules were also isolated by chemical etching of the organosilica material which was then analyzed by mass spectrometry to obtain structural information. Following extensive characterization, a survey to determine the ability of the supports to sequester the herbicide atrazine was performed.



Scheme 3.3

The incorporation of melamine-based dendrimers onto silica gel using convergent and divergent strategies is shown in Figure 3.5. The divergent approach – indicated with open arrows along the horizontal axis – only requires the solution-phase synthesis of **3**. Higher generations of dendrimers supported onto the surface of the silica gel are obtained by iterative deprotection and reaction steps which can be monitored using IR spectroscopy. The convergent approach relies on the solution phase synthesis of each dendrimer prior to its attachment onto the silica gel. The materials prepared by each of these two different strategies were compared using thermal gravimetric analysis to quantify

the amount of organic material in the composite, X-ray photoelectron spectroscopy to obtain C:N ratios, and mass spectrometry of the organic materials liberated from the support upon etching.

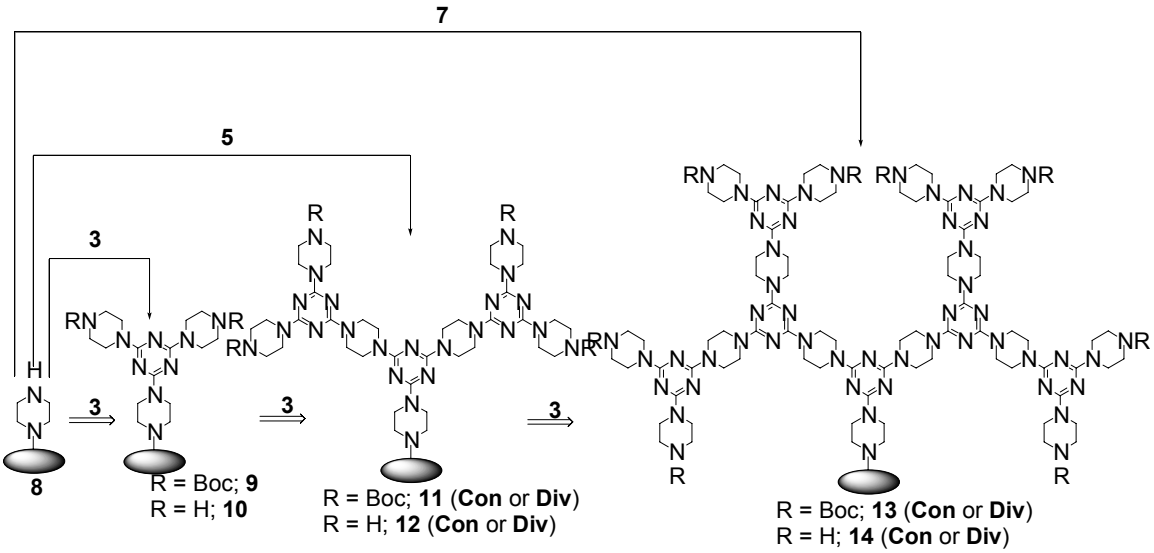


Figure 3.5. Incorporation of melamine-based dendrimers onto the silica gel surface by the convergent (regular arrow) and by divergent (open arrow) strategies. Materials are identified with the abbreviation "Con" or "Div" to indicate the route used for the preparation of the material.

Preparation of Materials by the Convergent Method. Dendrons **3**, **5** and **7** were synthesized in solution using the convergent strategy described in the experimental section. Unlike dendrons **1** and **2**, these three molecules contain an electrophilic monochlorotriazine group at the core. While the strategy to attach molecules **1** and **2** is slightly different than that of the attachment of **3**, **5**, and **7**, we relied on the reactivity of secondary amines to effect nucleophilic

aromatic substitution of monochlorotriazines. The change of strategy involved obtaining commercially-available piperazine-terminated silica gel. This shorted the time for preparation, and provided more homogenous materials. To obtain the materials by the convergent method, the appropriate dendrimer, **3**, **5**, **7**, is refluxed with **8** in THF overnight to produce composites **9**, **11-Con**, or **13-Con**, respectively.

Preparation of Materials Using the Divergent Approach. Composite **6** was refluxed in THF with excess of **3** to yield composite **9**, a material that contains *t*-Boc-protected amine groups. The protecting groups were easily removed in less than 30 minutes with 3 M HCl to give **10**. Washing **10** with aqueous sodium bicarbonate removed the hydrochloride salts and activated the amines for further reaction. The entire process is then repeated. Reaction of **10** with **3** produced **11-Div** and subsequent reactions yielded **12-Div** and **13-Div**.

Characterization Using ATR-IR Spectroscopy. Attenuated total reflection fourier transform infrared spectroscopy (ATR-IR) is valuable for monitoring the iterative nature of the divergent synthesis (Figure 3.6). Composite **8** show no IR bands in the region between 1200 cm^{-1} and 2000 cm^{-1}. The incorporation of **3** onto **8** to yield **9** can be seen with the appearance of the IR absorption band observed at 1696 cm^{-1} that corresponds to the carbonyl group present on the *t*-Boc-protecting groups. Accordingly, composites **11-Div**

and **13-Div** present similar IR bands as **9**. The disappearance of this band upon treatment of the material with HCl is consistent with the removal of the *t*-Boc groups. IR bands between 1400 cm^{-1} and 1600 cm^{-1} are diagnostic for the triazine rings on silica gel. These bands appear to be unaffected by the acidic deprotection and basic wash. Similar bands can be seen in materials produced using the convergent strategy.

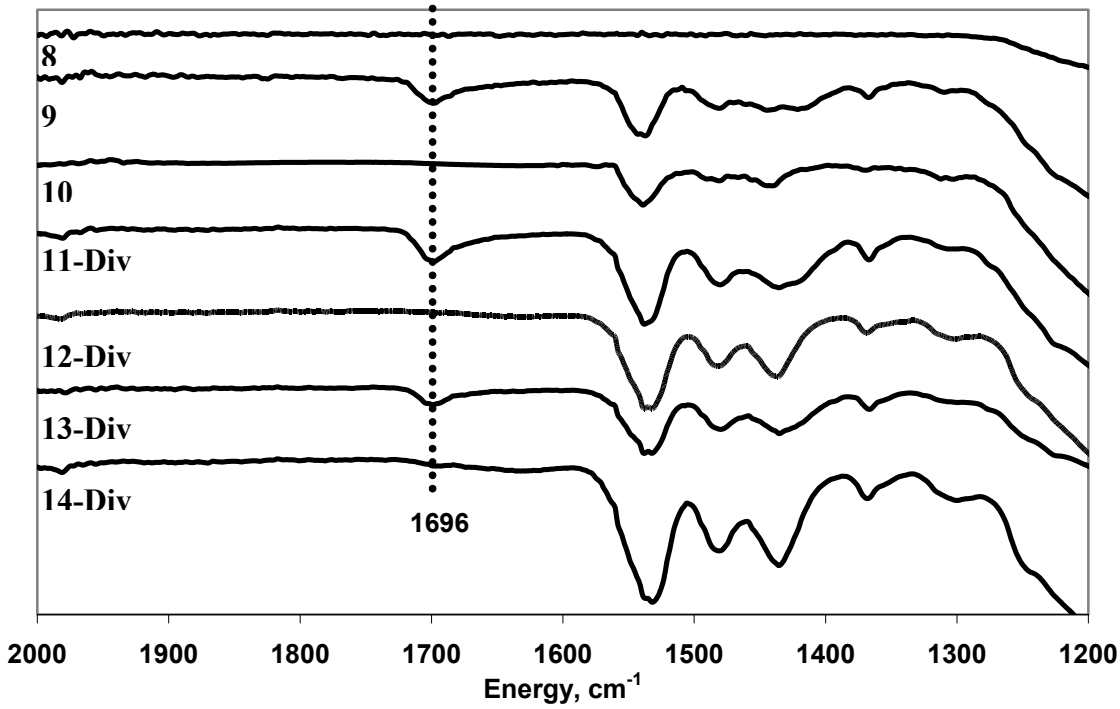


Figure 3.6. ATR-IR reveals the iterative reactions used in the divergent synthesis of dendrimers on silica gel.

Characterization Using X-ray Photoelectron Spectroscopy (XPS). Figure 3.7 (panel a) shows the XPS traces obtained for **8**, **9**, **11-Div** and **13-Div**. As expected, all these materials show similar ratios of C:N. The relative intensity of these two peaks increases with respect to those of silicon and oxygen as the synthesis proceeds, a trend that suggests increasing amounts of organic material on the surface of the silica gel. The appearance and disappearance of the carbonyl peak (not shown) can also be followed during the iterative steps of the synthesis. Table 3.2 summarizes the data from XPS experiments, showing the C/Si, N/Si and C/N ratios for all of these materials. The ratios obtained for composites **8**, **9**, **11-Div** and **13-Div** indicate that the thickness of the organic surface increases after each reaction with dendron **3**. For example, composite **8** has a C/Si ratio of 0.59 and after treating it with **3** to produce **9** the C/Si ratio increases to 0.81. In the case of composites **11-Div** and **13-Div**, the C/Si ratios are 1.16 and 1.80, respectively. The C/Si and the N/Si ratios for **13-Div** are boosted significantly when compared to **11-Div**.

The trend for the materials prepared by the convergent method is less apparent. Composite **11-Con** showed C/Si and N/Si ratios that are identical to material **9**. These ratios are smaller than those of **11-Div**. These ratios increase in **13-Con**, but these values remain smaller than those of **13-Div.** The data supports the previously proposed hypothesis suggesting that as dendrimer size increases, the reactivity of these molecules with solid supports decreases. From

these C/Si and N/Si ratios, we can calculate C/N ratios that roughly agree with what is predicted.

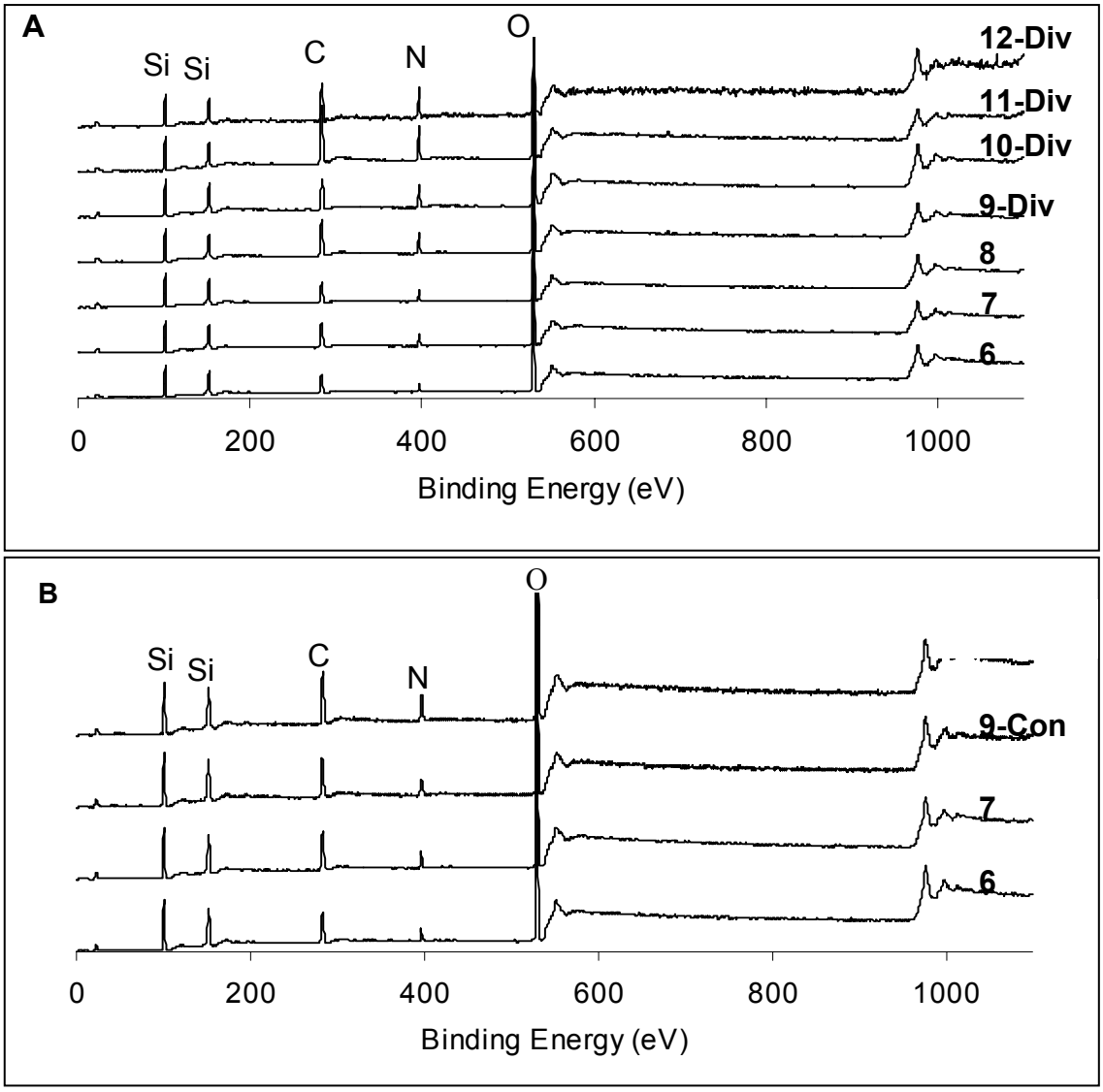


Figure 3.7. XPS traces for the dendronized silica prepared by divergent (panel A) and convergent (panel B) strategies.

Table 3.2. C/Si and N/Si ratios obtained from the XPS of materials prepared by divergent and convergent strategies.

Composite	C/Si	N/Si	C/N (Exp.)	C/N (Theoretical)
6	0.59	0.12	4.9	3.5
7	0.81	0.20	4.0	4.3
9-Div	1.16	0.35	3.3	3.0
11-Div	1.80	0.58	3.1	3.0
9-Con	0.79	0.16	4.9	4.7
11-Con	1.06	0.30	3.6	4.8

Characterization by Thermal Gravimetric Analysis (TGA). The total amount of organic material incorporated onto the silica gel can be measured using TGA. Table 3.3 shows the results of the TGA analysis for these materials. Commercially available *N*-propylpiperazine derivatized silica gel, **8**, contains 15% organic material (1.2 mmol/g). This value is consistent with the loading of 1.0 mmol/g reported by the manufacturer. The products of the convergent synthesis, **9**, **11-Con** and **13-Con**, have identical organic contents of ~21%, corresponding to an increase in organic content of 6%. In retrospect, this consistency is not surprising given our belief that the size of the dendrimer (and

the surface area it occupies) is directly related to molecular weight. Our conceptual model for this data is that the surface of the silica gel is uniformly covered with organic material. That is, since **11-Con** is twice as large as **9**, it covers twice as much surface area. This coverage precludes other surface amines from reacting. Similarly, **13-Con** is twice as large as **11-Con**, and occupies a surface area that is twice as large. The low loading of dendrons is a limitation that is overcome by applying the divergent approach for the synthesis of these materials. Higher organic content is observed in the TGA traces of **11-Div** and **13-Div**, namely 27% and 30%, respectively. However, given our hypothesis about surface crowding, these materials are expected to contain structural defects such as incomplete branching. These defects can be probed with mass spectrometry.

Table 3.3. Yields of products prepared by the convergent and divergent strategies.

	% Organic TGA	% Inorganic	% Organic Linker[a]	% Dendrimer Added[b]	Organic	MW mmol of piperazine /100 g silica gel from surface	mmol of piperazine /100 g silica gel from dendrimer	Total mmol of piperazine groups /100 g silica gel
8	15.0	85.0	15.0	0	127	120	0	120
9	21.1	78.9	13.9	7.2	575	110	21	131
9-Con	21.3	78.7	13.9	7.4	1269	110	23	133
11-Con	20.3	79.7	14.0	6.3	2660	110	19	129
9-Div	26.6	73.2	13.0	13.6	1269	100	43	143
11-Div	29.8	70.2	12.4	17.4	2660	97	52	150

[a]Calculated by assuming a constant ratio of aminopropylpiperazine groups per g silica gel. [b]Molecular weights of **8** (127 g/mol); **9** (575 g/mol); **11** (1269 g/mol); **13** (2660 g/mol).

Characterization by Mass Spectrometry after Etching. A more detailed characterization of the organic material is achieved by using mass spectrometry after the inorganic support is removed with aqueous HF. Molecular ions could be observed for all materials. For the products of convergent synthesis, the lowest ion corresponds to the desired deprotected dendrimer with the *N*-piperazinylpropyl silane linker. Higher molecular weight ions corresponding to SiF_3 adducts were also observed. We conclude from the quality of the spectra that the convergent synthesis proceeds as cartooned in Scheme 3.4. However, this scheme is not accurate for the divergent synthesis. Figure 3.8 shows the best MALDI-MS spectra obtained for **13-Div** after cleavage from the silica gel with aqueous HF. This spectrum shows a small peak at 1943 m/z, corresponding to the molecular ion of a generation three dendrimer covalently attached to a SiX_3 (X = F or OH). The spectrum also shows a slightly larger peak at 1860 m/z that belongs to the molecular ion of this dendrimer after loosing the SiX_3 group, presumably during the ionization process. The large number of other ions observed correspond to incomplete branching were also observed in the MALDI-MS spectrum of **13-Div**. The characteristic loss of an SiX_3 group (where X=F or OH) is observed in these spectra. The nature of the defects in many cases is not known, and the cartoons presented in Figure 3.8 are intended to communicate relative size and not exact structure in most cases. The utility of this technique may be limited to these small dendrimers; it is

difficult and operator-intensive to obtain signal from materials derived from **14-Div** or **14-Con**.

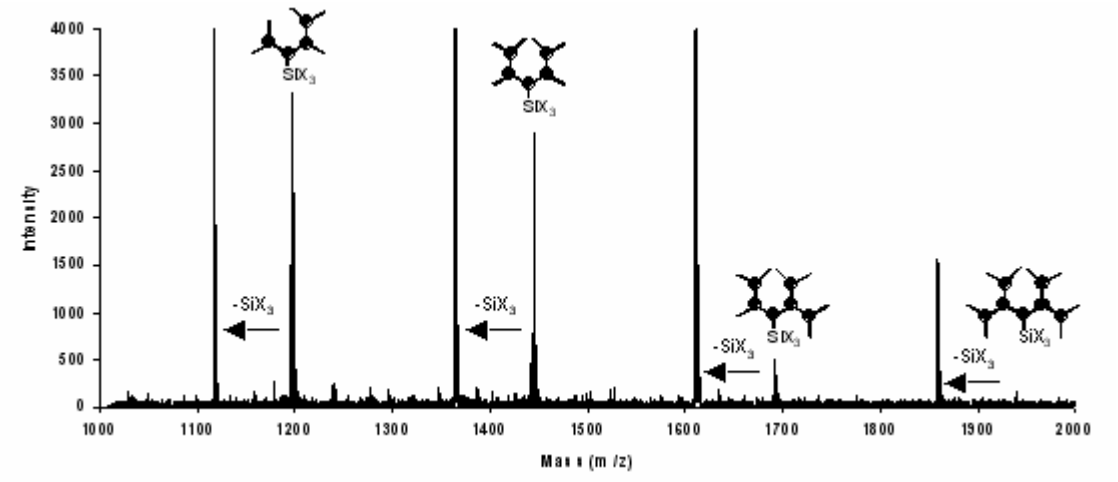


Figure 3.8. MALDI-MS analysis of **13-Div** after chemical etching with aqueous HF. In the dendrimer cartoons, the black dots symbolize melamine rings and the sticks are piperazines. In SiX_3, the X represents F or OH.

A Functional Assay for the Comparison of These Materials. The materials obtained by both the convergent and divergent methods were subjected to a functional assay of current interest to our group, the removal of atrazine (a commonly used herbicide) from water. Materials presenting reactive secondary amines – **8**, **10**, **12-Div**, **14-Div**, **12-Con** and **14-Con** – were incubated in a solution containing 10 mg/L aqueous solution of atrazine for 18 hours (Figure 3.9). Two trends are apparent from this data. First, increasing the

size of the dendrimer increases the amount of atrazine sequestered. That is, the amount sequestered increases in the convergently prepared materials from **8**<**10**<**12-Con**<**14-Con** as well as the divergent materials **6**<**8**<**12-Div**<**14-Div**. Second, the materials prepared divergently sequester more atrazine than those prepared convergently. While the materials prepared divergently contain more organic material, the amount of organic material for **10**, **12-Con** and **14-Con** is the same. The sequestration potential of these materials is different and we would expect similar sequestration profiles if sequestration were solely proportional to organic content. We cannot attribute these differences solely to the relative amounts of organic material or the number of piperazine groups available for reaction. This expectation holds even when the total number of reactive amines; unreacted surface piperazines; and dendrimer-displayed piperazines are considered. Thirdly, **14-Div** is remarkably effective: only 3% of the amines on the silica gel are modified, yet a 2.5-fold increase in the atrazine removal efficiency results when compared to **8**.

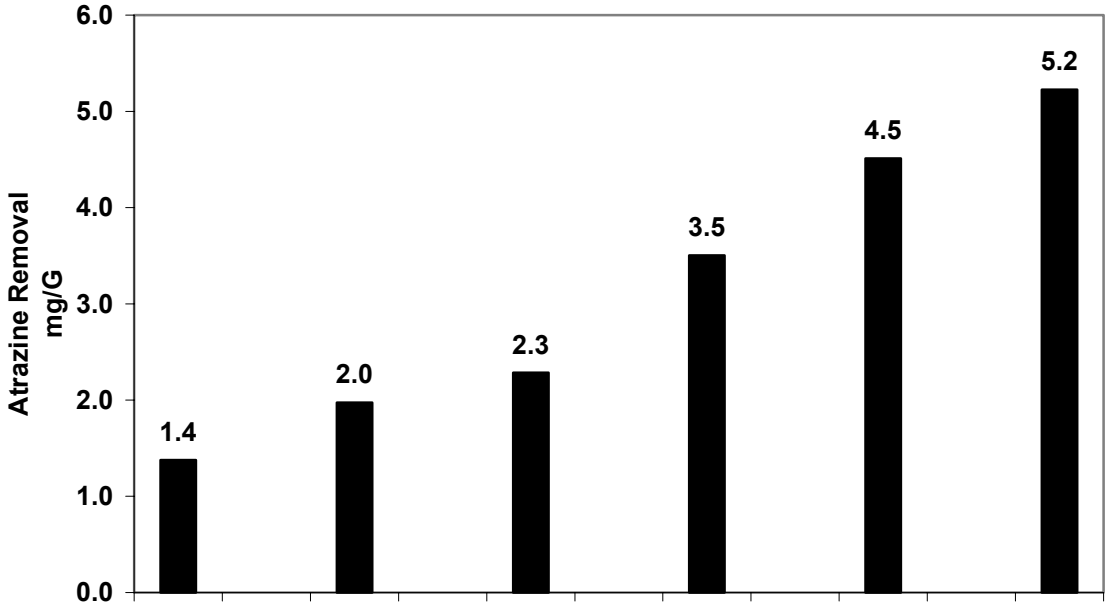


Figure 3.9. Sequestration of atrazine by **8**, **10**, **12-Con**, **14-Con**, **12-Div** and **14-Div**.

To summarize this section, the synthesis of dendritic composites using the divergent and convergent methods has been described. ATR-FTIR can be used to monitor the growth of dendrimers on the silica gel surface by looking at the carbonyl-stretching band at 1696 cm^{-1}. This analytical tool is also of value to observe the removal of the *t*-Boc-protecting groups from the solid-supported dendrimers when prepared by the divergent approach. XPS compliments the FTIR results by analyzing the relative concentration of nitrogen and carbon compared to silicon. The XPS results show a continuous increase in the C/Si and N/Si ratios for the materials prepared by the divergent approach. However, materials prepared by convergent approach presented smaller C/Si and N/Si ratios. TGA is consistent with the XPS results by showing that composites

produced by the convergent strategy contain a limited amount of dendrons attached to the silica gel surface. At the same time, TGA demonstrated that the divergent strategy is capable of producing materials with higher organic content. The most striking evidence of covalent attachment of the melamine-based dendrimers to the silica gel surface is obtained from mass spectrometry analysis of the organic portion. These results indicate that materials prepared by the convergent strategy contain well-defined dendritic structures covalently attached onto the silica gel surface. Unfortunately, the convergent strategy requires solution phase synthesis of the dendrimers prior to their attachment onto the silica surface. This fact narrows the application of this strategy to materials containing only small dendrimers since the synthesis and purification of large dendrimers in solution can be complicated and time consuming. Another drawback of the convergent strategy is the small loadings achieved when larger dendrimer generations are incorporated onto the silica gel surface.

The divergent strategy avoids complicated solution-phase synthesis and purification steps while increasing the loading of dendritic architectures onto the silica gel surface. The higher loadings obtained by this strategy are accompanied by incomplete branching of the dendritic structures as observed by MALDI-MS. Therefore, this synthetic strategy may yield hyper-branched polymers as well as the desired grafted dendrimers. Nevertheless, the incomplete branching does not seem to have a negative effect on the ability of these materials to sequester atrazine from water. On the contrary, composites

prepared by the divergent approach outperformed the perfectly-branched materials synthesized by the convergent methodology in this task. Future studies will be directed toward applications of these composites in the fields of catalysis, and as stationary phases for chromatographic separations.

Melamine-Based Molecules on Alumina. Another support with interesting potential for molecular recognition is alumina. The chemistry of alumina is very similar with that of silica gel, and the same synthetic protocols can easily be incorporated. Dr. David Ford in the Texas A&M Department of Chemical Engineering has been working on the modification of alumina membranes for gas separation. Collaboration with his group to modify such membranes is an ongoing project between chemistry and engineering. Membrane separation involves partially separating a feed containing a mixture of two or more components by the use of a semipermeable barrier (the membrane), through which one or more of the species moves faster than another or other species. The basic process of the membrane's function is illustrated in Figure 3.10. Separation involves a feed mixture separated into a *retentate* (part of the feed that does not pass through the membrane, i.e.,is retained) and a *permeate* (part of the feed that passes through the membrane).

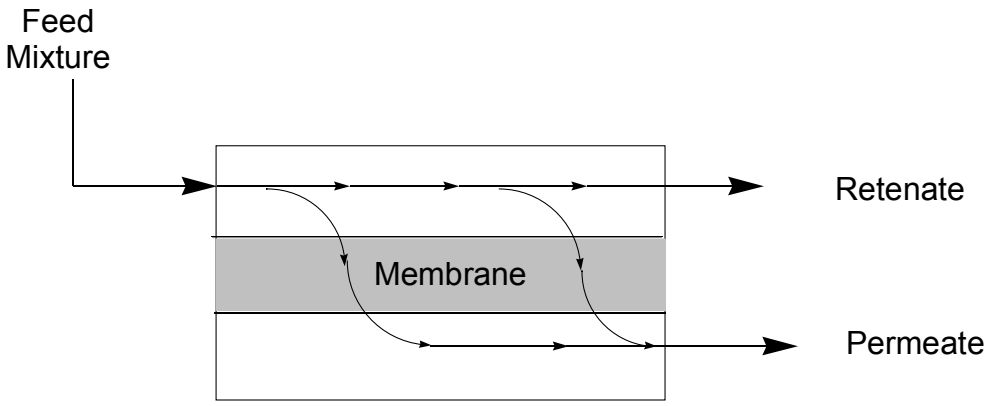


Figure 3.10. Basic membrane separation.

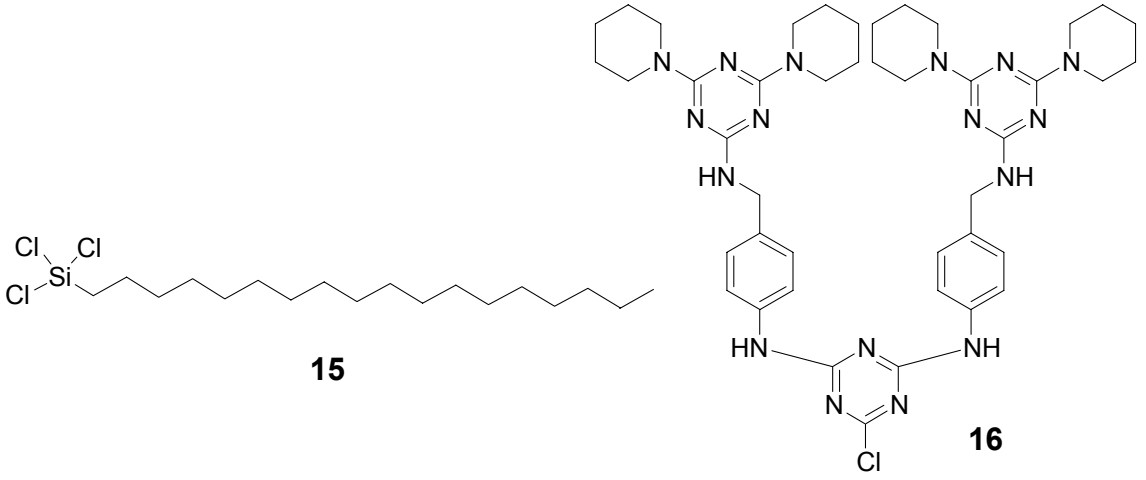
Ideal membranes will have high permeance. This requires a high gas flow (diffusivity), and a preference of one molecule *versus* another (selectivity). Permeance (P / l) is related to the measured gas permeation rate through the membrane, *Q*, as shown in Eq. 3.1:

$$P / l = Q / A \Delta p \qquad \textbf{Eq. 3.1}$$

where, P is the permeability coefficient of the separation layer, l is the effective thickness of the separation layer, A is the membrane surface area, and Δ p is the pressure differences between the retenate flow and the permeate flow.

The first part of the research was to compare membranes that have been modified with octadecyltrichlorosilane **15** (OTS), and a monochlorotriazine-generation 2 dendron, **16** (D2-Cl). These membranes have *p*-aminobenzylamine linking groups, and piperidine as surface groups, as

illustrated in Scheme 3.4. Details of the synthesis of **16** are in Chapter II. The organic/inorganic hybrid materials are prepared from commercially-available mesoporous alumina membranes. Most of the measurements presented in this section were conducted by Dr. Asad Javaid, and more detailed information can be found in his doctoral dissertation.[109] The main goal of this research was to prepare membranes with high selectivity, and high permeance.



Scheme 3.4

Modification of Membranes. The porous alumina membranes used in these experiments are commercially-available, with an average pore size of 5 nm. Three membranes were modified with **15** and will be referred to as membrane #1, membrane #2, and membrane #3, or OTS-modified membranes.

Another three membranes were modified with **16**, and will be referred to as membrane #4, membrane #5, and membrane #6, or D2-Cl-modified membranes. In both cases attachment of the organic material were done by submerging the membranes in a solution of **15** or **16**. While it is presumed that attachments of **15** happed by means of covalent substitution of the hydroxy groups on the membrane onto the silicon, the grafting of **16** is assumed to be compromised of non-covalent interactions (mainly hydrogen-bonding) between the surface of the membrane and the dendron. Evidence for the attachment of these molecules onto the membranes was established by XPS, compared against a bare membrane. These results are summarized in Table 3.4. From these results, it is assumed that the amount of organic material on the surface of the OTS-modified membranes is much greater than that on D2-Cl-modified membranes. The importance of the amount of organic material on the substrate will be explained in detail later. As expected, no silicon is found on the bare membrane or on the D2-Cl-modified membranes.

Table 3.4. The molar percentages of carbon and silicon on surface of bare and treated membranes by XPS. Standard deviation is given in parentheses.

Membrane	Carbon mol %	Silicon mol %
Bare	11.57 (3.64)	0
OTS-modified	73.44 (8.17)	5.10 (0.39)
D2-Cl-modified	22.61 (3.19)	0

Permeance and Selectivity of Modified Membranes. The permeance to nitrogen and propane of the membranes was measured, and is reported in Table 3.5. The selectivity of propane/nitrogen is also tabulated. The permeance of nitrogen was much higher for the bare membrane. One order of magnitude of decrease for the permeance of N_2 is observed when the membrane was modified with **16** and another drop of one order of magnitude was observed in the permeance of OTS-modified membranes. A similar trend was observed in the permeance of propane. The drop of permeance is directly related to amount of organic material on the surface. Selectivity of propane over nitrogen is about the same for the bare and D2-Cl-modified membranes, while the selectivity for the OTS-modified membrane is increased by an order of magnitude.

Table 3.5. Single gas permeance and selectivity data for untreated (bare) and modified (OTS-modified, and D2-Cl-modified) membranes. Standard deviation is given in parentheses.

Membrane	N_2 Permeance (mol sec^{-1} m^{-2} bar^{-1})	C_3H_8 Permeance (mol sec^{-1} m^{-2} bar^{-1})	Selectivity C_3H_8/N_2
Bare	0.621 (0.087)	1.047 (0.180)	1.681 (0.122)
OTS-modified	0.0012 (0.0002)	0.0218 (0.0172)	18.971 (4.132)
D2-Cl-modified	0.094 (0.041)	0.120 (0.041)	1.29 (0.150)

Toluene Permeance. While essentially no selectivity was observed for propane with the D2-Cl-modified membranes, toluene gave different results. These same membranes were tested in toluene *versus* nitrogen selectivity experiments. A commonly used method to evaluate the performance of a membrane is to plot separation factors as a function of permeance. The separation factors (S_F) of the membranes were calculated according to Eq. 3.2;

$$S_F = (T_p/N_p)/(T_f/N_f) \qquad \textbf{Eq. 3.2}$$

where T_f and N_f are the weight fractions of toluene (T) and nitrogen (N) in the gas feed, and T_p and N_p are the weight fractions of the components in the permeate, respectively. The plot of membranes # 2-6 is illustrated in Figure 3.11. As we can see from this plot, the selectivity of D2-Cl-modified membranes

is comparable to that of OTS-modified membranes, while the permeance of the D2-Cl-modified membranes is comparable to that of the bare membrane. This is one of the highest selectivity that has been observed without compromising permeance for this type of separation. Blume and co-workers observed high selectivity and high permeance by using a polymeric membrane based on poly(dimethoxysilane).[110] This result is also plotted in Figure 3.10, and labeled PDMS. The separation factor is still comparable to the alumina-modified membranes, while the permeance of the PDMS membrane is one order of magnitude higher than the OTS-modified membranes. It is also one order of magnitude smaller than the D2-Cl-modified membranes. A membrane prepared from treatment of the same alumina membranes with phenyltrichlorosilane was prepared in the same manner as the OTS-modified membranes, and is referred as membrane # 7. This membrane was prepared as a control to investigate if aromatic molecules on a surface can have selectivity for diffusing aromatic substrates such as toluene. As seen from the plot, we succeeded in essentially clogging the pores (very low permeance) on the membrane without accomplishing any improvement in selectivity relative to the bare membrane.

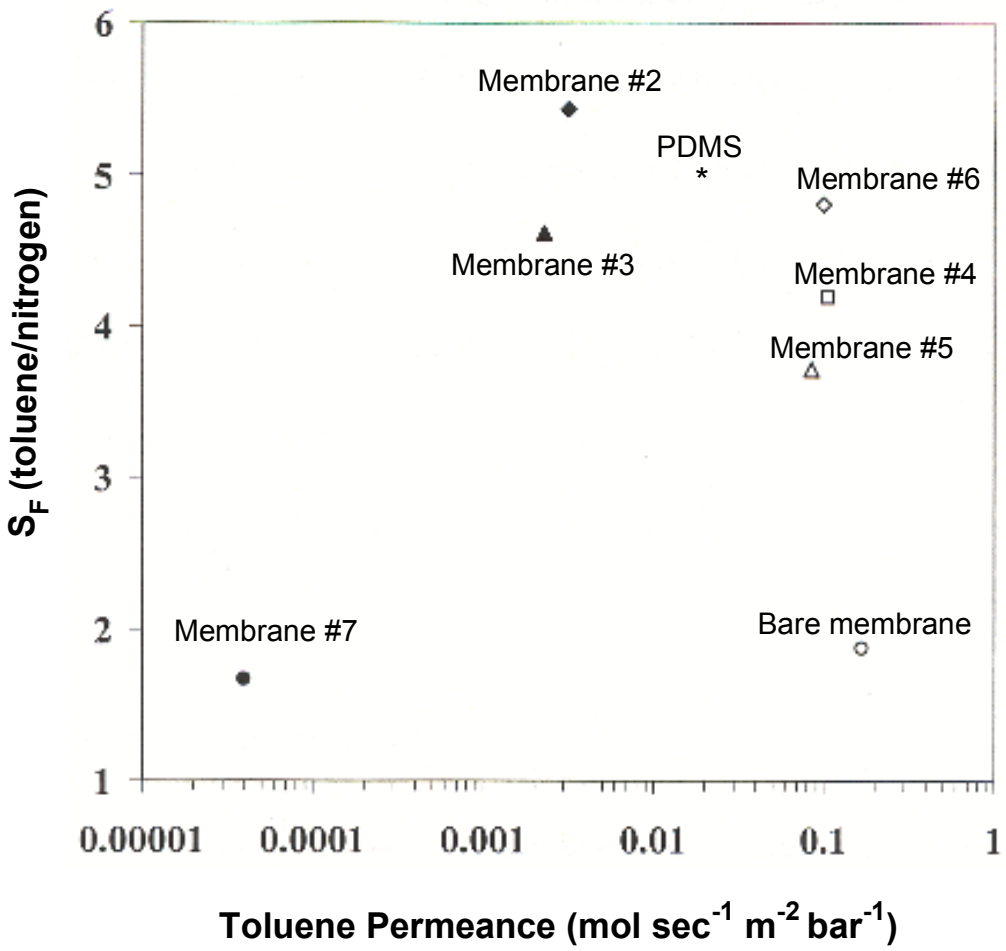


Figure 3.11 Separation factor (S_F) for toluene over nitrogen as a function of toluene permeance; for membranes # 1-7 and PDMS membrane.

Covalent Modification of Alumina Membranes by Melamine-Based Molecules. Encouraged by the early results of the organo-alumina membranes, we decided to pursue this project using a different approach. The established chemistry was also employed to modify the alumina membranes. The first set of membranes was refluxed in a solution of AMPS, treated with cyanuric chloride, and capped with a solution of docedecylamine. These membranes had very

small permeance (> 0.001), and no significant increase in selectivity of propane/nitrogen when compared with the bare membrane. The experimental conditions were altered to find the ideal conditions of high permeance and high selectivity; the same concentration was tried with no heating for the same amount of time. Membranes was treated with a smaller concentration of AMPS, and the same concentrations of cyanuric chloride and docedecylamine. While keeping the same concentration of AMPS with no heating improves the permeance of the membranes by an order of magnitude, there was no significant change in the selectivity of these membranes. Alternatively, changing the concentration of the first step in the preparation of the membrane improves permeance by two orders of magnitude, and the selectivity is increased from 1.39 to 2.55.

The protocol of using a low concentration of AMPS was used to make all of other membranes. Results in the permeance and selectivity data collected changed from batch to batch. It is hypothesized that the discrepancies in the measurements are due to the collection of organic and inorganic matter on the membranes before modification. The RCA-clean method applied to the glass surfaces was adopted to treat the membranes prior to organic modification. After adopting the RCA-clean method, membranes used just after the procedure have a propensity to incorporate a larger amount of organic material and consequently, the pores of the membranes get clogged. After revising the procedure, it was learned that surface water catalyzes the polymerization of

AMPS, and a thin film is form on the surface. This hypothesis was tested by varying the time the membranes were dried. Four membranes were exposed to the RCA-clean procedure, and one was submerged in a solution of AMPS immediately after flushing with nitrogen for 1 minute. The remaining three membranes were flushed with nitrogen for 1 minute and then dried for 0.5, 2, and 48 h respectively. These membranes were labeled membranes # 8-11 accordingly. After drying, they were submerged into a solution of AMPS. The propane permeance after this treatment is presented in Table 3.6. From the data, we can observe that no drying causes a considerable drop on permeance, while drying for at least 0.5 h is enough to remove all of the surface water and slow the polymerization of AMPS.

Table 3.6. Propane permeance of membranes prepared by varying their drying time.

Membrane # (drying time)	C_3H_8 Permeance (mol sec^{-1} m^{-2} bar^{-1})	% organic content
8 (0.0 h)	0.2066	0.98
9 (0.5 h)	0.7853	0.12
10 (2 h)	0.6407	0.13
11 (48 h)	0.5414	0.16

After investigating the effects of drying following the RCA-clean procedure, it was decided to dry the membranes for 2-4 hours before they were submerged in the solution of AMPS. Three membranes were prepared by the RCA-clean method and dried for 2.5 h. These membranes were sequentially dipped into solutions of AMPS, cyanuric chloride, and hexadecylamine. These membranes are labeled membranes # 12-14. The selectivity of propane over nitrogen is about the same for all three membranes (Table 3.7).

Table 3.7. Permeance and selectivity of membranes dried for 2.5 hours and capped with hexadecylamine.

Membrane	C_3H_8 Permeance (mol sec^{-1} m^{-2} bar^{-1})	Selectivity C_3H_8/N_2
12	0.1852	2.30
13	0.0978	2.68
14	0.0488	2.46

The small selectivity, the difficulty of getting consistent results, and the early results using dendrimers led us to change our strategy for surface functionalization. The reagent 3-aminopropyldimethylethoxysilane was used instead of AMPS. By making this change, we expected to see more consistent results since 3- aminopropyldimethylethoxysilane cannot be polymerized as

easily as AMPS. Another change in strategy was to begin growing dendrimers on the surface using the same covergent strategies used for the silica gel.

Three membranes were prepared by the same protocol as the silica gel, and labeled membranes # 15-17. The permeance and selectivity of these membranes were tested, and the results are presented in Table 3.8. As seen from the data, the permeance of the membranes dropped with each increasing generation. This behavior is expected, since we are increasing the amount of organic material at the pores of the membranes. By generation 3, the pores are so clogged that permeance is smaller than any previous examples. Selectivity of propane over nitrogen is best with membrane # 16, and is also the best selectivity observed for melamine-based materials observed during our studies. There are plans to continue investigating these organic-inorganic hybrids. A move to bigger pores is ideal for many reasons. Some of the reason is because they are cheaper, another is that we can more readily control the amount of organic material that is grafted on the surface. Finally, we believed that bigger pores would give us more consistency since they are bigger and more difficult to clog.

Table 3.8. Permeance and selectivity of dendrimer-modified membranes.

Membrane #	C_3H_8 Permeance (mol sec^{-1} m^{-2} bar^{-1})	Selectivity C_3H_8/N_2
15	1.2971	1.6758
16	0.0771	4.1091
17	0.0047	0.6239

Conclusion. Our group has developed a novel synthetic approach to new dendritic materials. The research focuses on developing techniques to graft molecules onto surfaces. These techniques are applied to wide range of solid supports including glass, silica gel, and alumina. The ability of these systems to sequester atrazine and separate gases was explored. The chemistry and analytical techniques allow the screening of compounds in a fast, cheap, and efficient manner. This research is aimed at creating systems for the removal and separation of small organic molecules.

Materials. All reagents and solvents were obtained from commercial sources and used without further purification unless specified. ^{1}H NMR spectra were obtained on Varian Inova 300, Mercury 300, or Inova 500 spectrometers at 300 or 500 MHz. ^{13}C NMR spectra were obtained on Varian Inova 300, Mercury 300, or Inova 500 spectrometers at 75 or 125 MHz. ^{1}H and ^{13}C chemical shifts are reported in ppm referenced to tetramethylsilane or residual solvent peaks, respectively.

Synthesis. Details of the solution-phase synthesis and the characterization of the dendrimers used in this chapter are in Erick Acosta's doctoral dissertation.[111]

RCA-Clean Protocol. Distilled (DI) water (100 mL) was placed in a Pyrex beaker, and 20 mL of 30 % aqueous hydrogen peroxide was added. To this solution, 20 mL of ammonium hydroxide solution were added. The solution was heated to 70° ± 5° C on a hot plate. The glass slide or alumina membrane was dipped into the solution for 15 min. The slide or membrane was then transferred to a container with 150 mL of DI water. After several water changes, the slide or membrane was removed and placed in 100 mL of DI water in a Pyrex beaker. To this beaker, 20 mL of 30% aqueous hydrogen peroxide solution was added., and then 20 mL of 12 M hydrochloric acid was also added. The solution was then warmed to 70° ± 5° C on a hot plate. The glass slide or alumina membrane was dipped in the solution for 15 min. The slide or membrane was rinsed with 100 mL of DI water. After several water washes, the slide or membrane was removed and placed in 100 mL of DI water in a Pyrex beaker. The slide or membrane was removed from the water and dried under nitrogen for 1 min and then stored in an oven set at 80° C.

General Activation by AMPS. Toluene (100 mL) was added to a Pyrex flask, and then 3-aminopropyltriethoxysilane (AMPS) (0.221 g, 0.01 mol) was

added to make a 0.01 M solution of AMPS. The glass slide, silica, or alumina membrane was then submerged in this solution. The solution was warmed to 80° C and heated for 8 h. The slide, silica, or membrane was removed and rinsed with 100 mL of toluene. The support was then submerged in 40 mL of toluene and placed in a sonicator for 30 min. The slide, silica, or membrane was then rinsed with THF, submerged in 40 mL of THF, and placed on a sonicator for 30 min. The THF was decanted, and the slide, silica, or membrane was stored in dry THF.

General Activation by Cyanuric Chloride. A 0.1 M solution of cyanuric chloride was prepared by adding cyanuric chloride (1.84 g, 0.10 mol) to 100 mL of THF. *N,N*'-diisopropylethylamine (1.0 g 0.77 mmol) was added as proton scavenger. The AMPS glass slide, silica gel, or alumina membrane was submerged into this solution. The flask was gently shaken for 8 h at room temperature. The slide, silica gel, or membrane was removed and rinsed with 100 mL of THF. The slide, silica or membrane was then submerged in 40 mL of THF, and placed on a sonicator for 30 min. This step was repeated one more time in a fresh THF solution. The THF was decanted, and this slide, silica gel or membrane was stored in dry THF.

Addition of 4-Iodoaniline. A 0.1 M solution 4-iodoaniline was prepared by adding 4-iodoaniline (2.19 g, 0.10 mol) to 100 mL of THF. *N,N*'-

diisopropylethylamine (1.0 g 0.77 mmol) was added as a proton scavenger. This solution of iodoaniline was used to cap the inorganic substrate after activation by cyanuric chloride. Into this solution the glass slide was submerged. The flask was gently shaken for 48 h at room temperature. The slide was removed and rinsed with 100 mL of THF. The slide was then submerged in 40 mL of THF, and placed in a sonicator for 30 min; this step was repeated in a fresh THF solution. The THF was decanted, and the glass slide was stored in THF.

Addition of 3-Trifluoromethylbenzylamine. A 0.1 M solution 3-trifluoromethylbenzylamine was prepared by adding 3-trifluoromethylbenzylamine (1.75 g, 0.10 mol) to 100 mL of THF. *N,N*'-diisopropylethylamine (1.0 g 0.77 mmol) was added as a proton scavenger. This solution of trifluoromethylbenzylamine was used to cap the inorganic substrate. Into this solution, the iodoaniline glass slide was submerged, and the flask was gently shaken for 48 h at 80 °C. The slide was removed and rinsed with 100 mL of THF. The slide was then submerged into 40 mL of THF and placed in a sonicator for 30 min; this step was repeated in a fresh THF solution. The THF was decanted and the slide was stored in dry THF.

Addition of 1. A 0.1 M solution **1** was prepared by adding **1** (3.79 g, 0.05 mol) to 50 mL of THF. *N,N*'-diisopropylethylamine (1.0 g 0.77 mmol) was

added as a proton scavenger. This solution of **1** was used to cap the surface of the inorganic substrate after activation by cyanuric chloride. Into this solution, the cyanuric chloride glass slide or silica was submerged. The flask was gently shaken for 48 h at 80° C. The slide or silica was removed and rinsed with 100 mL of THF. The slide or silica was then submerged in 40 mL of THF and placed in a sonicator for 30 min; this step was repeated in a fresh THF solution. This THF was decanted, and the slide or silica was stored in THF.

Addition of 2. A 0.1 M solution **2** was prepared by adding **2** (5.02 g, 0.02 mol) to 50 mL of THF. *N,N*'-diisopropylethylamine (1.0 g 0.77 mmol) was added as a proton scavenger. This solution of **2** was used to cap the surface of the inorganic substrate after activation by cyanuric chloride. Into this solution, the cyanuric chloride glass slide or silica was submerged. The flask was gently shaken for 48 h at 80° C. The slide or silica was removed and rinsed with 100 mL of THF. The slide or silica was then submerged in 40 mL of THF and placed in a sonicator for 30 min; this step was repeated in a fresh THF solution. This THF was decanted, and the slide or silica was stored in dry THF.

General Procedure for the Convergent Strategy. One gram of 3-(1-piperazino)propyl-functionalized silica gel **8** (2.0 mmol N/g) was mixed with 10 mL of THF. Then, 2 mmol of the dendron (**3**, **5** or **7**) and *N,N*'-diisopropylethylamine (0.5 g 0.39 mmol) was added to the THF-silica mixture.

This suspension was heated at reflux with stirring overnight. The silica gel was then washed with 50 mL portions of THF, saturated aqueous $NaHCO_3$, methanol and dichloromethane. The silica gel was then dried under reduced pressure and characterized.

General Procedure for the Divergent Strategy. One gram of **9** was treated with 20 mL of 3 M HCl for 30 min to remove the *t*-Boc-protecting groups. The silica gel was washed with saturated aqueous $NaHCO_3$, and with distilled water. This deprotected silica gel, **10**, was dried under vacuum and characterized. Composite **10** was mixed with 10 mL of THF. Then, **3** (4 mmol) and *N,N*'-diisopropylethylamine (0.5 g 0.39 mmol) were added to the suspension of **10**. The suspension was heated at refluxing temperature and stirred overnight to produce composite **11**. Subsequently, the silica gel was washed with 50 mL portions of THF, saturated aqueous $NaHCO_3$, methanol and dichloromethane. The silica gel was then vacuum dried and characterized. Removal of the *t*-Boc-protecting groups with HCl produces composite **12**. Reaction of **12** with **3** (as described previously) gives composite **13**.

Chemical Etching. The silica gel composites (~50 mg) were placed in plastic vials and dissolved in 0.5 mL of 24% HF aqueous solution and stirred for 1 h. The solvent was evaporated under vacuum to yield a white solid that was analyzed by mass spectrometry.

Atrazine Sequestration. An aqueous solution containing 10 mg/L of atrazine was prepared by stirring 5 mg of atrazine in 500 mL of purified water for about 24 hours at room temperature. A 10 mL aliquot of the atrazine solution was placed in 20 mL glass vial, and 10 mg of the desired organosilica was added. The glass vial was capped and incubated at room temperature while shaking for 18 h. Afterwards, the aqueous solution was filtered, and analyzed by reverse-phase high performance liquid chromatography (HPLC). The area under the atrazine peak was compared to a calibration curve to determine the amount of atrazine left in solution.

Preparation of OTS-Membranes and D2-Cl-Mebranes. The preparation of OTS membranes and D2-Cl membranes are described in Asad Javaid's doctoral dissertation.[109]

General Procedure for the Capping of Membranes with Long-Chain Amines. To a glass beaker, 100 mL of THF was added, and then either dodecylamine (1.85 g, 0.10 mol) or hexadecylamine (2.41 g, 0.10 mol) was added to make a 0.1 M solution of trifluoromethyl-benzylamine. The cyanuric chloride membrane was then submerged in this solution. The flask was gently shaken for 24 h at 80° C. The membrane was removed and rinsed with 100 ml of THF. The membrane was then submerged in 40 ml of THF and placed in a

sonicator for 30 min; this step was repeated with a fresh THF solution. This THF was decanted, and the membrane was stored in dry THF until analysis.

CHAPTER IV

LATENT SOLID-PHASE EXTRACTION USING THERMORESPONSIVE SOLUBLE POLYMERS *

Linear Polymers *versus* Dendrimers. The properties of dendrimers such as discrete molecular weight, exquisite control of functionalities, and the ease of characterization make these molecules ideal candidates for basic research. However the use of linear polymers in applied science is advantageous over dendrimers. The main difficulty of using dendrimers as a part of an applied science is their lengthy preparation. As of now, the laborious polymerization of dendrimers, coupled with the cost of such a polymerization, makes these macromolecules unsuitable candidates for large scale production (such as the production needed for the removal of atrazine runoff accumulated through 50 years of use). On the other hand, we believe that applied dendrimer chemistry can still find applications in the field of drug delivery.[112,113] For this reason, we wanted to apply the knowledge accumulated in our basic investigation of dendrimers for separations to find a suitable polymerization technique that is useful for large scale application.

During our investigations of secondary cyclic amines either in solution as low molecular weight species, as insoluble polymer-bound reagents, or as highly

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branched organic-inorganic hybrids, we determined that this class of nucleophile readily reacts with monochlorotriazines.[30,114] We took note of the work reported by the Bergbreiter group that describes thermoresponsive polymers as a latent solid-phase. The combination of these two chemistries created a collaboration that is the basis for this new latent solid support strategy for chlorotriazine scavenging.

Poly(*N-iso*propylacrylamide) as a "Smart" Material. Solid-phase extractions using insoluble crosslinked polymer supports are a well established method to separate or concentrate trace contaminants from solution.[115,116] Reactive insoluble polymer-bound reagents are also routinely used as scavengers for reagents, by-products or products in solution-state high-throughput synthesis.[117] We describe how poly(*N-iso*propylacrylamide) (PNIPAM) and PNIPAM derivatives can be used as latent solid phase supports for the physical sequestration or reactive scavenging of low concentrations of hydrophobic contaminants from aqueous solutions. PNIPAM is a thermoresponsive polymer that is soluble in water at low temperature, but it has the feature that it quantitatively precipitates from solution above a lower critical solution temperature (LCST).[118] This behavior has been exploited in the design of "smart" materials for catalysis,[119,120] of thermally responsive coatings,[121] for soluble polymeric ligands,[122] in the development of supports for heavy-metal scavenging,[123] and as temperature or pH-sensitive materials in drug delivery

applications.[124] More recently, PNIPAM has been conjugated with a variety of biologically-relevant molecules.[125] Here we expand the use of such thermoresponsive supports for the physical sequestration or reactive scavenging of hydrophobic monochlorotriazines from aqueous solutions.

The polymers and guests used in this study are shown in Figure 4.1. Poly(*N*-*iso*propylacrylamide), **1**, was chosen as an unreactive thermally-responsive polymer. This polymer has an LCST of 30.2 °C.[126] A reactive piperidine-functionalized copolymer, **2**, containing a 95:5 mol:mol mixture of *N*-*iso*propylacrylamide and 4-(acrylamidomethyl)piperidine groups was also prepared. This latter polymer had an LCST of 40 °C. In both cases, solutions of these polymers precipitated above their LCST temperature to form a solid hydrogel phase.[118,126] As shown below, this hydrogel phase can physically absorb a significant amount of a nonpolar monochlorotriazine from a dilute aqueous solution. Incorporation of a nucleophilic secondary amine covalent scavenger produces an even more efficient reactive scavenger. This modified thermally responsive polymer leads to recovery of > 98% of these same monochlorotriazines when compared to **1**. Such sequestration and covalent scavenging, coupled with the ability to effect nearly quantitative removal of the precipitated polymer by filtration or centrifugation makes these and related polymers potential candidates for applications in remediation and scavenging technology.

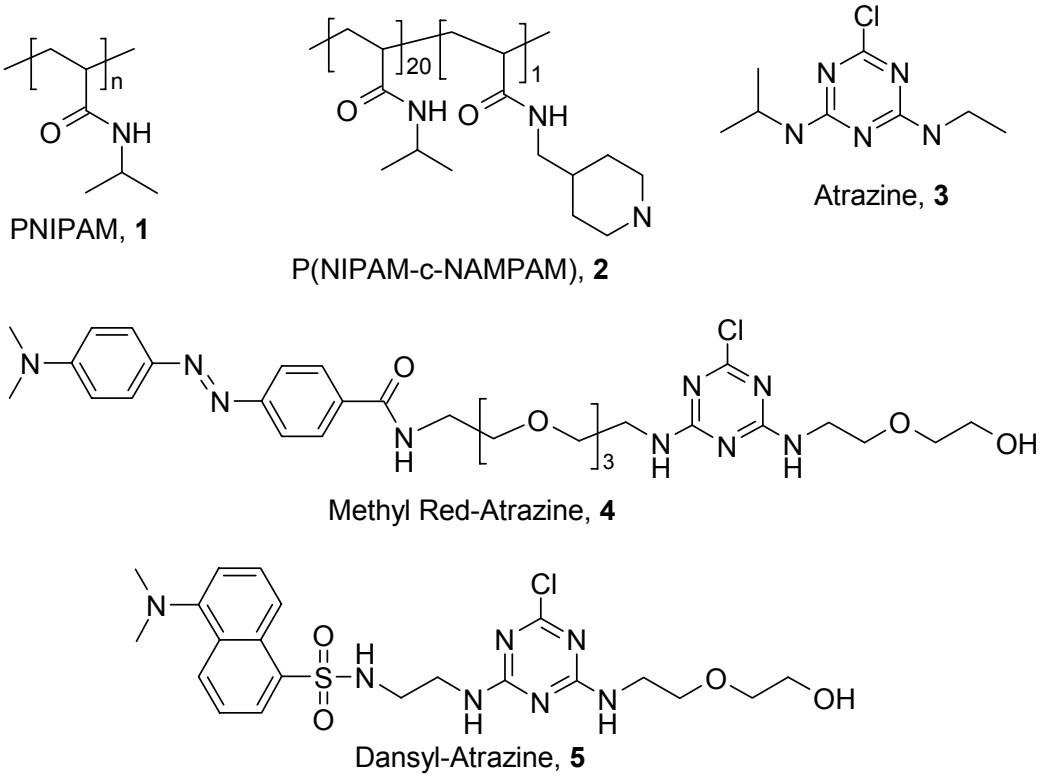
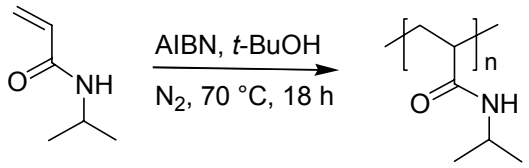


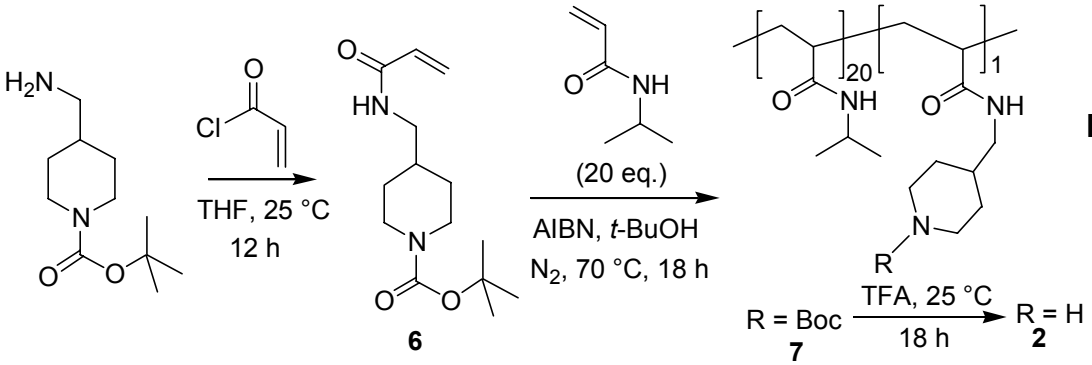
Figure 4.1. Thermoresponsive polymeric sequestration or scavenging agents (**1** or **2**), atrazine (**3**) and dye-labeled atrazine analogs (**4** or **5**).

Polymers and Monochlorotriazines. Atrazine, **3,** was chosen as a substrate because it is an example of an environmental contaminant of current concern. Two more dye-labeled analogs of atrazine examined in this study included the monochlorotriazines **4** and **5**. In one case, an atrazine analog was designed to contain a dansyl group for fluorescence analysis (**5**). In the second case, an atrazine analog was labeled with a methyl red group to facilitate visual and spectrophotometric analysis (**4**). Atrazine (**3**) concentrations were measured by liquid chromatography-mass spectrometry.

Results and Discussion. The thermoresponsive polymers **1** and **2** were prepared to compare physical and chemical scavenging of monochlorotriazines by a latent solid phase extractant. Polymer **1** is a homopolymer of *N-iso*propyl-acrylamide, and was prepared accordingly to eq. 4.1. It was not expected to chemically react with **3**, **4**, or **5**. Polymer **2** is a copolymer of *N-iso*propyl-acrylamide and **6**, and was prepared as shown in eq 4.2. The secondary amine groups in polymer **2** were expected to react in a covalent manner with a monochlorotriazine based on earlier studies.[28,30,114] performed in our research group.



Eq. 4.1



Eq. 4.2

Sequestration Experiments. A general representation of our sequestration procedure is shown in Figure 4.2. In these experiments, an initial homogenous solution of analyte (**3-5**) in water was first prepared. Then, polymer **1** or **2** was added as a solution (in the fast precipitation protocol) or as a solid (in the slow precipitation protocol). The resulting solutions were heated to precipitate the polymer sequestrant or scavenger (15 min for fast precipitation protocol, and 8 h for slow precipitation protocol). Salt was added to facilitate separation of the polymeric precipitate.[127] Separation of the supernatant containing residual monochlorotriazine from the polymer **1** or **2**, and any sequestered monochlorotriazine was then accomplished by centrifugation at temperatures above the LCST of **1** or **2**.

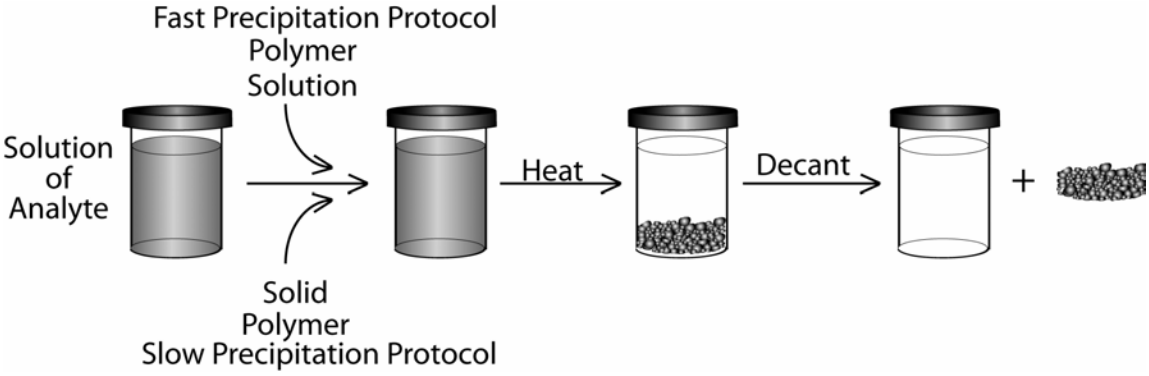


Figure 4.2. The protocols used for sequestration of monochlorotriazines.

The sequestration of analytes **3**-**5** was monitored over a concentration range that varied depending on the analyte. In the case of **3**, relatively low concentrations of *ca*. 100 ppb were used. This level of **3** was studied because the "safe" concentration of atrazine (**3**) in water is 3 ppb, and typical atrazine concentrations in runoff are *ca*. 120 ppb.[31,32] Higher concentrations of 5-10 ppm were used for the dansyl- and methyl red labeled monochlorotriazines. These labeled substrates provided a spectroscopic handle for a higher concentration of atrazine **3** or other chlorotriazine herbicides. In the cases where the reactive polymer **2** was used, the concentration of reactive groups on the polymer was *ca*. 10^{-3} N, which amounted to a >100-fold excess over the concentration of any of the analytes.

Analysis of the effectiveness of polymers **1** or **2** to effect sequestration of monochlorotriazines derivates was carried out using several techniques. For low 100 ppb concentrations of **3**, a LCMS procedure was used. For **5**, fluorescence spectroscopy was used. For the UV-visible dye labeled atrazine analogue **4**, quantitative analysis was carried out by UV-visible spectroscopy, although qualitative visual analyses were also possible. For example, non-covalent sequestration of **4** by **1** was visually evident since both the supernatant and precipitated polymer were visually yellow in color. The solution was nearly colorless when **4** was sequestered by the reactive polymer **2**.

Results of Sequestration. The results of the sequestration experiments are listed in Table 4.1. In general, non-covalent sequestration occurs with all analytes, but a significant amount of the analyte remains in solution regardless of whether a “fast” or “slow” precipitation protocol was used. Quantitative sequestration was achieved using the “slow” precipitation protocol for polymer **2** with all the monochlorotriazine substrates **3** – **5**. However, polymer **2** was not as effective in the “fast” protocol for the most relevant triazine substrate **3**. While the reason for this difference was not examined in detail, we presume it reflects kinetic problems associated with the bimolecular reaction of low concentrations of a substrate like **3,** even in the presence of an excess of amine groups. The rates for complete reaction of a very low concentration of monochlorotriazine with the soluble polymer-bound secondary amine **2** were comparable to the rates seen with insoluble polymer-bound secondary amines which also required extended reaction times to reduce concentrations of **3** to < 1 ppb. There is a notable difference between the effectiveness of polymers **1** and **2**. We attribute the efficiency of **2** to be due to the reactivity of the pendant piperidine groups. These groups can undergo nucleophilic aromatic substitution with monochlorotriazines derivatives.

Table 4.1. Sequestration of atrazine (**3**) or atrazine analogs **4** or **5** from dilute aqueous solutions using thermally responsive polymers **1** and **2**.

	Fast Precipitation Protocol			Slow Precipitation Protocol		
Polymer	Analyte	Initial [Analyte]	% Sequestered[a]	Analyte	Initial [Analyte]	% Sequestered[a]
1	**3**	96 ppb	46	**3**	100 ppb	56
	4	6.4 ppm	78	**4**	8 ppm	83
	5	8 ppm	60	**5**	10 ppm	71
2	**3**	96 ppb	72	**3**	100 ppb	> 99[b]
	4	6.4 ppm	97	**4**	8 ppm	98
	5	8 ppm	96	**5**	10 ppm	98

[a]The values for the % sequestered are based on the average of two experiments in each case. [b]The concentration of atrazine remaining in the solution was below the detection limit (1 ppb) of the LCMS analysis.

Non-covalent v*ersus* Covalent Sequestration. Distinguishing between non-covalent sequestration and covalent sequestration was possible using a simple thin layer chromatography experiment. When a precipitate formed from reaction of **2** with **4** or of **1** with **4** using either the “slow” or “fast” protocol was redissolved, a qualitative analysis of the solution indicated that most of the dye was back in solution. This result superficially corresponds to earlier results, where most of the atrazine sequestered by an insoluble reactive polymer could be released from the polymer by an acid digestion. However, the qualitative

reappearance of color in a solution of redissolved polymer does not distinguish between non-covalent and covalent sequestration of **4** by the polymer. TLC experiments were successful in making this distinction. When a precipitate of polymer **2** that had essentially quantitatively sequestered **4** was spotted on a TLC plate and developed with CH_2Cl_2-MeOH (10:1), the only dye species detectable was a species at the origin. Under the same conditions, **4** had an R_f of *ca*. 0.35 (Figure 4.3). In a similar experiment, TLC of a solution prepared from a precipitate of **4** and **1** (a precipitate that was presumed to be a physical mixture of **1** and **4**) had a spot at an R_f of 0.35 coincident with the R_f of free **4**. TLC experiments using the products from the coprecipitation of **1** and **5**, or of **2** and **5**, had similar results. In the latter case, no free **5** was detected by TLC when the precipitate of **2** and **5** was redissolved. In the former case with physical entrapment, a fluorescent spot for free **5** was detectable by TLC when the precipitate of **1** and **5** was redissolved.

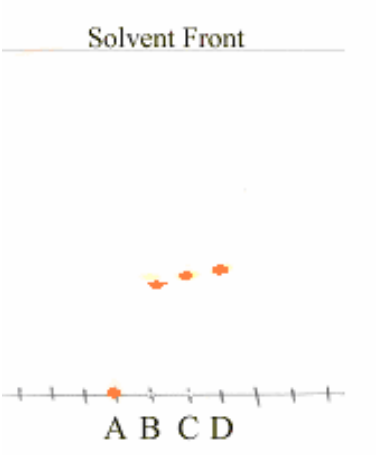


Figure 4.3. TLC plate to corroborate the covalent sequestration of **4**. TLC spots of polymer **2** (**A**) and polymer **1** (**B**) after sequestration of **4**. Co-spot of **4** added to polymer **1** after sequestration of methyl red atrazine (**C**). Spot for methyl red atrazine **4** (**D**).

Conclusions. The experiments above show that soluble polymers that precipitate under mild heating can serve both as physical and chemical sequestrants. In the case of chlorotriazines, chemical sequestration using a functional polymer containing a secondary amine is significantly more successful at sequestering a chlorotriazine. Quantitative sequestration of trace quantities of a chlorotriazine requires an 8 h reaction.

Synthesis of Analytes and Polymers. All reagents and solvents were obtained from commercial sources and used without further purification unless specified. ^{1}H NMR spectra were obtained on Varian Inova 300, Mercury 300, or Inova 500 spectrometers operating at 300 or 500 MHz. ^{13}C NMR spectra were

obtained on Varian Inova 300, Mercury 300, or Inova 500 spectrometers operating at 75 or 125 MHz. ^{1}H and ^{13}C chemical shifts are reported in ppm referenced to tetramethylsilane or residual solvent peaks, respectively. Light scattering experiments were carried out using a Brookhaven Instruments BI-200SM goniometer, BI-9000AT digital correlator, and a Melles Griot HeNe laser. M_w analysis of light scattering data was performed using Brookhaven Instruments Zimm Plot Software.

Poly(*N*-Isopropyl-Acrylamide) (1). This material was prepared according to a literature procedure.[126]

Atrazine (3). This material was prepared according to a literature procedure.[128]

***N*-(2-{2-[2-(2-{4-Chloro-6-[2-(2-Hydroxyethoxy) Ethylamino]-[1,3,5]Triazin-2-Amino}-Ethoxy)Ethoxy]Ethoxy}Ethyl)-4-(4-Dimethylaminophenylazo)Benzamide (Methyl Red Atrazine, 4).** A solution of **8** (100 mg 0.226 mmol) in 40 mL of THF was added to an ice-cold solution of cyanuric chloride (40 mg, 0.217 mmol) and *N,N-diisopropylethylamine* (0.2 mL, 1.4 mmol) in 10 mL of THF. The reaction mixture was stirred for 4 h at 0 °C, and then warmed to 25 °C. 2-(2-Aminoethoxy)ethanol (0.15 mL 1.4 mmol) was then added to the reaction flask, and the mixture was stirred at 25 °C for 8 h. The

solvent was removed under reduced pressure, and the crude product was dissolved in 150 mL of CH_2Cl_2. The organic solution was washed with 0.1 M aqueous acetic acid (2 x 100 mL), saturated aqueous $NaHCO_3$ (3 x 100 mL), and brine (2 x 100 mL). The organic solvent was removed under reduced pressure, and the crude product was purified by column chromatography (19:1 CH_2Cl_2:MeOH, with 0.5 % NH_4OH). The solvent was removed under reduced pressure, and the resulting red crystals were dried under vacuum to yield 90 mg (60%) of the product **4**. ^1H NMR ($CDCl_3$) δ 3.19 (6H, s), 3.39-3.82 (24H, m), 5.91 (1H, bs), 6.05 (1H, bs), 6.74 (2H, d, *J* = 8.8 Hz), 7.07 (1H, bs), 7.88 (2H, d, *J* = 8.8 Hz), 7.92 (2H, d, *J* = 8.8 Hz); ^{13}C NMR ($CDCl_3$) δ 30.23, 39.73, 40.20, 40.53, 61.46, 69.22, 69.66, 70.05, 70.22, 70.38, 72.28, 111.34, 121.98, 125.27, 127.88, 127.93, 134.45, 134.62, 143.46, 152.67, 154.78, 165.20, 165.46, 167.15, 168.27. MS (ESI): calcd for $C_{30}H_{42}N_9O_6Cl$: 659.29; found 660.29 $(M+H)^+$, 330.65 $(M+2H)^{2+}$. A standard solution of 8.0 ppm of **4** was prepared by dissolving 8.0 mg of **4** in 1.0 mL of DMSO. This solution was diluted to 1 L by the addition of distilled water in a volumetric flask. Further dilutions using serological pipettes and volumetric flasks were carried out to prepare solutions of 0.08, 0.80, 1.60, 4.00, 5.60 ppm. The concentrations of **4** in water were determined by measuring the absorbance at λ_{max} = 474 nm. UV-visible analysis of a series of aqueous solutions of **4** showed that the extinction coefficient of **4** was 29,960.

5-Dimethylaminonaphthalene-2-Sulfonic Acid ({4-Chloro-6-[2-(2-Hydroxyethoxy)Ethyl-Amino]-[1,3,5]Triazin-2-Amino}Methyl)Amide (Dansyl Atrazine, 5). 5-Dimethylaminonaphthalene-1-sulfonic acid (2-aminoethyl)amide (dansylamine) (50 mg, 0.17 mmol) was added to an ice-cold solution of cyanuric chloride (30 mg, 0.16 mmol) and *N,N*-diisopropylethylamine (0.2 mL, 1.4 mmol) in 10 mL of THF. The reaction mixture was stirred for 1 h at 0 °C and then warmed to 25 °C. 2-(2-Aminoethoxy)ethanol (0.15 mL 1.4 mmol) was then added to the reaction flask and the mixture was stirred at 25 °C for 8 hours. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (19:1 CH_2Cl_2:MeOH, with 0.5 % NH_4OH). The solvent was removed under reduced pressure and the resulting product was dried under vacuum to yield 70 mg (80%) of the product **5**. ^{1}H NMR ($CDCl_3$) δ 2.83 (6H, s), 2.93 (2H, m), 3.21 (2H, m), 7.25 (1H, d, *J* = 8 Hz), 7.60 (3H, m), 7.70 (1H, t, *J* = 6 Hz), 7.81 (1H, t, *J* = 6 Hz), 8.10 (1H, m), 8.25 (1H,m), 8.45(1H, d, *J* = 8 Hz); ^{13}C NMR ($CDCl_3$) δ 45.06, 60.17, 68.38, 72.05, 72.17, 115.10, 118.95, 123.52, 127.83, 128.15, 129.04, 129.44, 135.88, 151.34, 165.21, 165.45, 167.55, 168.06. MS (ESI): calcd for $C_{21}H_{28}N_7O_4ClS$: 509.16; found 510.18 $(M+H)^+$. A standard solution of 10.0 ppm of 5 was prepared by dissolving 10 mg of 5 in 1.0 mL of DMSO. This solution was diluted to 1 L by the addition of distilled water in a volumetric flask. Concentrations of **5** were determined by fluorescence spectroscopy using a λ_{Ex} at 357 nm and a λ_{Em} at 548 nm.

4-(Aminomethyl)Piperidine-1-Carboxylic Acid *tert*-Butyl Ester. This material was prepared according to a literature procedure.[129]

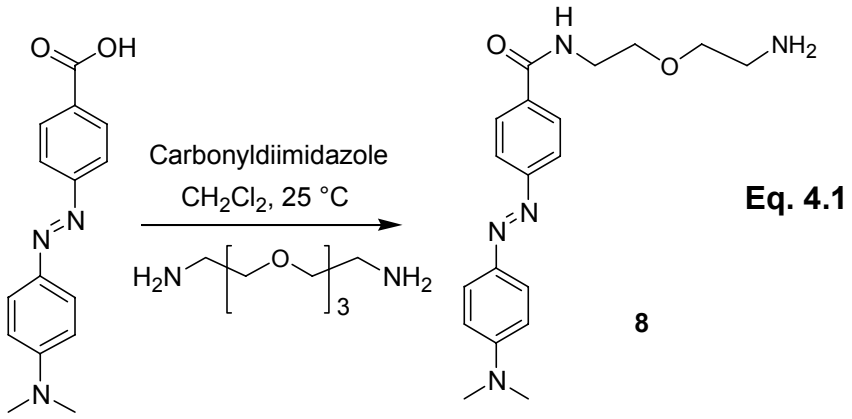
4-(Acryloylaminomethyl)Piperidine-1-Carboxylic Acid *tert*-Butyl Ester (6). A solution of acryloyl chloride (3 g, 33 mmol) in 100 mL of THF was added dropwise to a solution of 4-(aminomethyl)piperidine-1-carboxylic acid *tert*-butyl ester (5 g, 23 mmol) and triethylamine (2.5 mL, 19 mmol) in 100 mL of THF over 6 h. The reaction was stirred at 25 °C for an additional 6 h. The solvent was removed under reduced pressure, and the resulting oil was dissolved in 200 mL of CH_2Cl_2. The solution was washed with aqueous acidic acid 0.1 M (3 x 100 mL), saturated aqueous $NaHCO_3$ (3 x 100 mL), brine (3 x 100 mL), and was then dried over $MgSO_4$ overnight. Following filtration, the solvent was removed under reduced pressure, and the resulting oil was dried under reduced pressure, yielding 5.56 g (90%) of the product **6**. ^{1}H NMR ($CDCl_3$) δ 6.28 (1H, dd), 6.11 (1H, dd), 5.64 (1H, dd), 4.07 (2H, bs), 3.12 (2H, bs), 2.66 (2H, bs), 1.67 (3H, m), 1.43 (9H, s), 1.11 (2H, m); ^{13}C NMR ($CDCl_3$) δ 165.96, 155.03, 130.98, 126.75, 79.66, 45.16, 36.63, 30.00, 28.66. MS (ESI): calcd for $C_{14}H_{24}N_2O_3$: 268.18; found 269.17 $(M+H)^+$, 291.15 $(M+Na)^+$.

4-(Acryloylaminomethyl)Piperidine-1-Carboxylic Acid *tert*-Butyl Ester (7). A solution of *N-iso*propylacrylamide (10.95 g, 97.00 mmol) and **6** (1.3 g, 4.80 mmol) in 200 mL of *tert*-butanol was degassed and heated to 70 ºC

under positive pressure of N_2. Then, a degassed solution of 2,2´-azo*bisiso*butylnitrile (30 mg, 0.18 mmol) in 15 mL of *tert*-butanol was added to the reaction flask via forced siphon. After 18 h of heating, the solvent was removed under reduced pressure, and the polymer product was dried under vacuum. The crude product was dissolved in 150 mL of THF and purified by precipitation using 2 L of hexanes to yield 11.03 g (90%) of the product. ^{1}H NMR ($CDCl_3$) ȡ 6.30 (21H, bs), 4.00 (20H, bs), 2.60-1.50 (56H, bm), 1.45 (9H, s), 1.18 (120H, bs).

Poly(*N*-Isopropylacrylamide)-C-Poly(*N*-4-(Acrylamidomethyl)Piperidine-1-Carboxylic Acid *tert*-Butyl Ester) (8). This amine terminated hydrophilic derivative of methyl red was prepared as shown in eq. 4.3. A solution of *p*-dimethylaminoazobenzene-*p*-carboxylic acid (1.75 g, 6.6 mmol) and 1,1´-carbonyldiimidazole (1.07 g, 6.6 mmol) in 100 mL of CH_2Cl_2 was stirred at 25 °C under N_2 for 5 h. The solution was then transferred to an addition funnel, and added dropwise to a solution of 2-{2-[2-(2-aminoethoxy)ethoxy]ethoxy}-ethylamine (8.82 g, 46 mmol) in 250 mL of CH_2Cl_2 under N_2. Once all of the activated acid solution was added, the mixture was stirred for 8 h under N_2. The solution was then washed with water (4 x 125 mL), and brine (4 x 125 mL), and then dried over $MgSO_4$. The solvent was removed under reduced pressure and the resulting red oil was dried under vacuum to yield 2.61 g (90%) of the product **8**. ^{1}H NMR $CDCl_3$ ȣ 2.83 (2H, bs), 3.10 (6H, s),

3.47 (2H, t, *J* = 5.3 Hz), 3.56-3.76 (14H, m), 6.76 (2H, d, *J* = 8.5 Hz), 7.59 (1H, bs), 7.86 (2H, d, *J* = 8.5 Hz), 7.89 (2H, d, *J* = 8.5 Hz), 7.97 (2H, d, *J* = 8.5 Hz); ^{13}C NMR ($CDCl_3$) δ 39.83, 40.24, 41.41, 53.40, 69.96, 69.99, 70.14, 70.38, 70.47, 72.75, 111.39, 122.00, 125.29, 128.09, 134.74, 143.56, 152.69, 154.84, 167.14. MS (ESI): calcd for $C_{33}H_{33}N_5O_4$: 443.25; found 444.22 $(M+H)^+$, 222.60 $(M+2H)^{2+}$.



Eq. 4.1

8

Poly(*N*-Isopropylacrylamide)-C-Poly(*N*-4-(Acrylamidomethyl))-Piperidine (2). A solution of **7** (5.00 g, 2 mmol) was added to 100 mL of TFA, and the resulting mixture was stirred at 25 °C for 18 h. The solvent was removed under reduced pressure, and the polymer product was dissolved in 100 mL of ice-cold deionized water. Saturated aqueous Na_2CO_3 was added until the polymer solution was basic (pH~9 by pH paper). The polymer precipitate that formed was separated from the supernatant solution using centrifugation at 50

°C (1,500 rpm) for 1 h followed by decantation of the supernatant. The solid polymer product was dissolved in 100 mL of ice-cold deionized water, and separated again as a solid after a second centrifugation at 50 °C (1,500 rpm) for 1h. On some occasions the centrifugation produced a milky suspension. In those cases, brine was added. This facilitated formation of a separable solid after centrifugation. After centrifugation, the supernatant was separated from the solid polymer product by decantation. This process was repeated a total of 3 times. The white solid polymer product was dried under vacuum. The polymer was added to 75 mL of THF and stirred for 1 h. The resulting THF solution contained a small amount of solid that was separated by centrifugation. Then the polymer product was recovered as a precipitate by slowly adding this THF solution to 800 mL of hexanes. The polymer powder **2** obtained in this way was dried to yield 4.32 g (90%) of product. ^{1}H NMR ($CDCl_3$) δ 6.30 (21H, bs), 4.00 (20H, bs), 2.60-1.50 (56H, bm), 1.18 (120H, bs). M_w = 3.8 x10^5 g/mol (light scattering in MeOH using literature value for the parent polymer PNIPAM of 0.201 mL/g for dn/dc.).[130]

Analytical Procedures. UV-Vis spectroscopic measurements were performed on a Cary 100 UV-Visible spectrophotometer. Fluorescence spectroscopic analyses were carried out on either a Fluorolog-3 spectrofluorometer or on a SLM-Aminco spectrofluorometer. LC-MS experiments were conducted on a Waters XTerra MS using a 2.0-mm × 150-mm

C18 column, eluting fractions with a 60:40 water:methanol gradient. Total ion count (area under the curve) was determined after atmospheric pressure chemical ionization using a Thermofinnigan LC Q Deca mass spectrometer and was compared to a calibration curve.

Polymer Solutions. Stock solutions of polymers **1** and **2** (50 mg/mL) in water were prepared by adding 2 g of polymer **1** or **2** to flasks equipped with magnetic stirring bars containing 40 mL of distilled water. The flasks were then placed in an ice bath and stirred for 2 h until the polymers dissolved.

Solutions of 3 for LC-MS Analysis. Two stock solutions of **3** were prepared. For the fast precipitation protocol, a solution of 12.0 ppm of **3** was prepared by dissolving 12.0 mg of **3** in 1 mL of DMSO and diluting it to 1 L in a volumetric flask by the addition of distilled water. The solution was diluted to a concentration of 120 ppb, by taking 10.0 mL of this 12.0 ppm solution and diluting it to 1 L in a volumetric flask with distilled water. Further dilutions using serological pipettes and 100-ml volumetric flasks were carried out to prepare solutions with 1.2, 9.6, 12.0, 24.0, 48.0, 60.0, and 96.0 ppb concentrations of **3**. These solutions were used to make the calibration curve. For the slow precipitation protocol, a solution of 10 ppm of **3** was prepared.

Fast Precipitation Protocol. A 8 mL solution of analytes **3**-**5** were placed in a 40 mL centrifuge tube. A previously prepared solution of either polymer **1** or **2** was added (2 mL, 100 mg of polymer) to the desired analyte solution. Within 5 min of mixing, the solution was heated in an oil bath for 15 min at 40 °C for solutions containing polymer **1**, and 60 °C for 15 min for solutions containing polymer **2**. A 100 mg portion of NaCl was added, and the polymer that precipitated (**1** or **2**) was separated from the supernatant by centrifugation at 55 °C (463 g, 20 min). The supernatant was then decanted and analyzed by liquid chromatography mass spectrometry, UV-Vis spectroscopy, or fluorescence, spectroscopy for analytes **3**-**5** respectively.

Slow Precipitation Protocol. A 10 mL solution of analytes **3**-**5**, were placed in a 40 mL centrifuge tube. Either polymer **1** or **2** was added (100 mg) as a solid to the analyte solution. The polymer was dissolved by placing the flask in an ice bath. The process of dissolving the polymer took between 1 to 1.5 h. The resulting solution was then heated in an oil bath for 8 h at 40 °C for solutions containing polymer **1**, and at 60 °C for 8 h for solutions containing polymer **2**. A 100 mg portion of NaCl was added, and the polymer precipitate (**1** or **2**) was separated from the supernatant by centrifugation at 55 °C (463 g, 1 h). The supernatant was then decanted and analyzed by liquid chromatography mass spectrometry, UV-Vis spectroscopy, or fluorescence, spectroscopy for analytes **3**-**5** respectively.

CHAPTER V

CONCLUSION

Dendrimer chemistry was born in the laboratories of Vögle in the middle of the 1970's. Later papers discuss the synthesis and characterization of such molecules and the elegance of a stepwise polymerization to produce monodiperse molecules. A rapid interest on the properties of such discrete and well-characterized architectures grew exponentially. By the middle of the 1990's research of dendrimers discuss the possibilities of using them in a variety of applications.

A similar journey was followed in the research presented in this dissertation. Melamine-based dendrimers were first prepared in our laboratory about the same time that the research in this dissertation began. A continuation and complementation to the early work of melamine-based dendrimers was presented in Chapter II. The synthesis of the dendrimer presented was significant to complete the structure-activity relation of this new family of dendrimers. The results presented help us to understand the self-recognition and hydrogen bonding properties of melamine-based dendrimers.

The journey takes a new direction in Chapter III. In research, there is a basic drive to find an application from the basic science. We were successful in showing the capacity of melamine-based molecules to be grafted in different types of inorganic supports. Furthermore, we showed the ability of these

materials to sequester and separate small organic molecules. These types of applications have important consequences in environmental and industrial chemistry.

The research was completed with the demonstration that we can use what was learned from basic research and apply it into other technologies. In Chapter IV, we show the advantage of using a latent solid phase to separate small analytes from an aqueous solution. In addition, we used some of knowledge we gained from the use of dendrimers on surfaces for separation and applied to a different technology. We knew that the use of secondary amines to sequester monochlorotriazines was practical. Therefore, we synthesized a polymer that had pedant secondary amines to sequester the herbicide atrazine, and atrazine-like analytes from solution.

This dissertation demonstrates the skill in taking a research subject from the very basic questions of bio-physico-chemical properties to the possibility of discovering an applied technology.

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102 The shorter retention time for **2** is not a reflection of a difference in size between it and **1** but instead reflects a replumbing of the instrument and our desire not to remake a majority of the samples. When **1** is reanalyzed on the replumbed instrument, no appreciable differences in retention times are observed between it and **2**.

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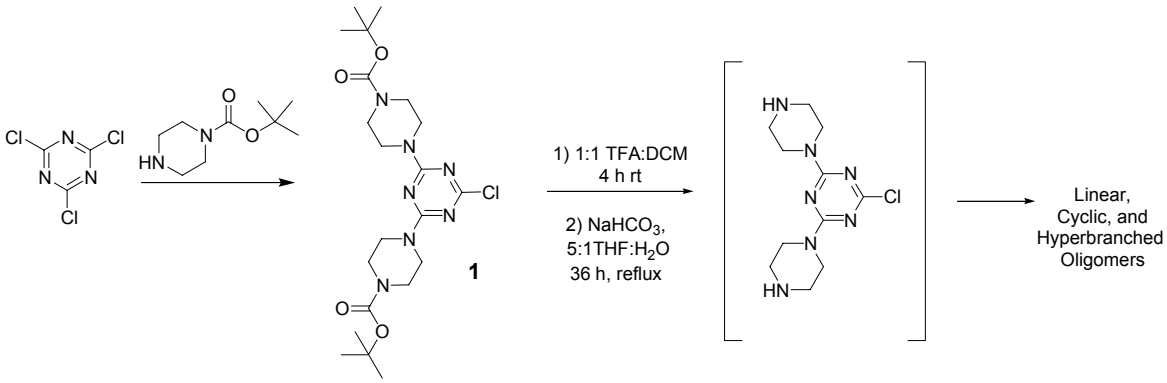
APPENDIX A

HYPERBRANCHED POLYMERS

Melamine-Based Hyperbranched Polymers. In our efforts to investigate melamine-based macromolecules with dendritic architectures, we began studies in hyperbranched polymers. Hyperbranched polymers were first described in a theoretical paper by Flory in 1952.[1] These polymers often give rise to dendritic shapes without the effort required for true dendritic architecture. The degree of branching in a polymer lies between 0 (as in a linear polymer) and 1 (as in a dendrimer). In general hyperbranched polymers have more dendritic character than linear charater. That is to say the degree of branching is greater than 0.5.[2] Hyperbranched polymers are usually prepared from an A_nB_m monomer (where n is usually 1, and m is usually > 2, But m > n). The monomer we chose to polymerize is the monochlorotriazine **1** illustrated in Scheme A.1. This monomer is prepared from the substitution of two chlorine atoms in cyanuric chloride with piperazine-1-carboxylic acid tert-butyl ester (monoboc-pipearzine). This monomer is then deprotected with a 1:1 solution of triflouro acetic acid (TFA) and dichloromethane (DMC). After four hours, the solvent was removed under reduced pressure and the resulting oil was dissolved in tetrahydrofuran (THF). Sodium bicarbonate was added as a solution (1 M) in water, the reaction was heated to reflux and run for 24 or 60 hours. The resulting material is analyzed by ^{1}H NMR and mass spectrometry.



Scheme A.1

Results and Discussion. The highest molecular weight observed for this polymerization corresponded to the 16-mer oligomer. No high molecular weight polymer was observed by mass spectrometry. Figure A.1 is the mass spectrum of the reaction after 24 hours. As we can see there is evidence for oligomers from the dimmer (label M2) to a dodemer that is missing 36 mass units (label M12 – HCl). We presume that this loss of mass is due to cyclization of the oligomers. This phenomenon as been observed by Wooley and coworkers while polymerization of fluorinated ethers.[3] The weight of the monomer is calculated to be 247 mass units and is consistent with the differences in molecular weight observed from one oligomer to the next. From the data in Figure A.1 we can see that no cyclic product smaller than a tetramer is observed. Lowe and group synthesize a cyclic trimer based on triazine and phenylenediamine linkers.[4] They also reported a second trimer based on triazine and piperazine. We did not observe a trimer. If the reaction is run for 60

hours the dimers and trimers disappear, also the peak belonging to uncyclic material become smaller and disappear. Also the longer reaction time gives us bigger macroclycles up to the hexadecamer. We know that more work needs to be done in this area. Investigation of the structures and sizes of the macrocycles will be an important addition to this research. Since the cyclization is ending the reactivity of the polymer hyperbranched chains, different conditions must be used to create higher molecular weights.

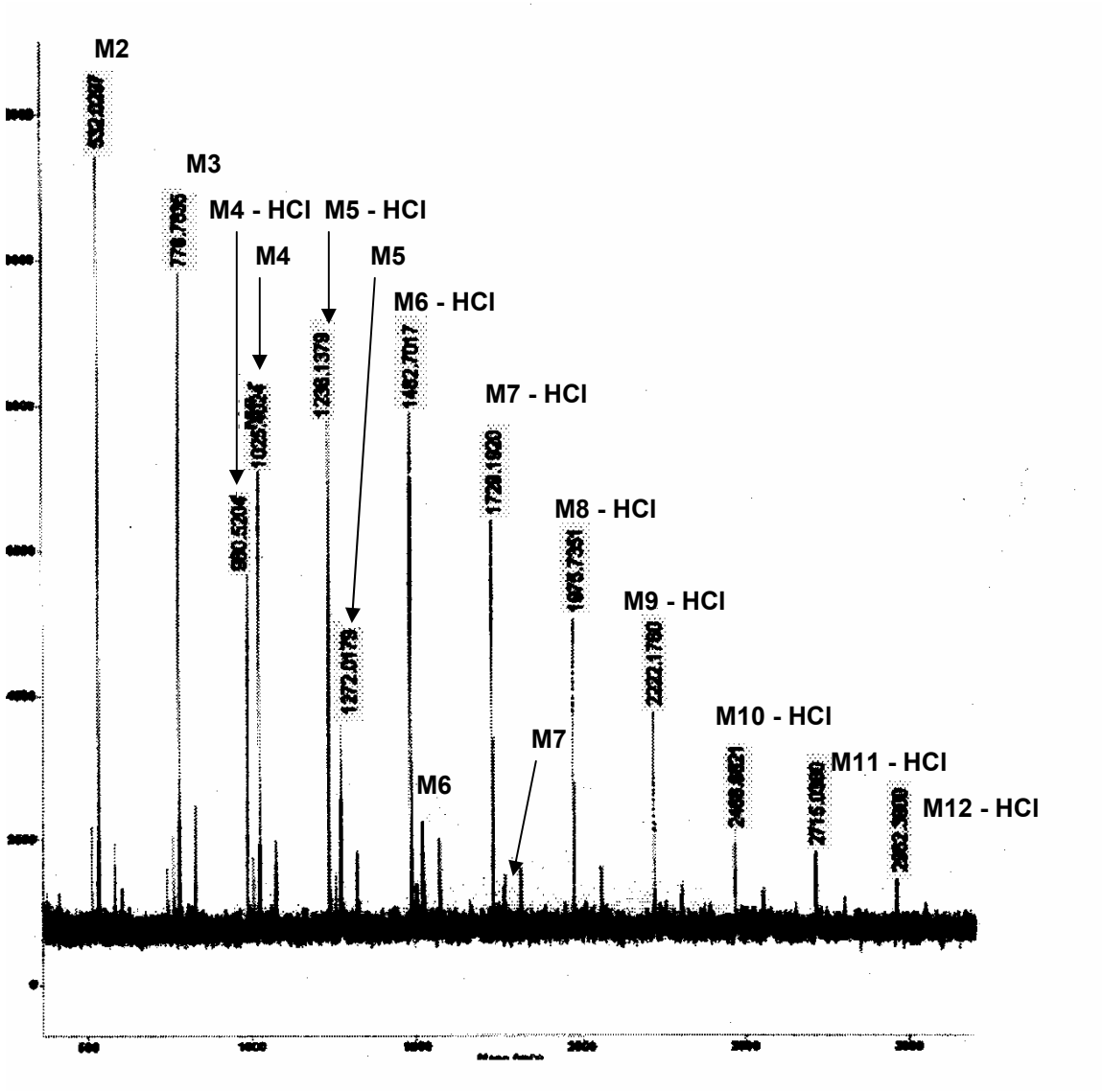


Figure A.1. MALDI mass spectrometry of the polymerization run for 24 hours.

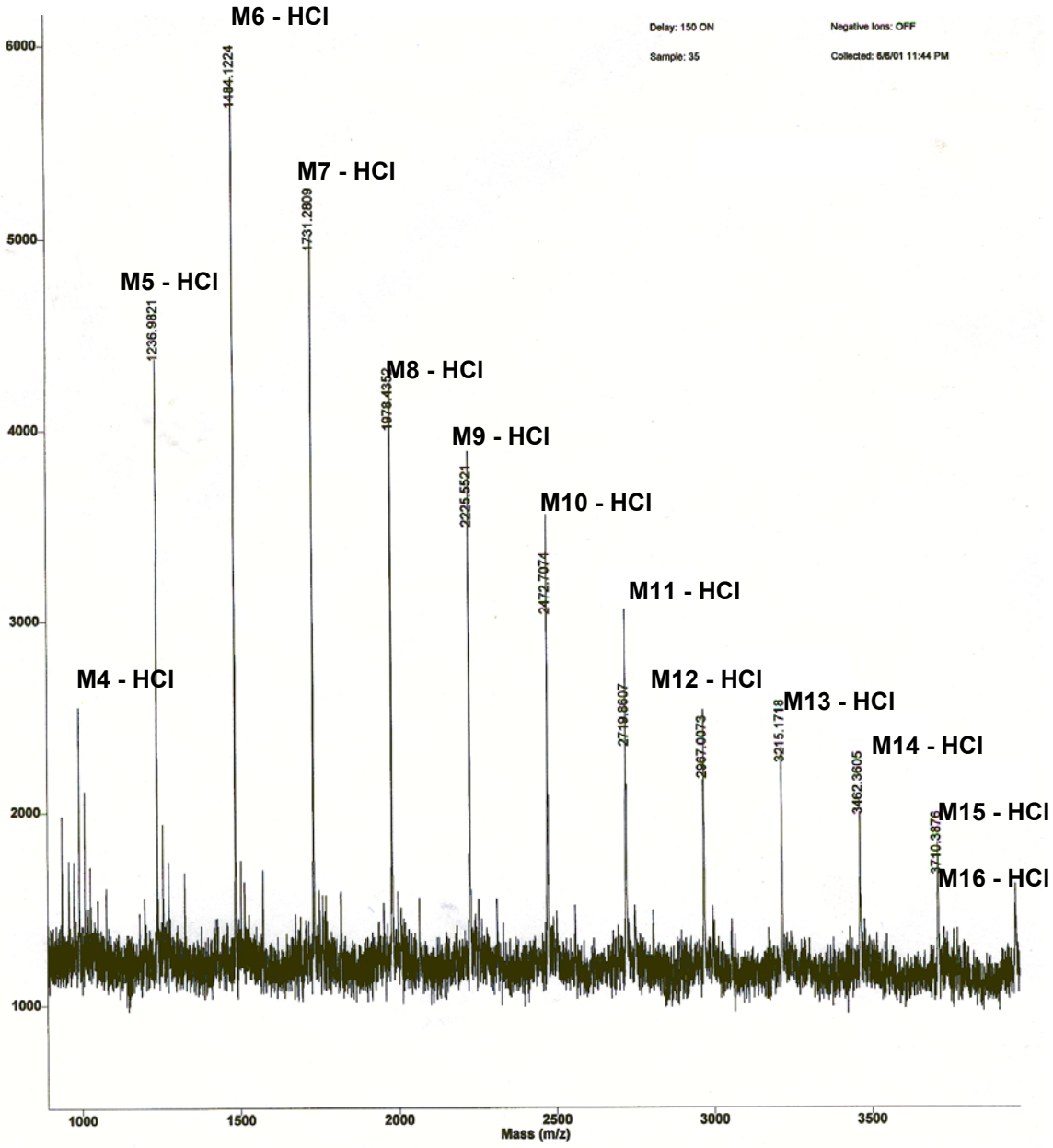


Figure A.2. MALDI mass spectrometry of the polymerization run for 60 hours.

General. All reagents and solvents were obtained from commercial sources and used without further purification unless specified. ^{1}H NMR spectra were obtained on Varian Inova 300, Mercury 300, or Inova 500 spectrometers at 300 or 500 MHz. ^{13}C NMR spectra were obtained on Varian Inova 300, Mercury 300, or Inova 500 spectrometers at 75 or 125 MHz. ^{1}H and ^{13}C chemical shifts are reported in ppm referenced to tetramethylsilane or residual solvent peaks, respectively.

Synthesis of 1. Synthesis of **1** is described in chapter III.

Polymer Synthesis. Monomer **1** (100 mg, 207 mmol) was dissolved in 50 mL of a solution of 1:1 TFA:DCM. The solution was stirred for 4 h at room temperature. The solvent was removed under reduced pressure. The resulting gel was dissolved in 30 mL of THF and 20 mL of a 0.1 M solution of sodium bicarbonate was added. The reaction was heated to reflux and run for either 24 h or 60 h. The solvent was removed under reduced pressure and the resulting material was wash with ether. ^{1}H NMR ($CDCl_3$) δ 4.40 – 3.35 (70 H, b), 3.30 – 2.80 (b, 30 H).

REFERENCES AND ASSOCIATED SPECTRA FOR APPENDIX A.

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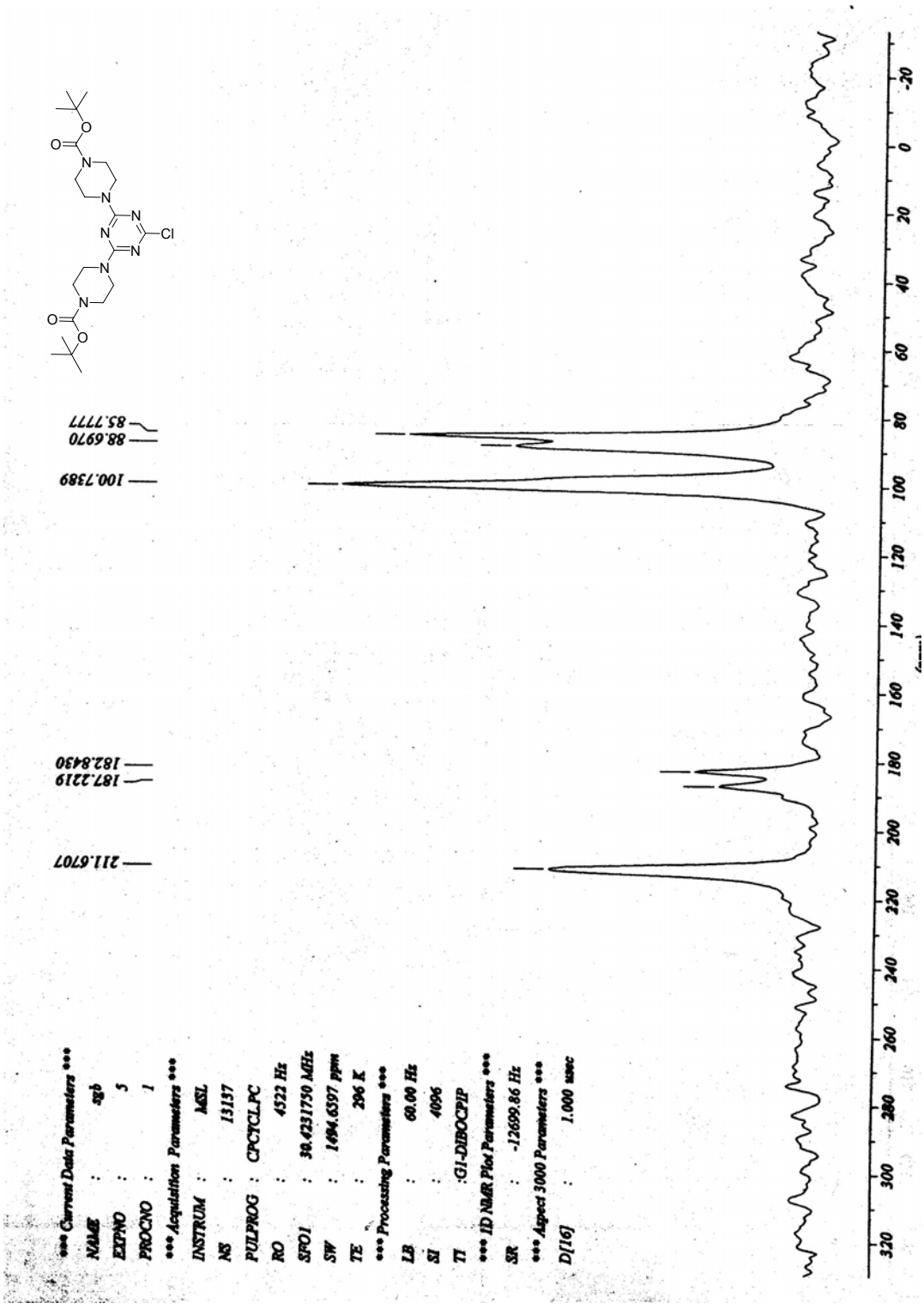

Figure A.3. ^{15}N solid state NMR spectrum of **1**.

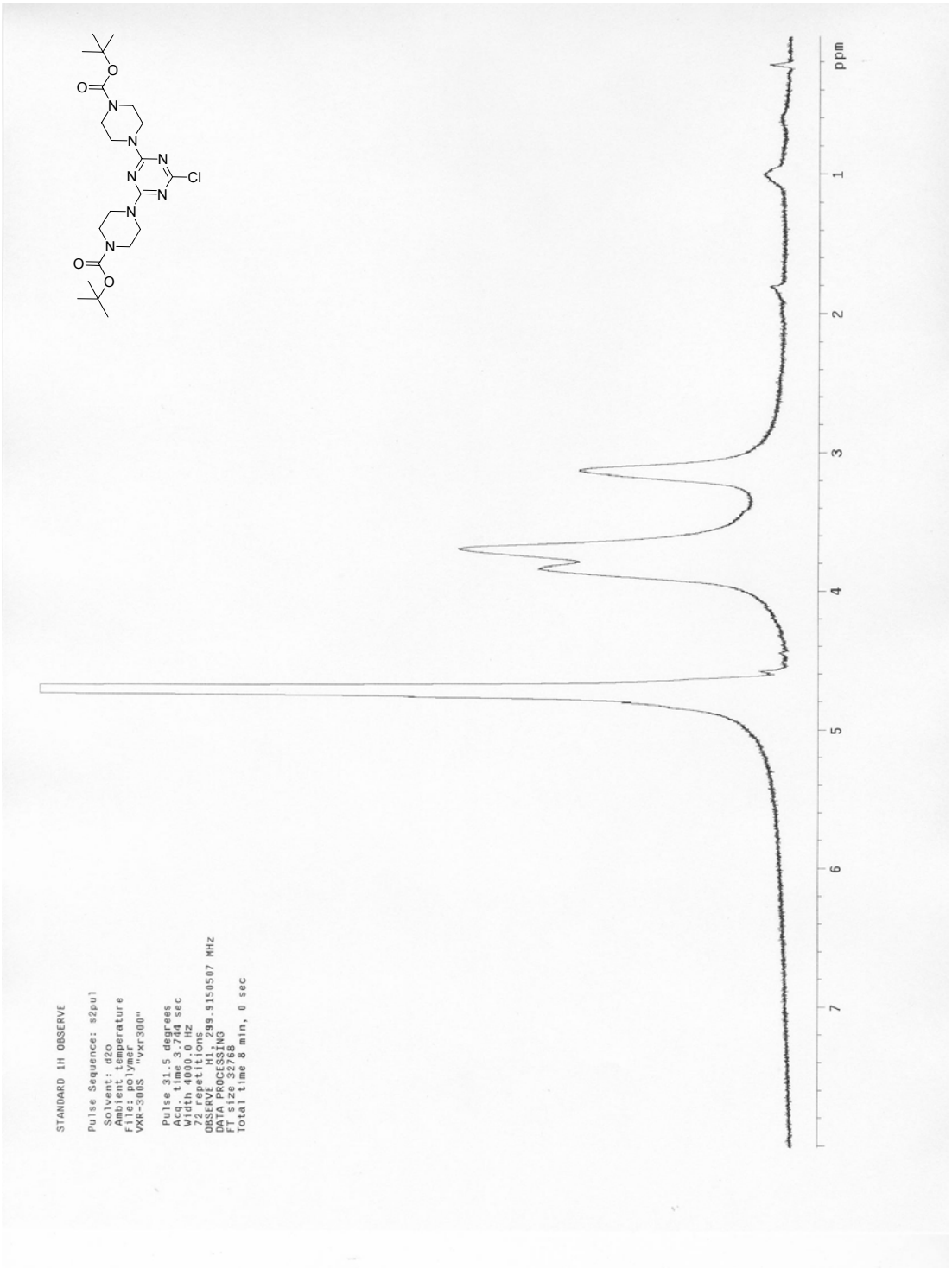

Figure A.4. ^{1}H NMR spectrum of polymer.

APPENDIX B

SPECTRA RELEVANT TO CHAPTER II

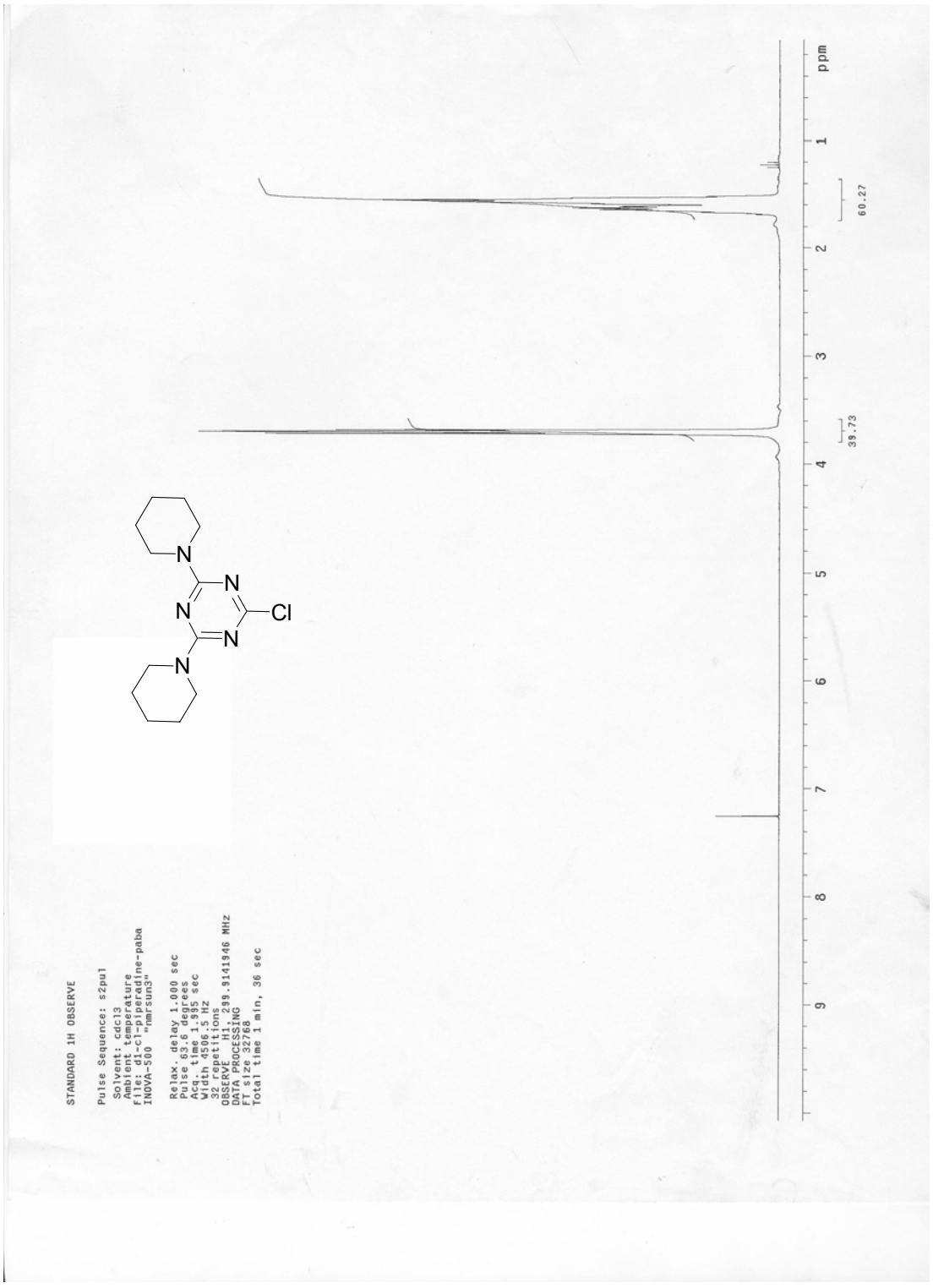

Figure B.1. ^{1}H NMR of spectrum of **9**.

Figure B.2. ^{13}C NMR spectrum of **9**.

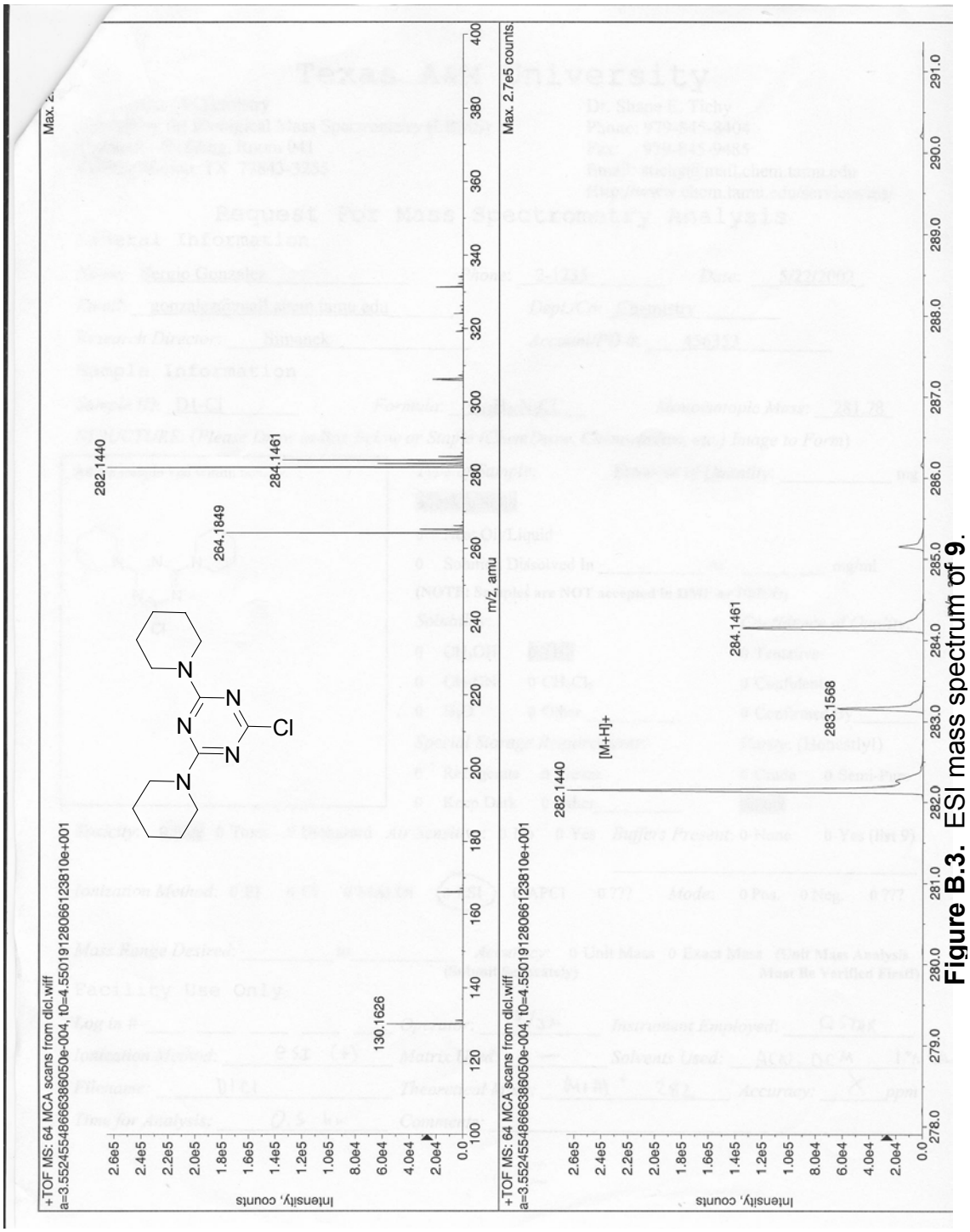

Figure B.3. ESI mass spectrum of **9**.

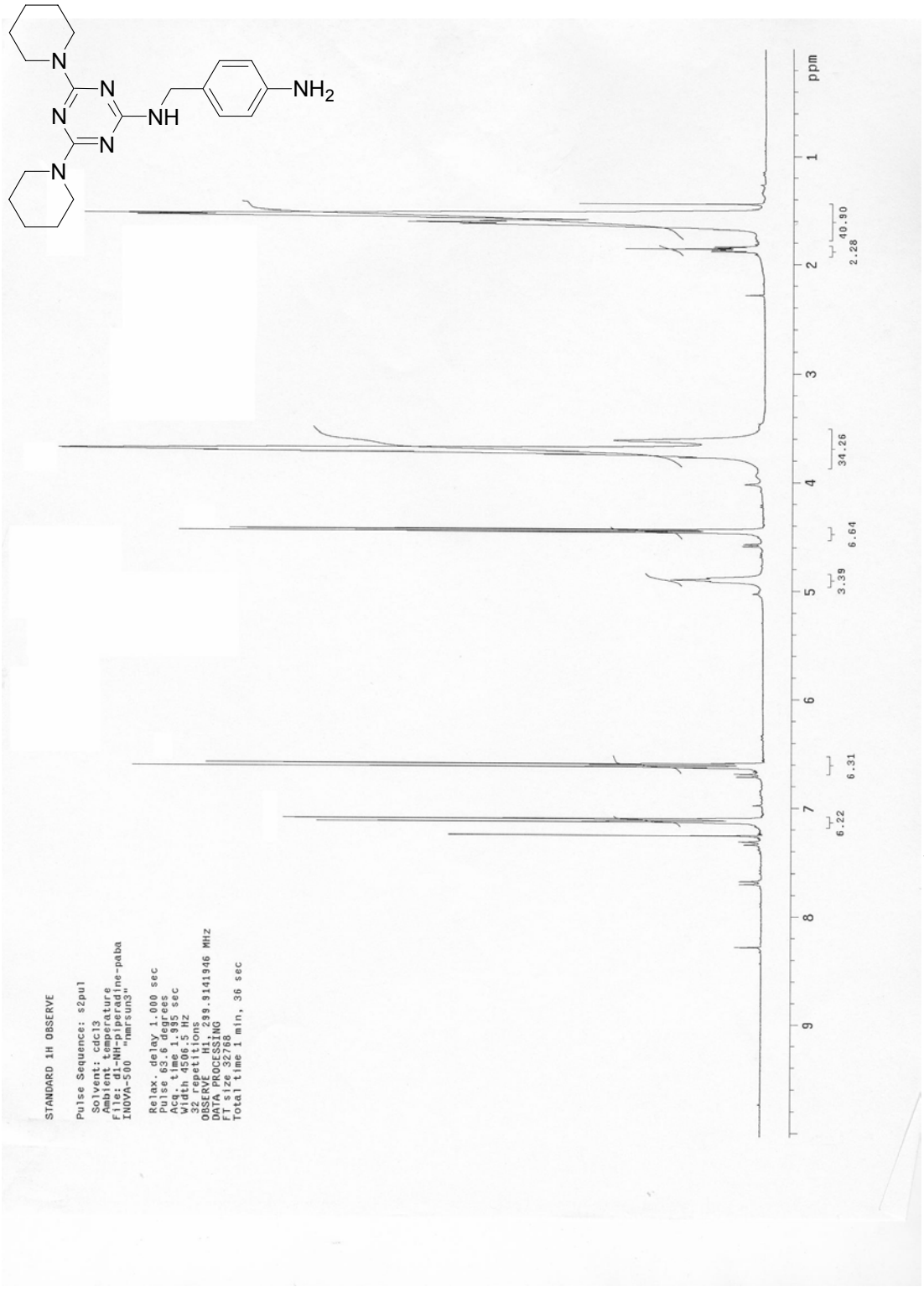

Figure B.4. ^{1}H NMR spectrum of **10**.

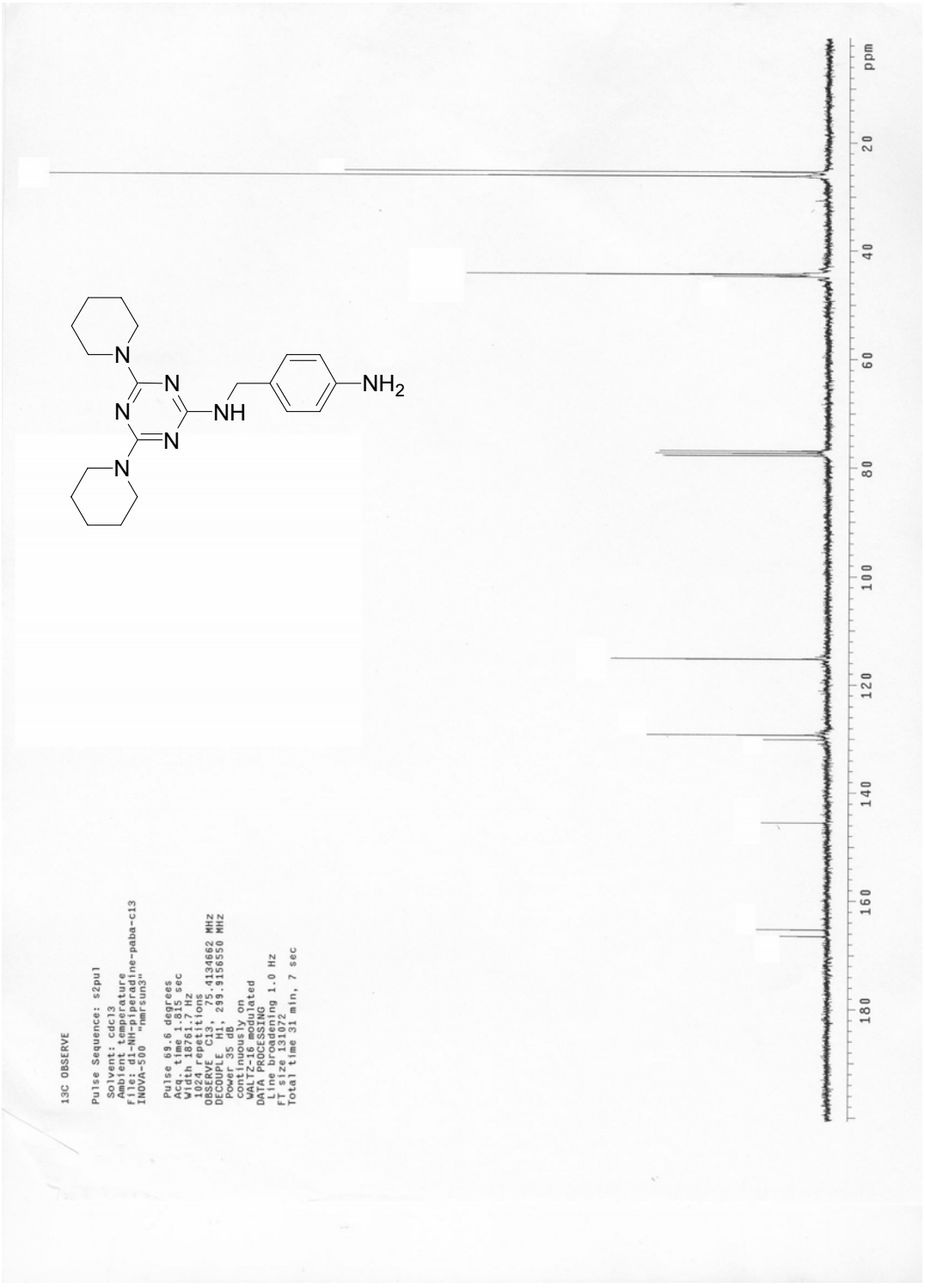

Figure B.5. ^{13}C NMR spectrum of **10**.

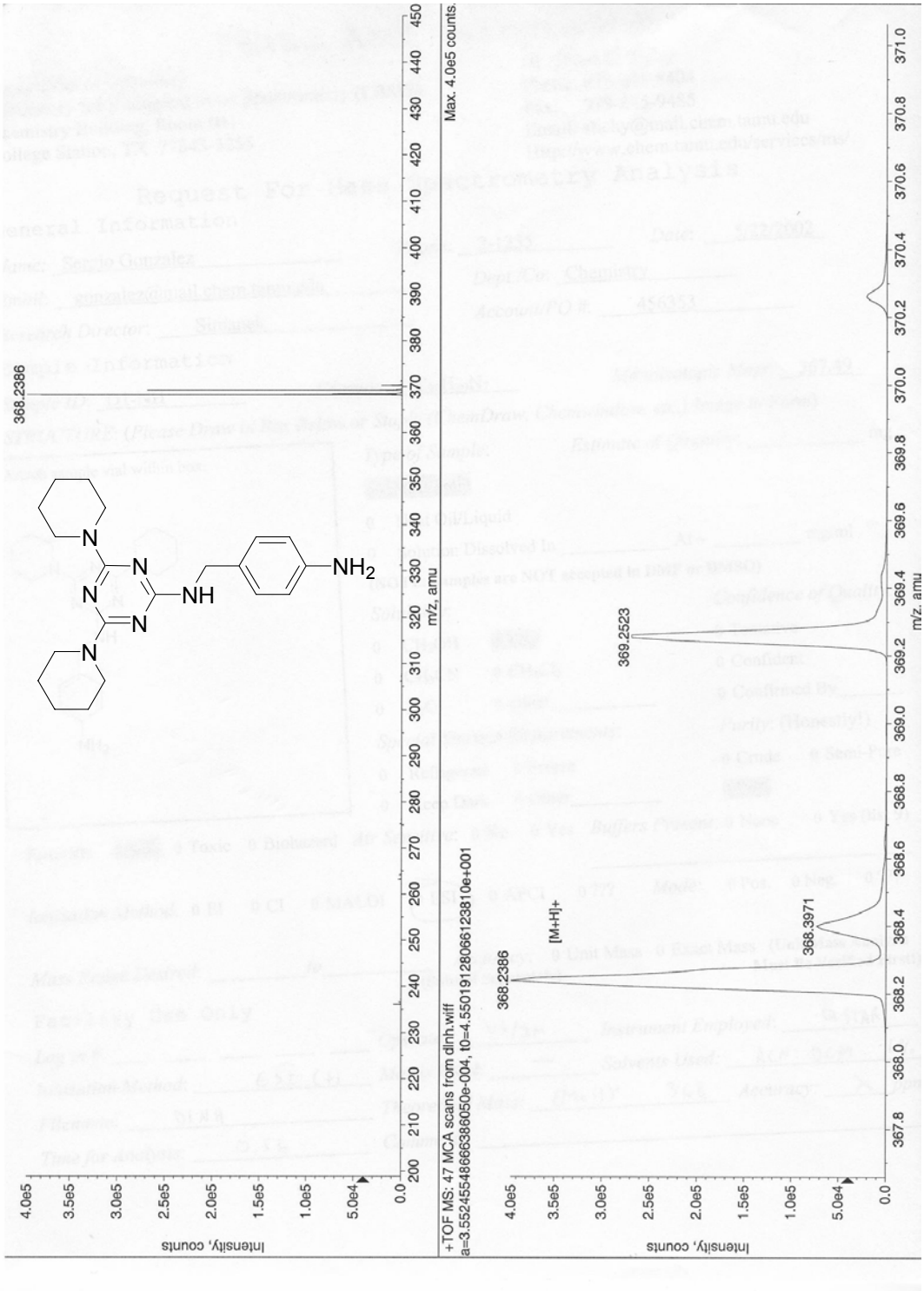

Figure B.6. ESI mass spectrum of **10**.

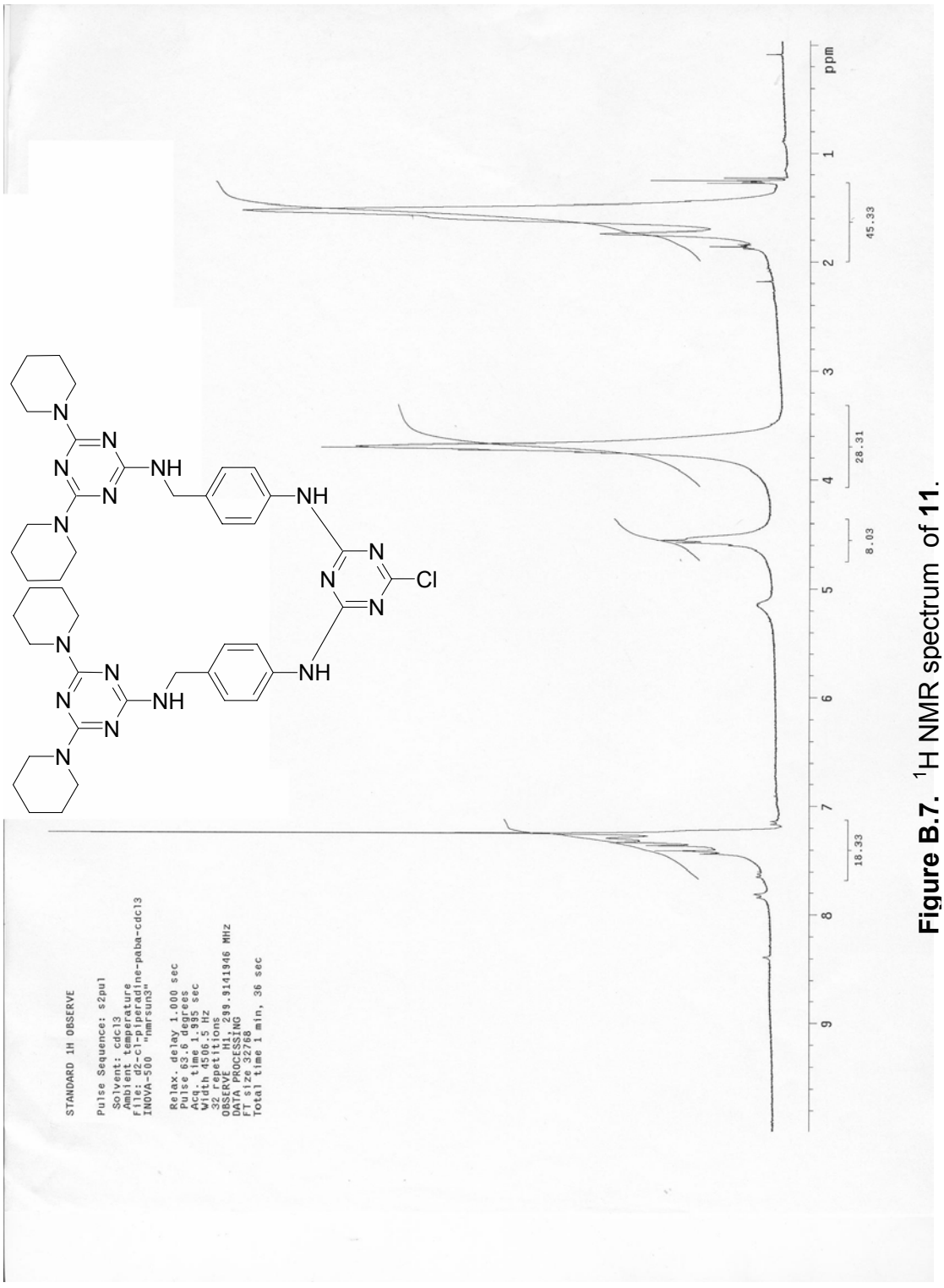

Figure B.7. ^{1}H NMR spectrum of **11**.

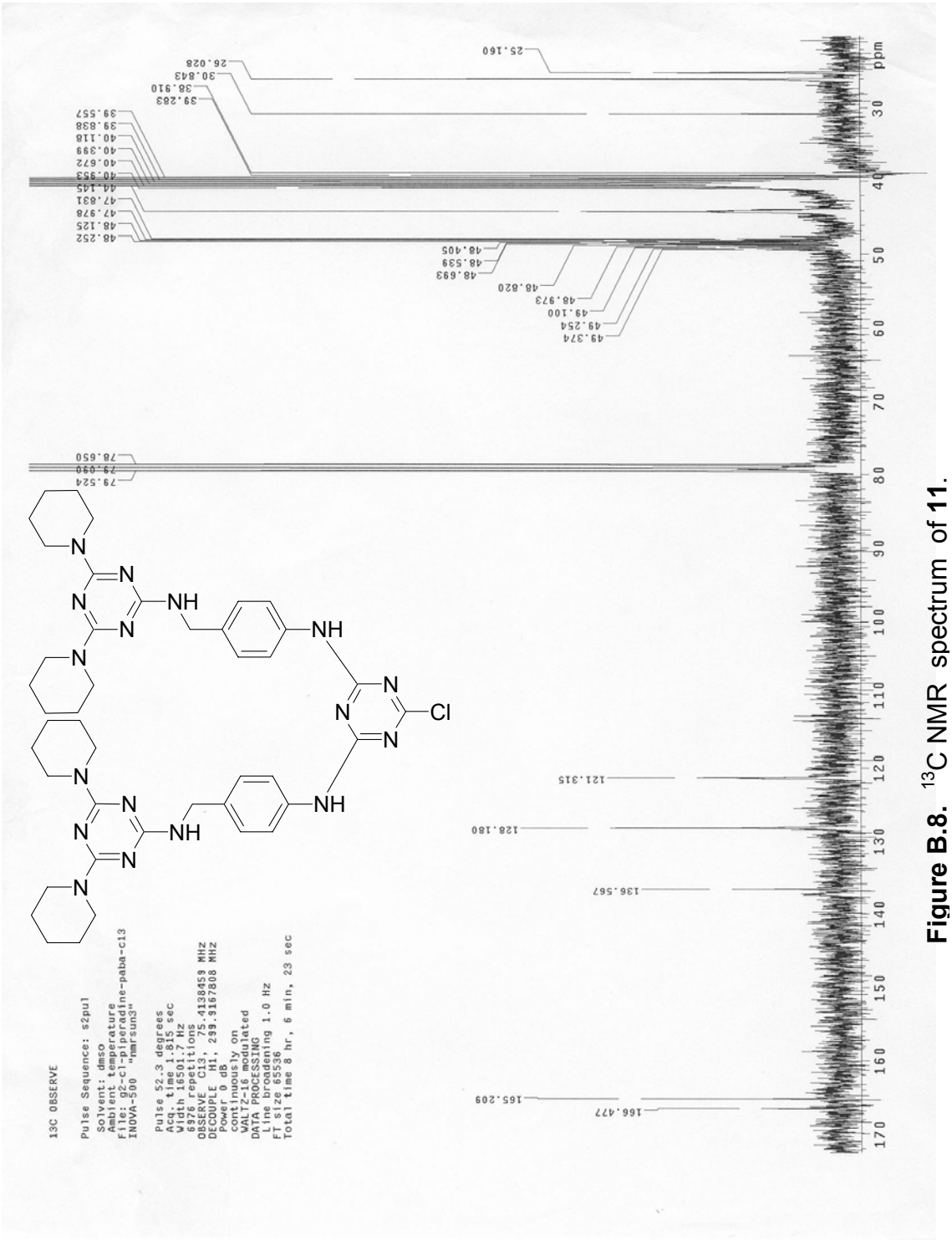

Figure B.8. ^{13}C NMR spectrum of **11**.

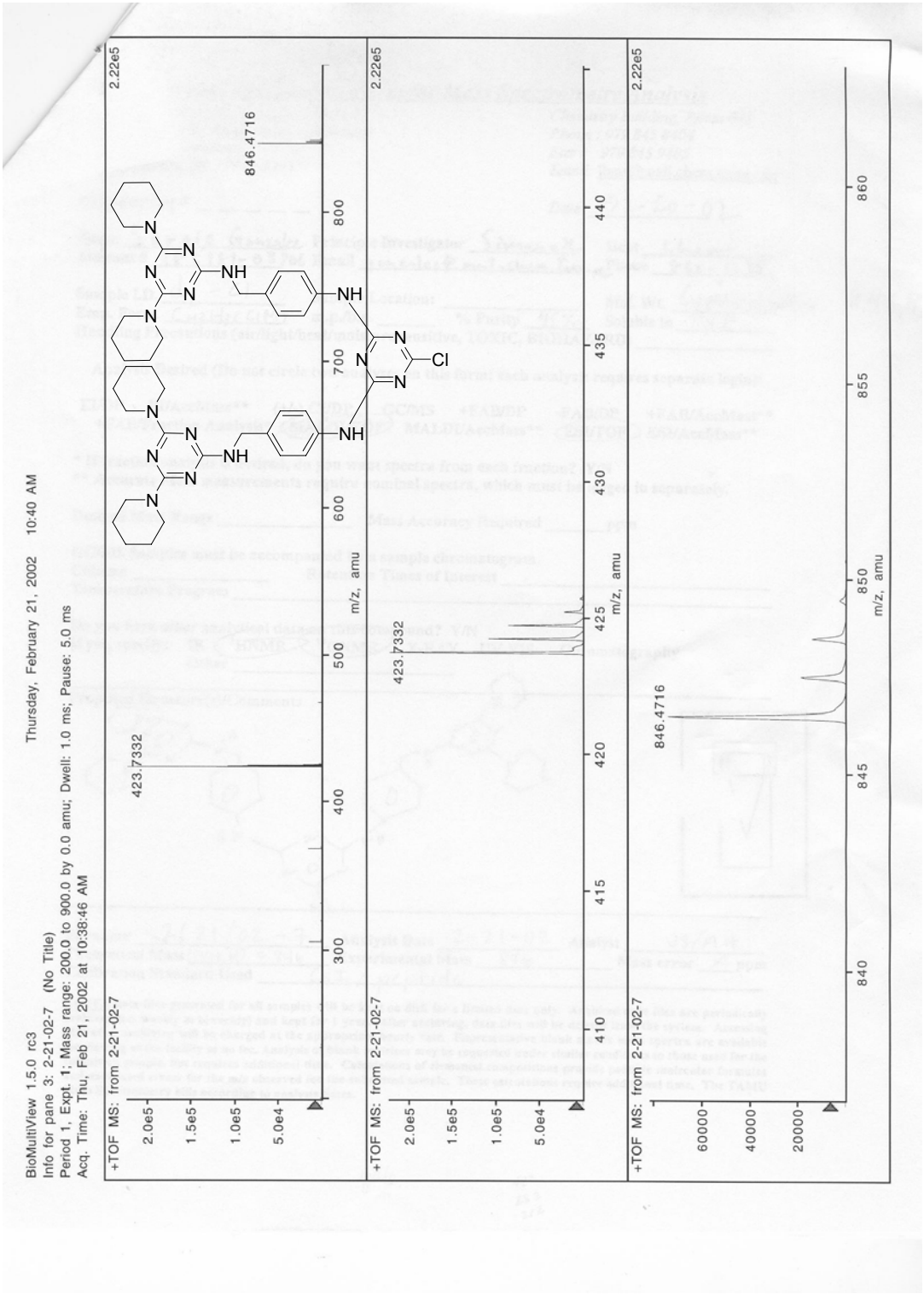

Figure B.9. ESI mass spectrum of **11**.

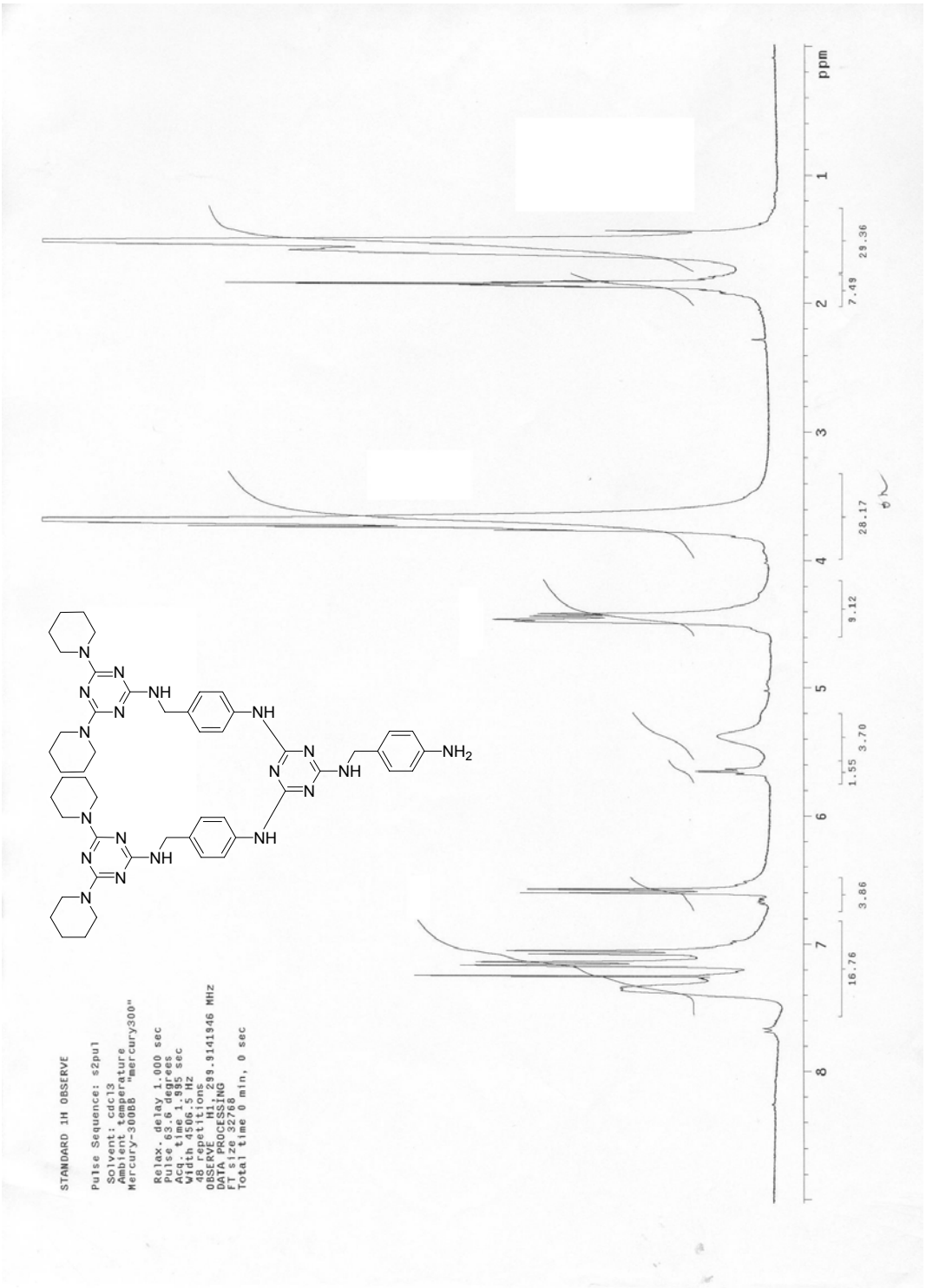

Figure B.10. ^{1}H NMR spectrum of **12**.

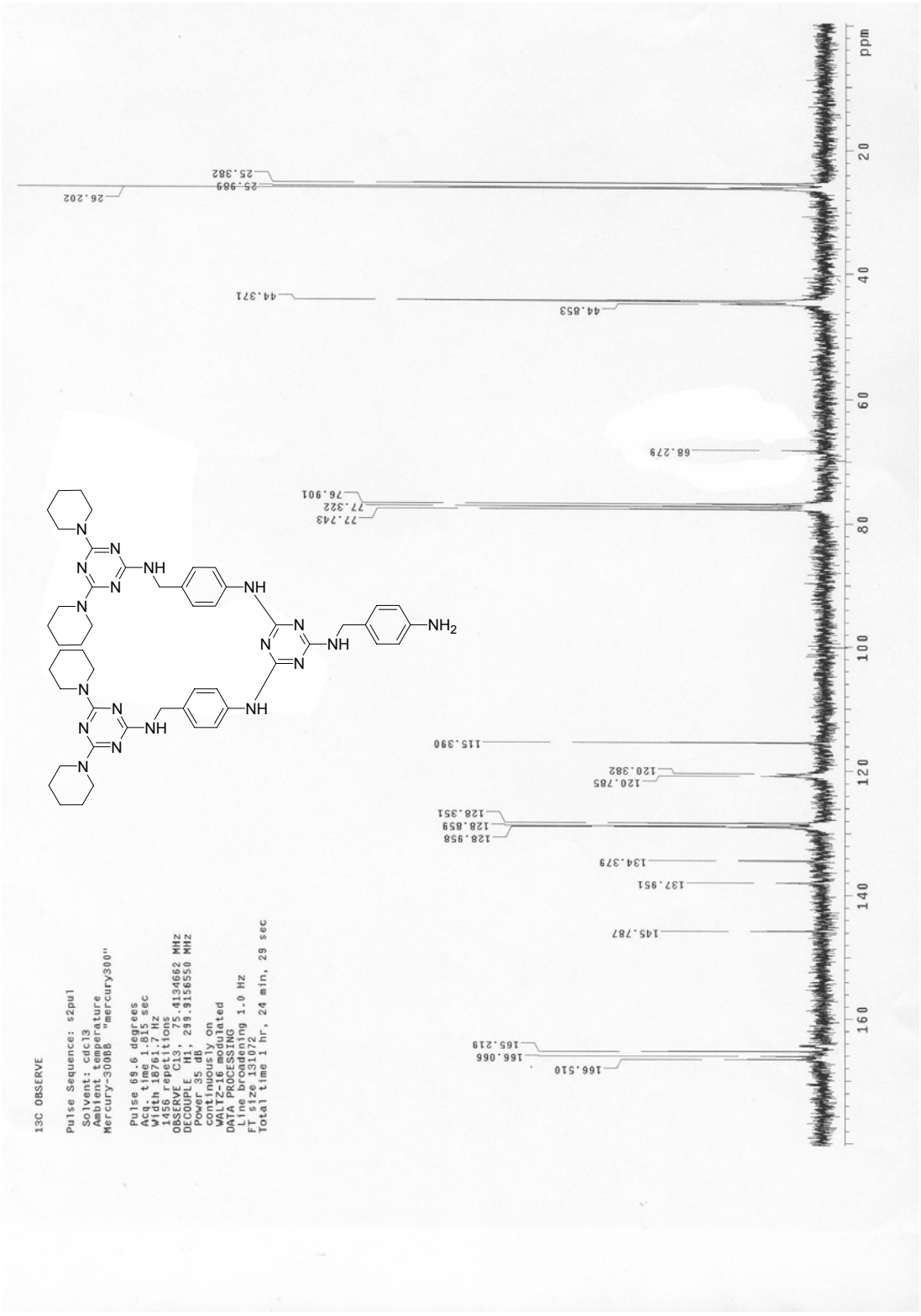

Figure B.11. ^{13}C NMR spectrum of **12**..

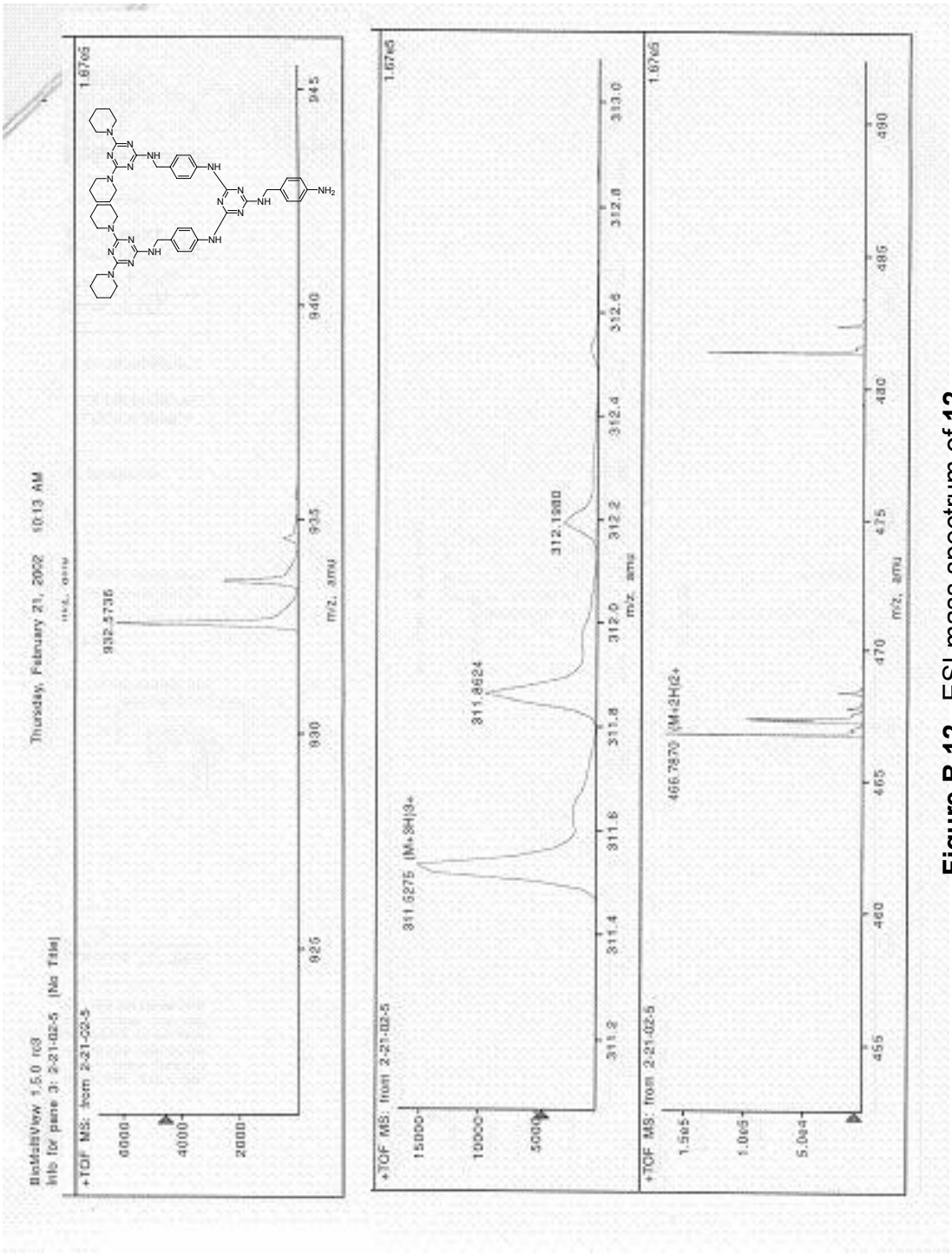

Figure B.12. ESI mass spectrum of **12.**

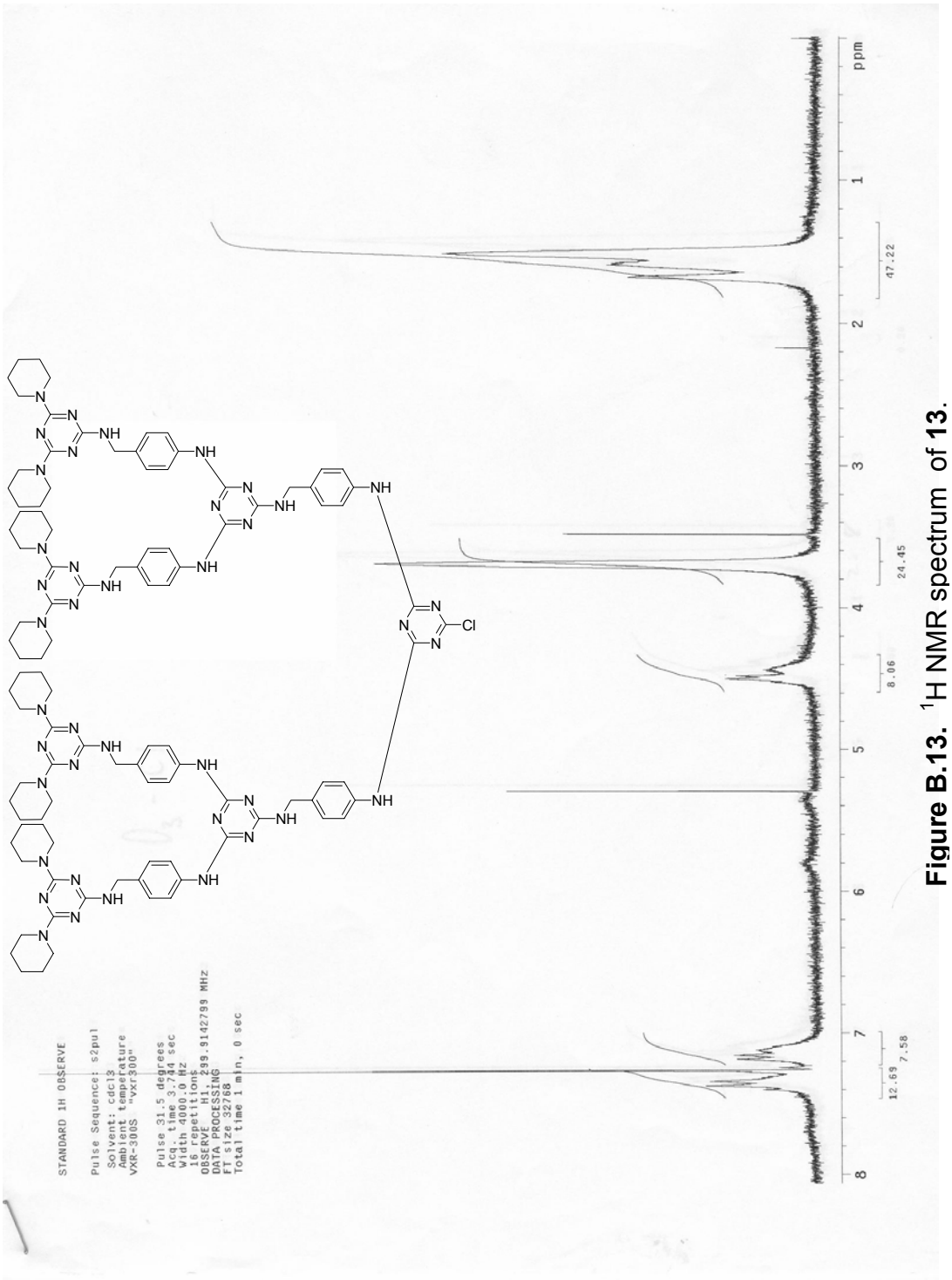

Figure B.13. ^{1}H NMR spectrum of **13**.

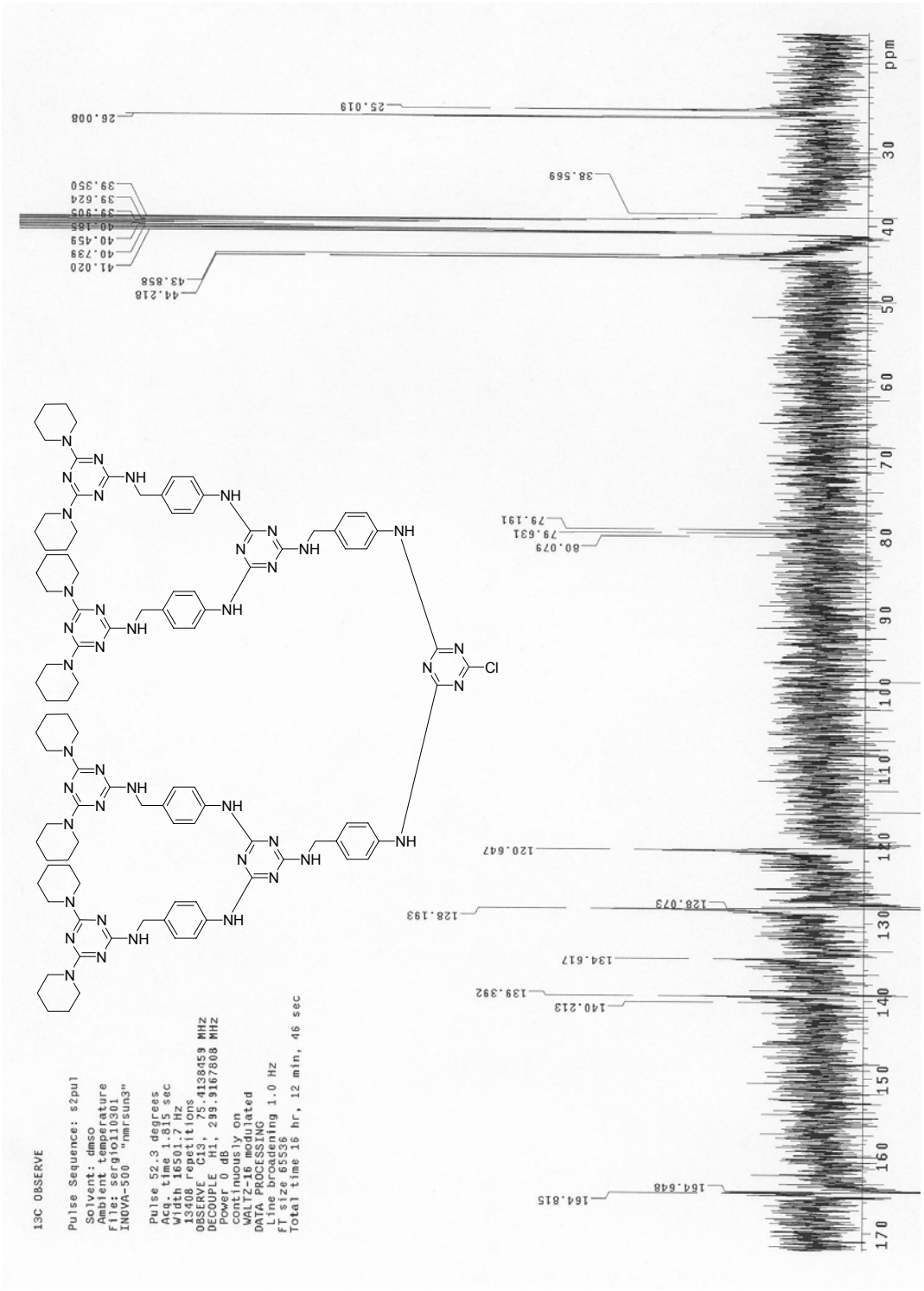

Figure B.14. ^{13}C NMR spectrum of **13**.

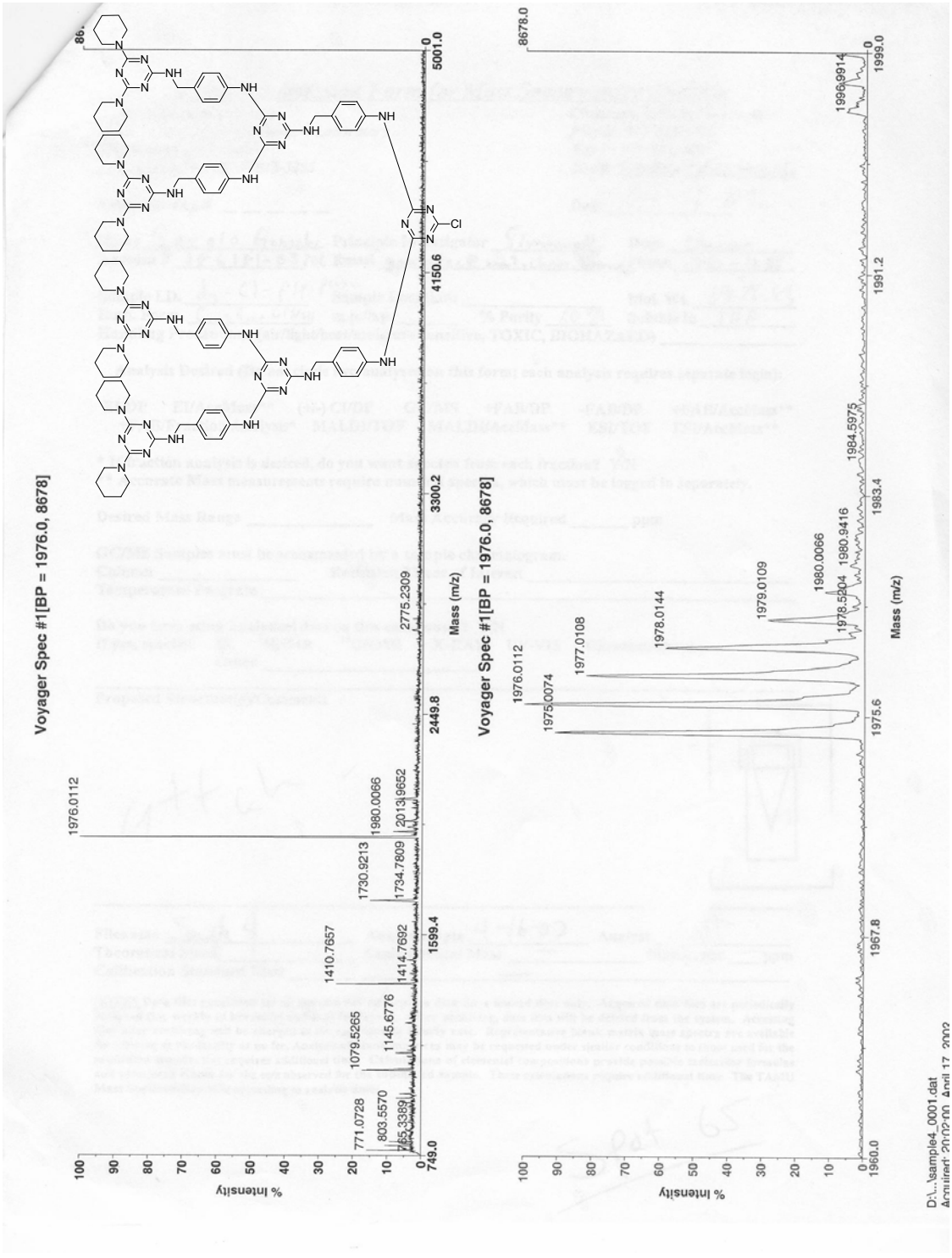

Figure B.15. MALDI mass spectrum of **13**.

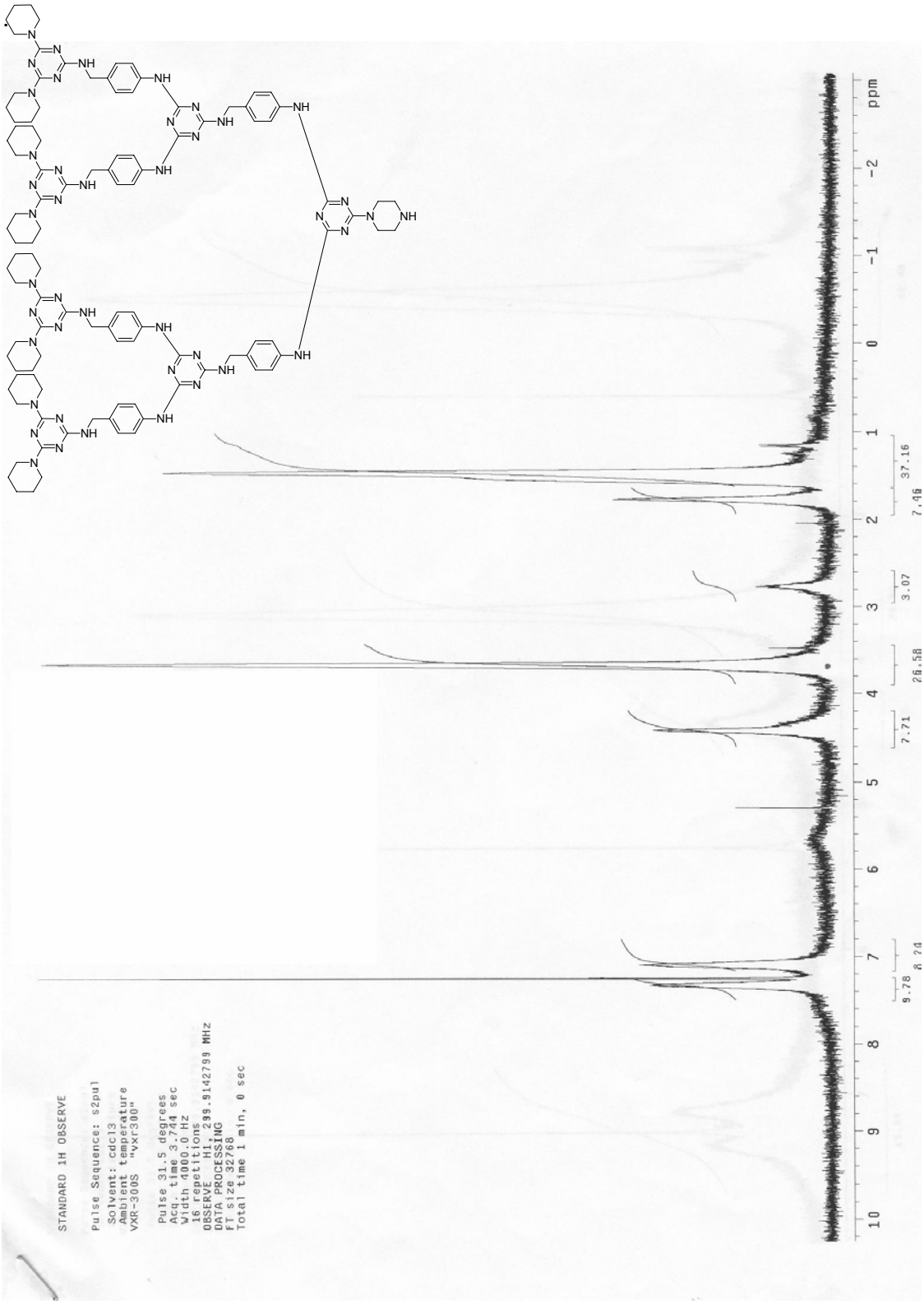

Figure B.16. ^{1}H NMR spectrum of **14**.

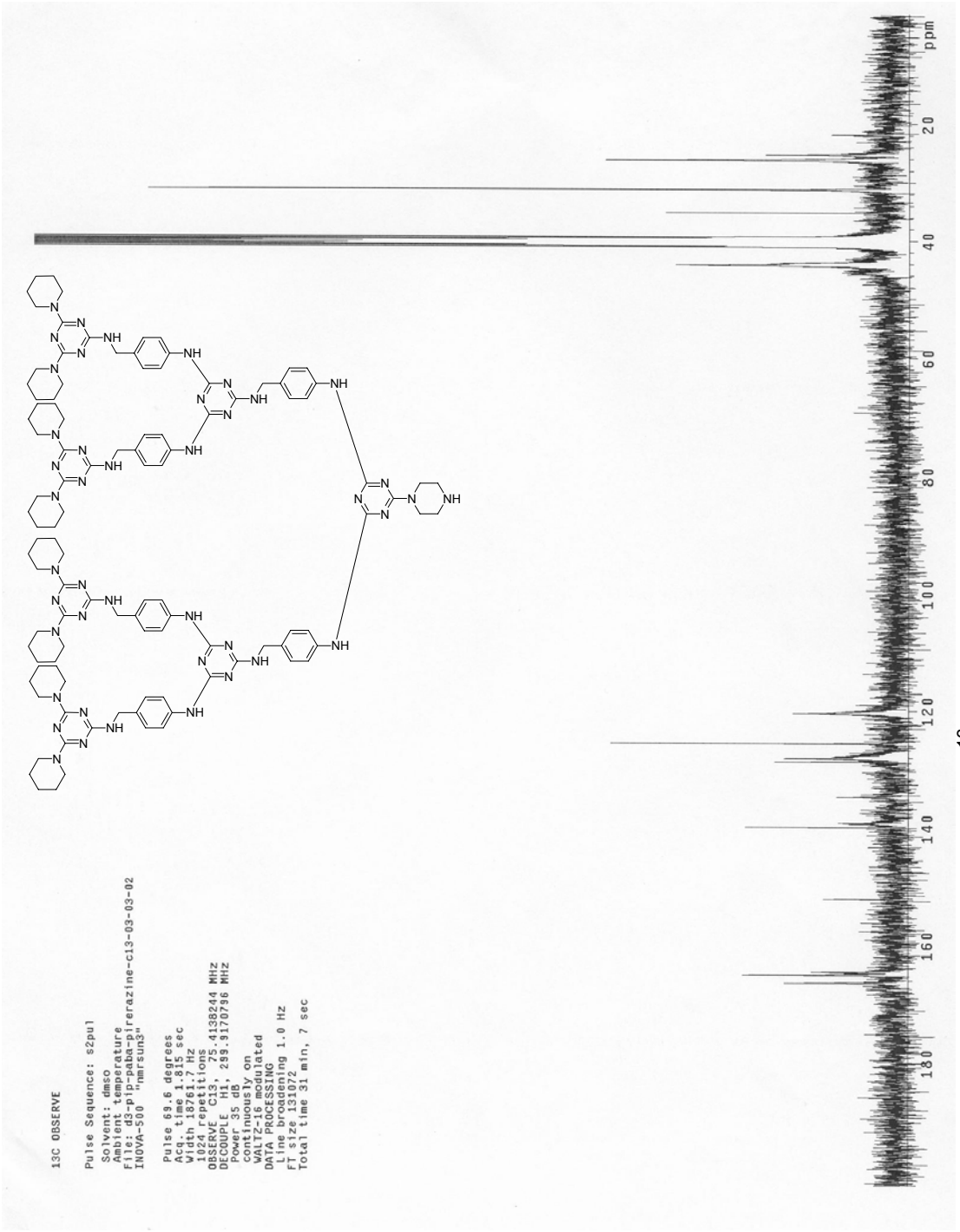

Figure B.17. ^{13}C NMR spectrum of **14**.

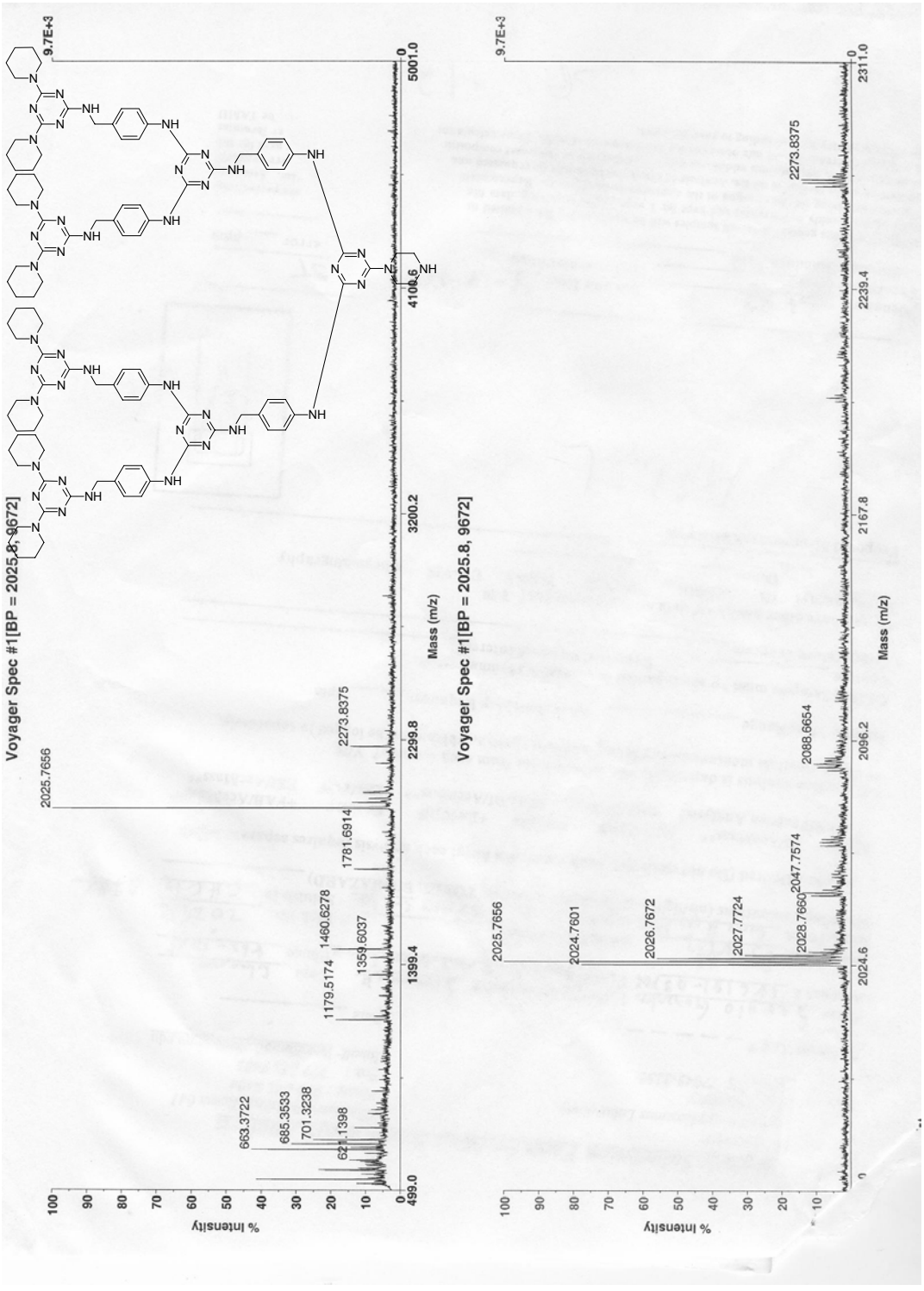

Figure B.18. MALDI mass spectrum of **14**.

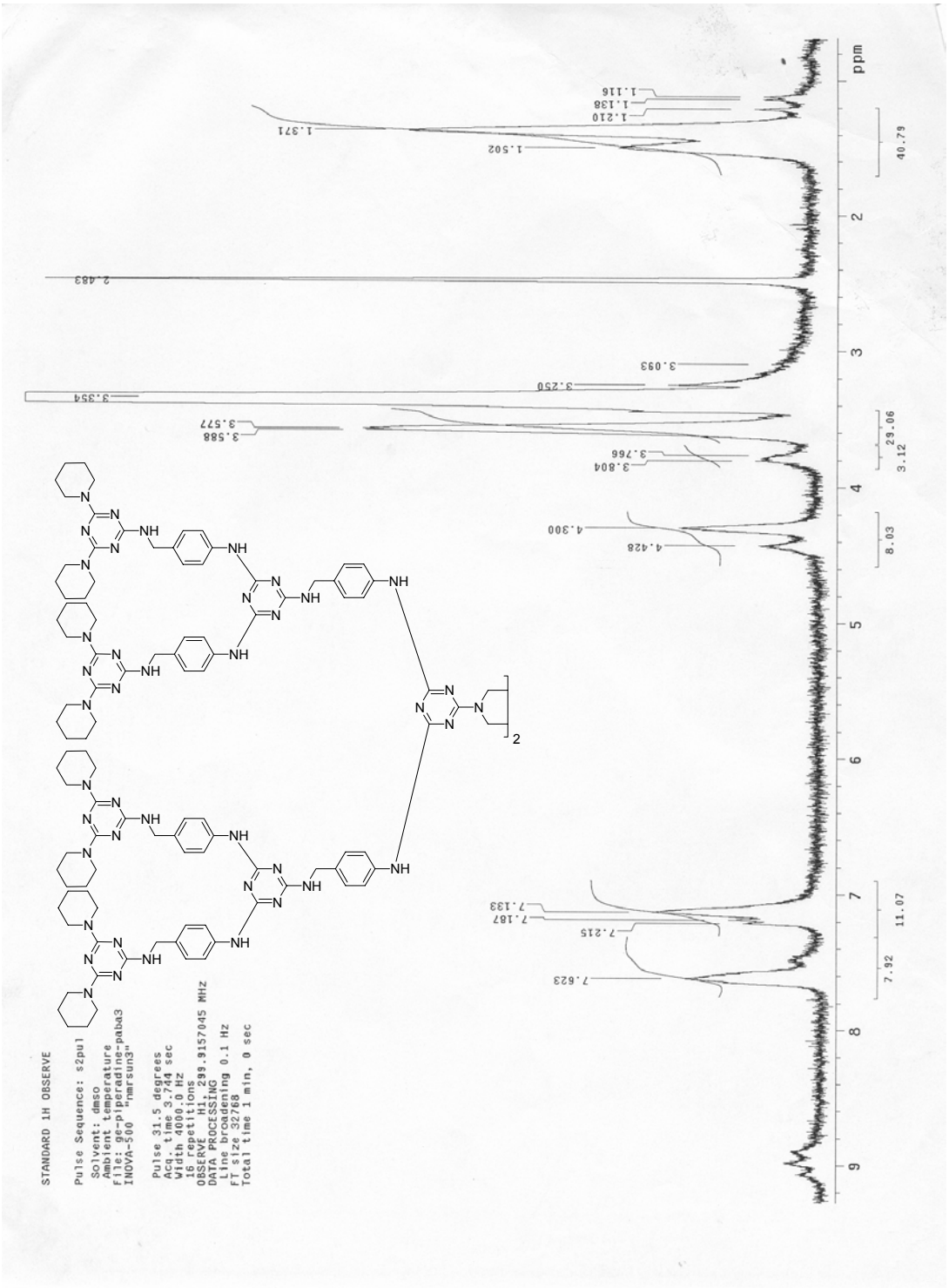

Figure B.19. ^{1}H NMR spectrum of **8**.

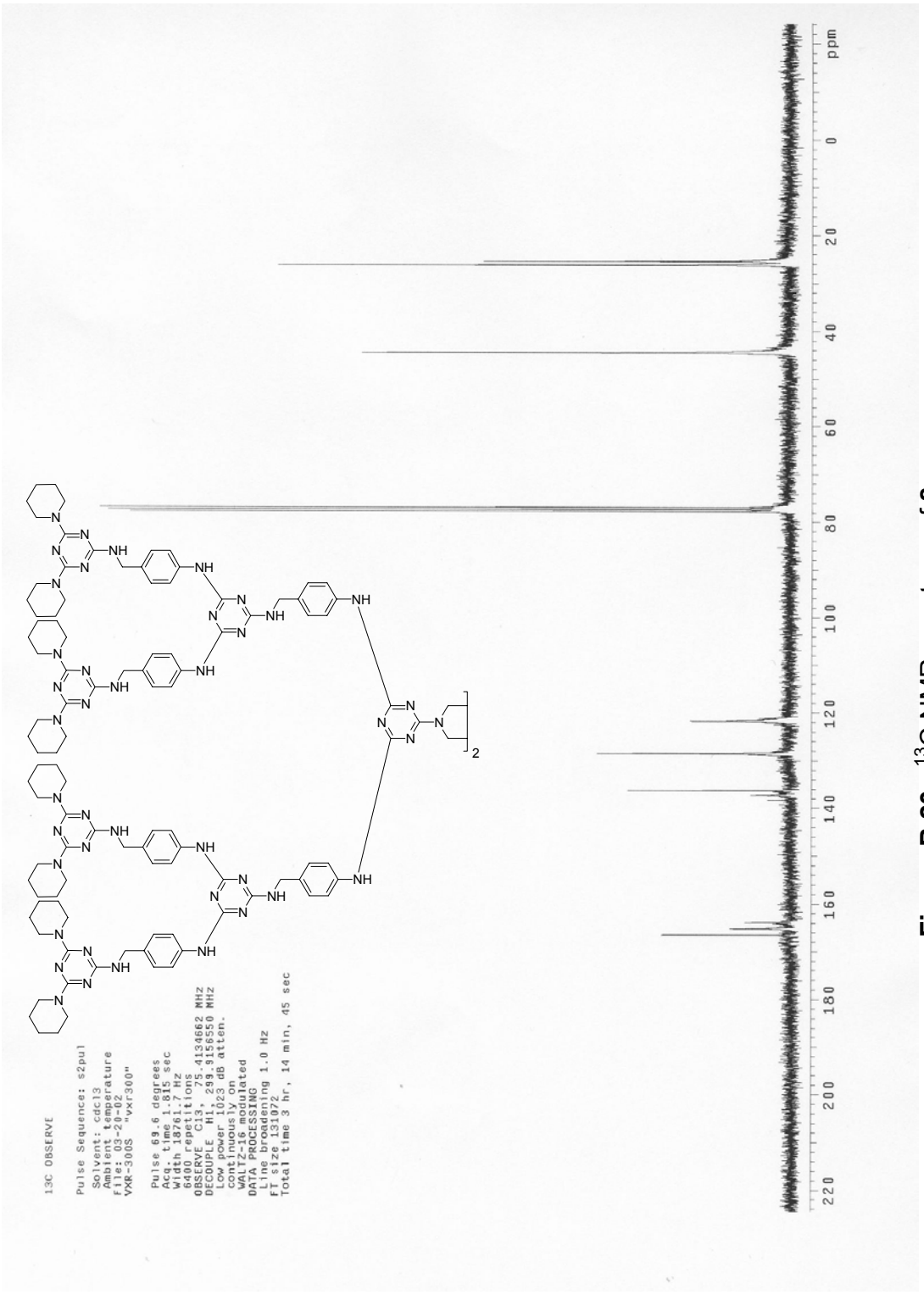

Figure B.20. ^{13}C NMR spectrum of **8**.

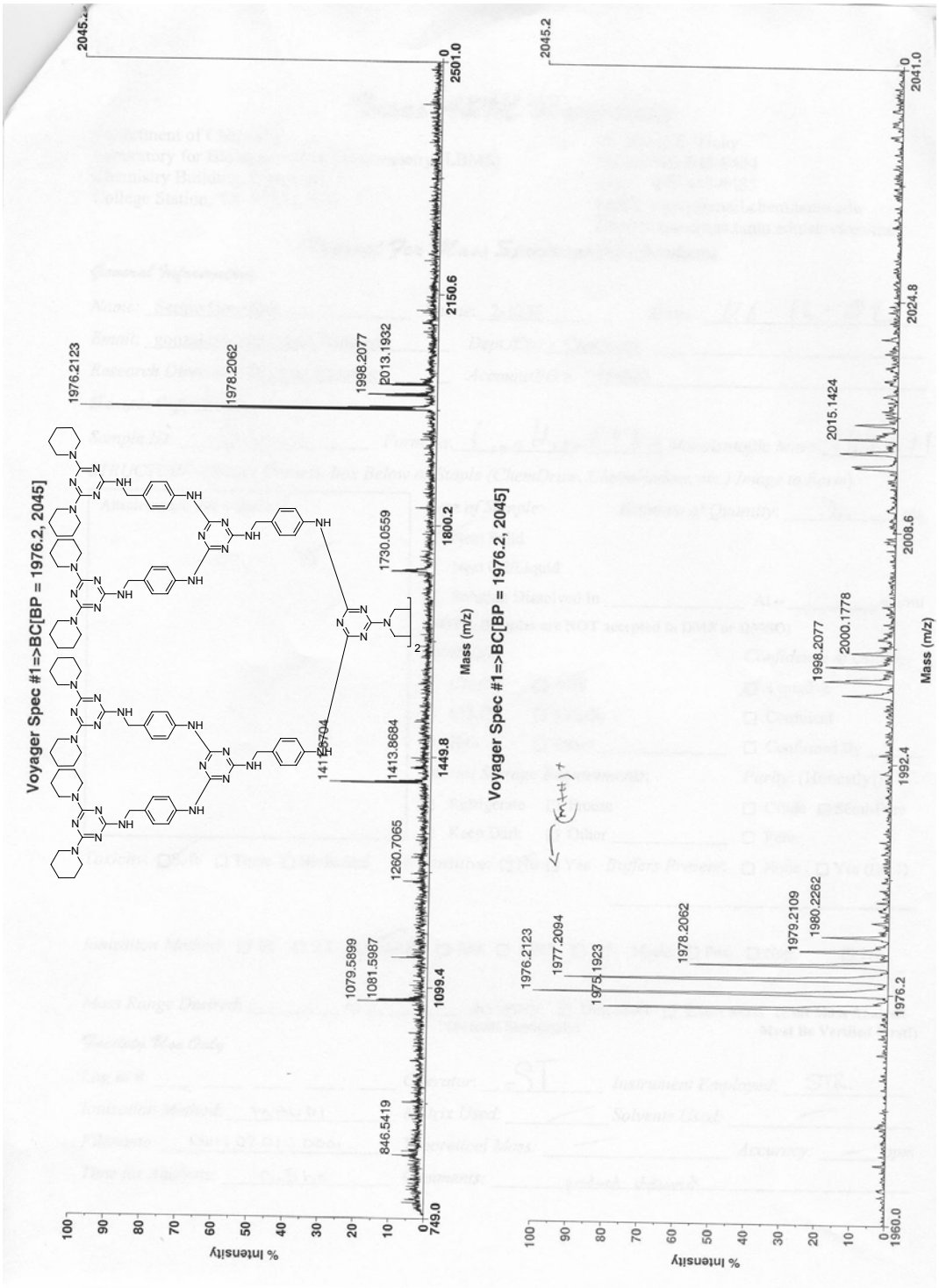

Figure B.21. MALDI mass spectrum of **8**.

APPENDIX C

SPECTRA RELEVANT TO CHAPTER III

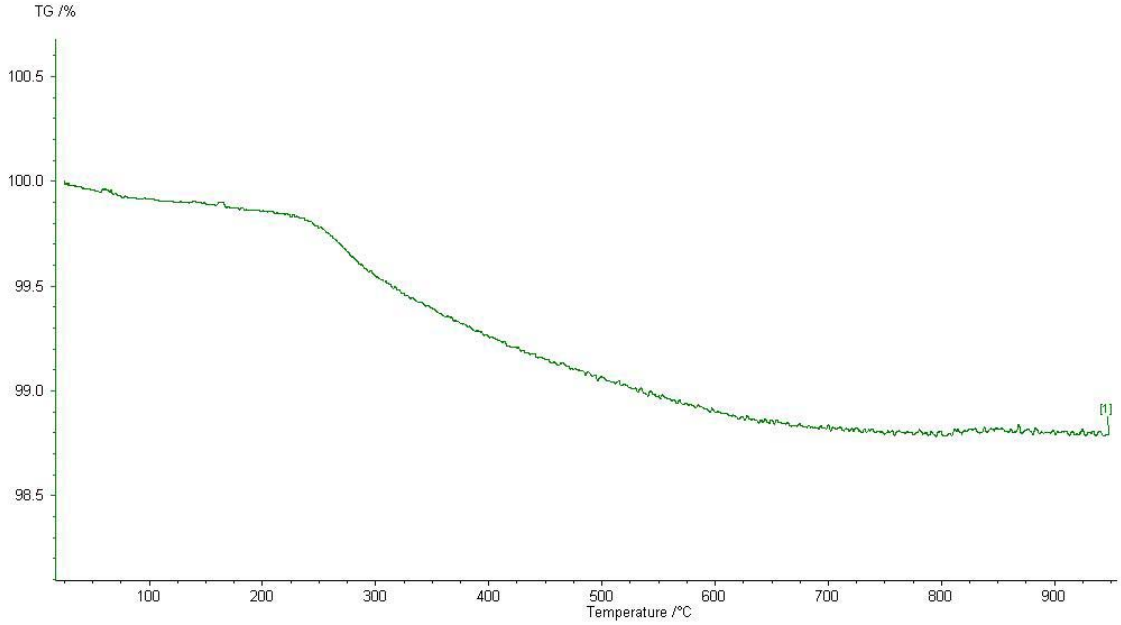

Figure C.1. TGA of alumina membrane 0.0 h.

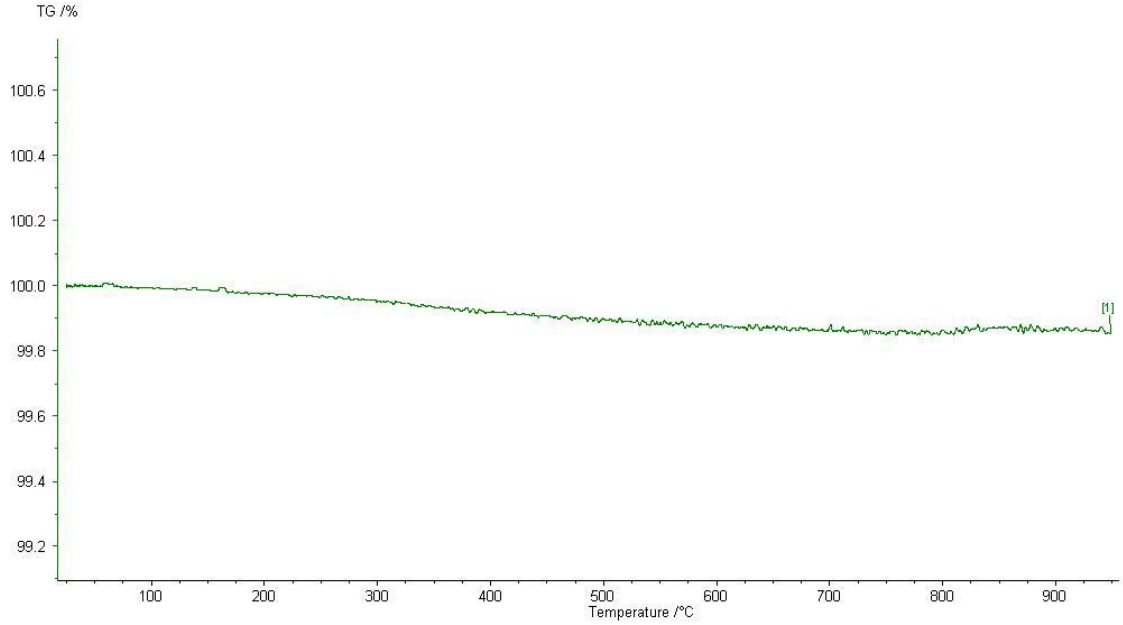

Figure C.2. TGA of alumina membrane 0.5 h.

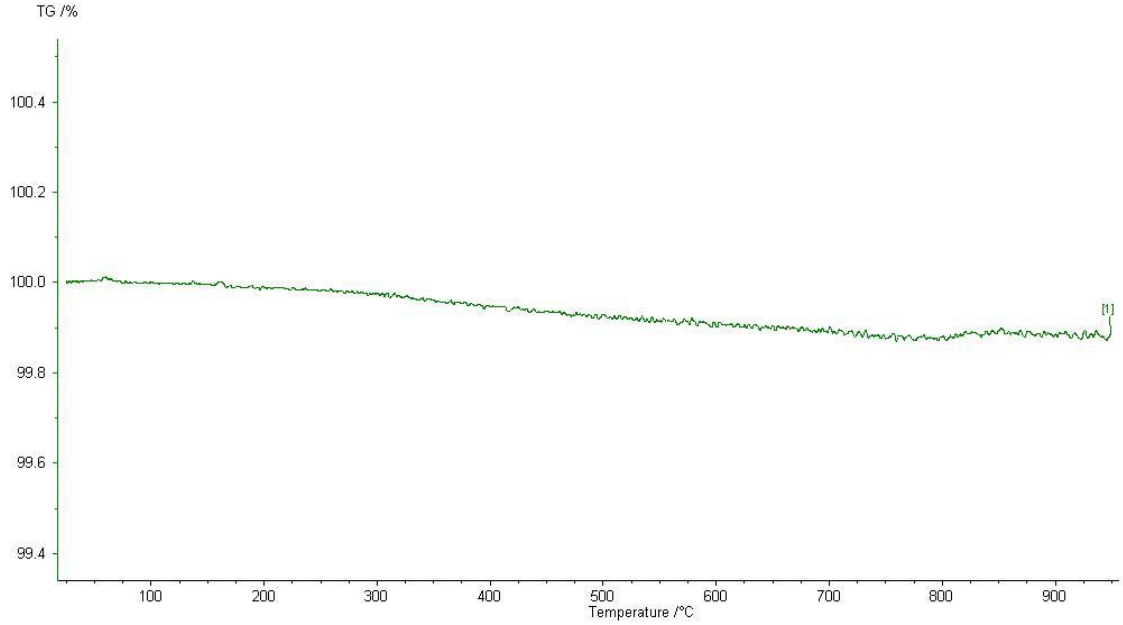

Figure C.3. TGA of alumina membrane 2 h.

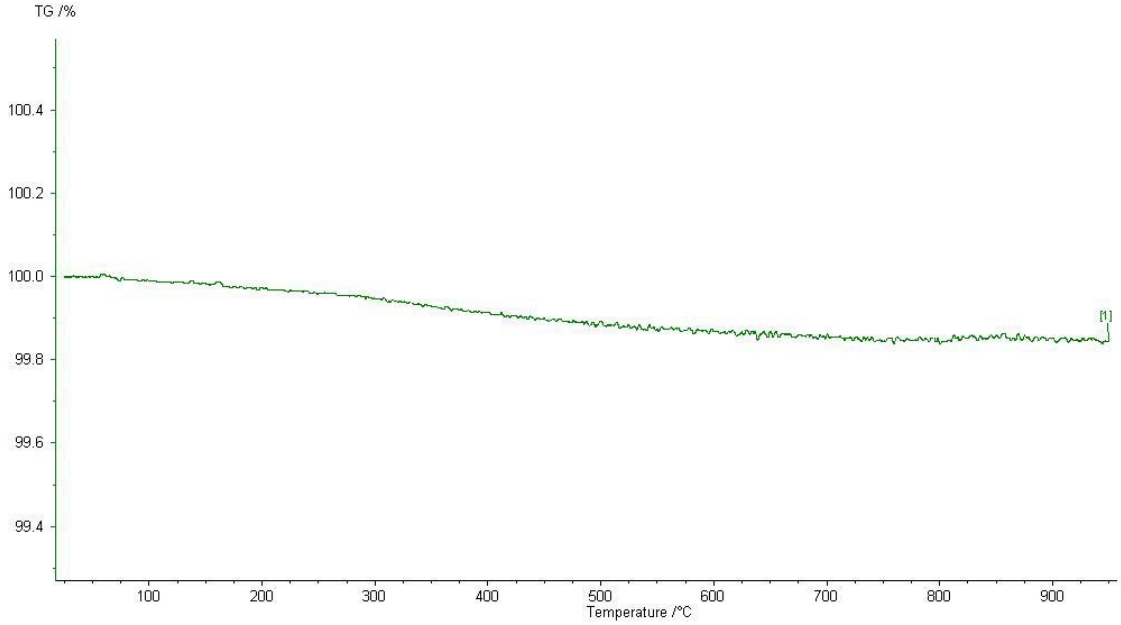

Figure C.4. TGA of alumina membrane 2 d.

APPENDIX D

SPECTRA AND CALIBRATION CURVES RELEVANT TO CHAPTER III

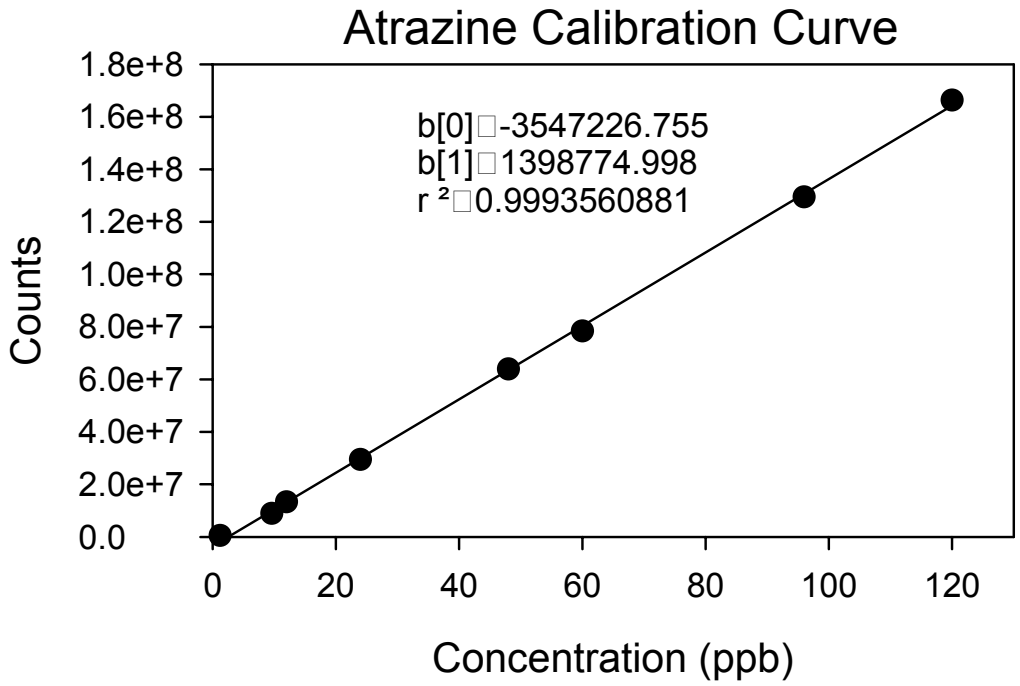

Figure D.1. Calibration curve of atrazine based on 8 data points. The curve had an r^2 value of 0.999.

Table D.1. Sequestration data of fast precipitation protocol on a 96 ppb solution of atrazine.

Polymer	Exp	Counts	Concentration (ppb)	Sequestration
1	1	665,58,923	50	48%
	2	71,011,254	54	44%
2	1	35,021,245	28	71%
	2	33,551,996	27	72%

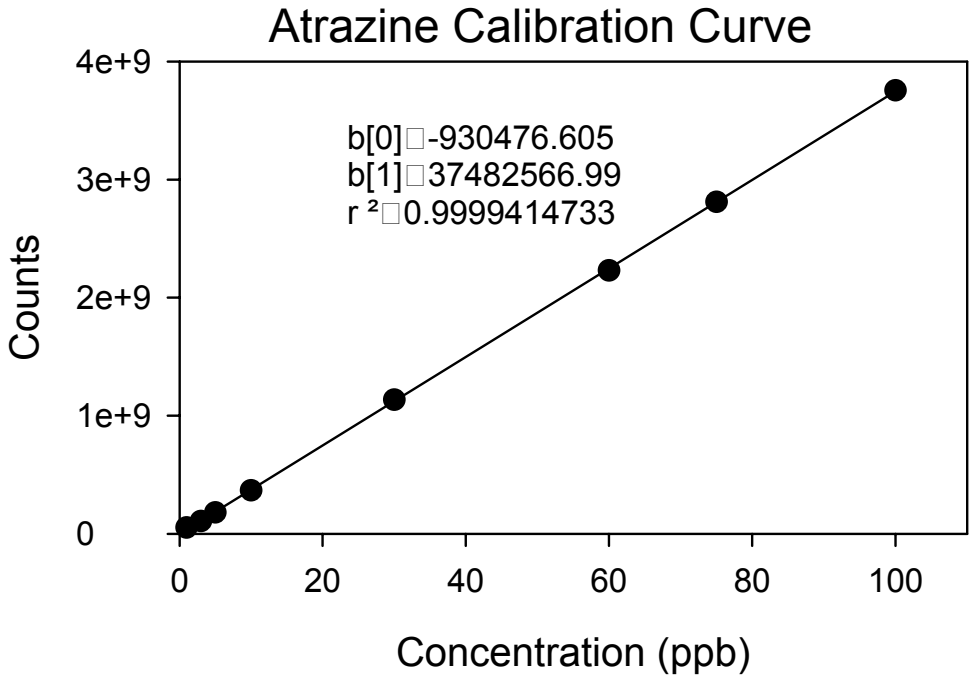

Figure D.2. Second calibration curve of atrazine based on 8 data points. The curve had an r^2 value of 0.999.

Table D.2. Sequestration data of slow precipitation protocol on a 100 ppb solution of atrazine.

Polymer	Exp	Counts	Concentration (ppb)	Sequestration
1	1	1,638,165,307	44	56%
	2	1,638,625,954	44	56%
2	1	0.00	0.00	100%
	2	0.00	0.00	100%

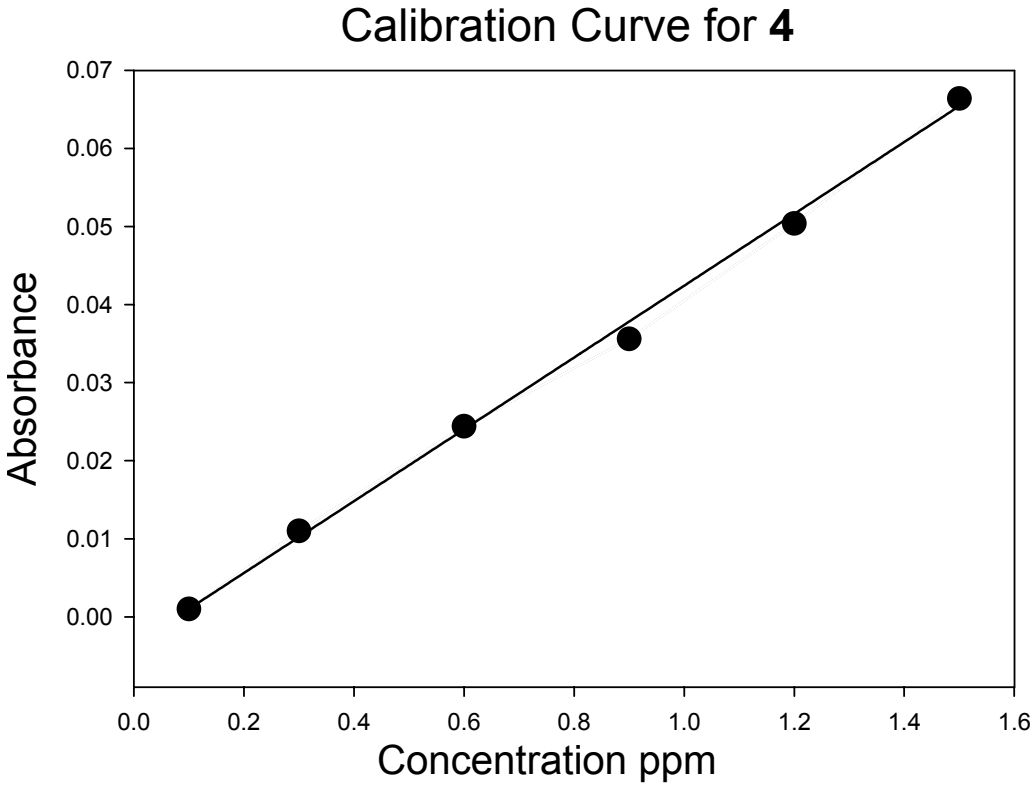

Figure D.3. Calibration curve of **4** based on 6 data points. The curve had an r^2 value of 0.997. The molar absorptivity of **4** was calculated to be 3.0×10^4.

Table D.3. Sequestration data of fast precipitation protocol on a 6.4 ppm solution of methyl red atrazine.

Polymer	Exp	Absorbance	Concentration (ppm)	Sequestration
1	1	0.0774	1.77	72 %
	2	0.0775	1.78	72 %
2	1	0.0055	0.20	97 %
	2	0.0060	0.20	97 %

Table D.4. Sequestration data of slow precipitation protocol on an 8 ppm solution of methyl red atrazine.

Polymer	Exp	Absorbance	Concentration (ppm)	Sequestration
1	1	0.0585	1.36	83 %
	2	0.0583	1.36	83 %
2	1	0.0050	0.22	97 %
	2	0.0064	0.19	98 %

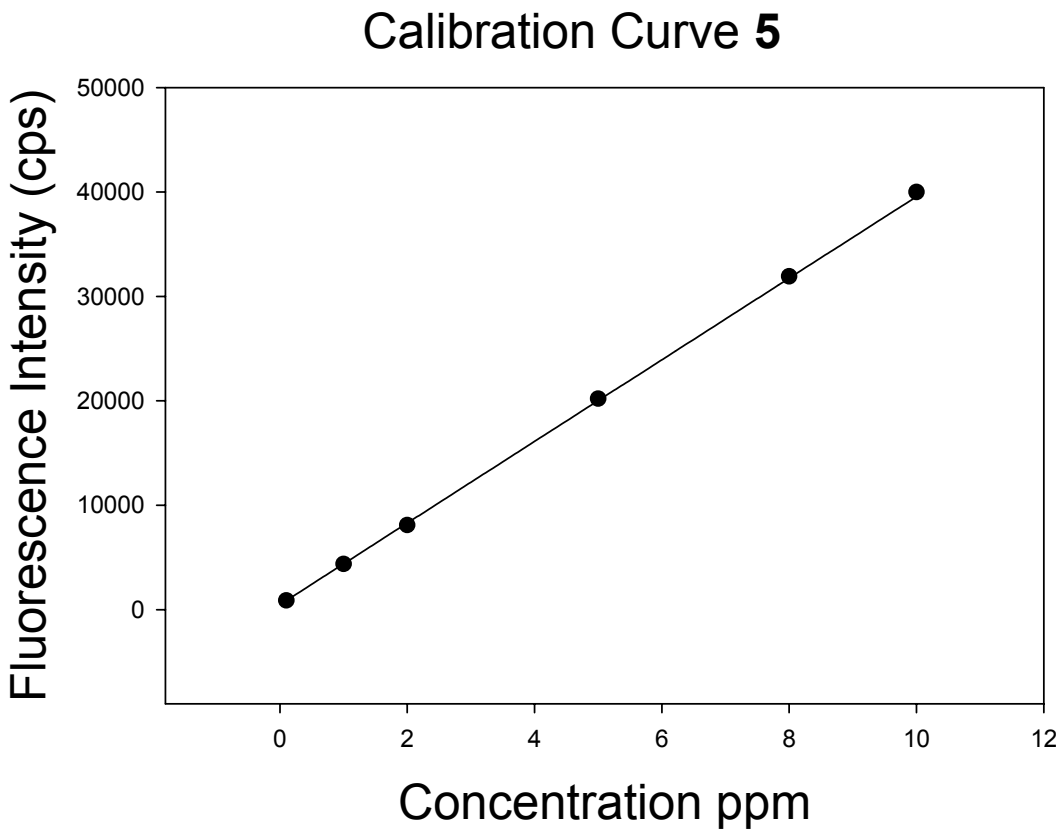

Figure D.4. Calibration curve of **3** based on 6 data points. The curve had an r^2 value of 0.999.

Table D.5. Sequestration data of fast precipitation protocol on an 8 ppm solution of dansyl atrazine.

Polymer	Exp	Fluorescence Intensity (cps)	Concentration (ppm)	Sequestration
1	1	13,480	3.31	59%
	2	12,470	3.05	62%
2	1	1720	0.34	96%
	2	1604	0.30	96%

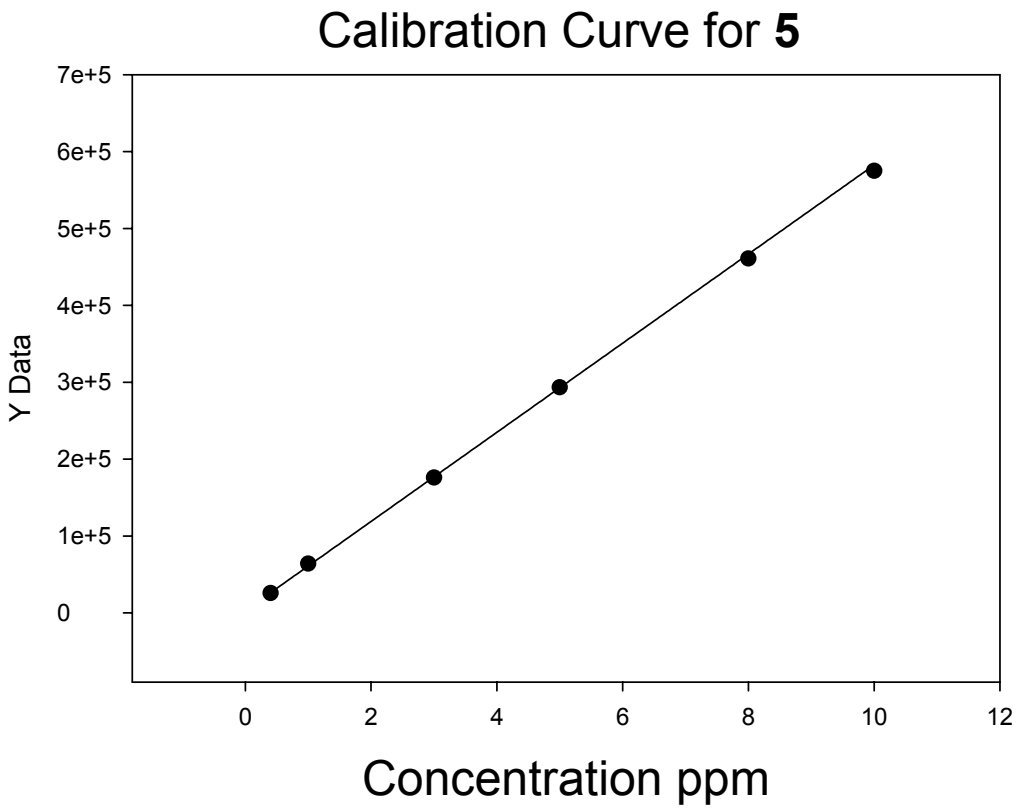

Figure D.5. Calibration curve of **5** based on 6 data points. The curve had an r^2 value of 0.999.

Table D.6. Sequestration data of slow precipitation protocol on a 10 ppm solution of dansyl atrazine.

Polymer	Exp	Fluorescence Intensity (cps)	Concentration (ppm)	Sequestration
1	1	171,781	2.9	71%
	2	171,233	2.9	71%
2	1	18,080	0.2	98%
	2	18,163	0.2	98%

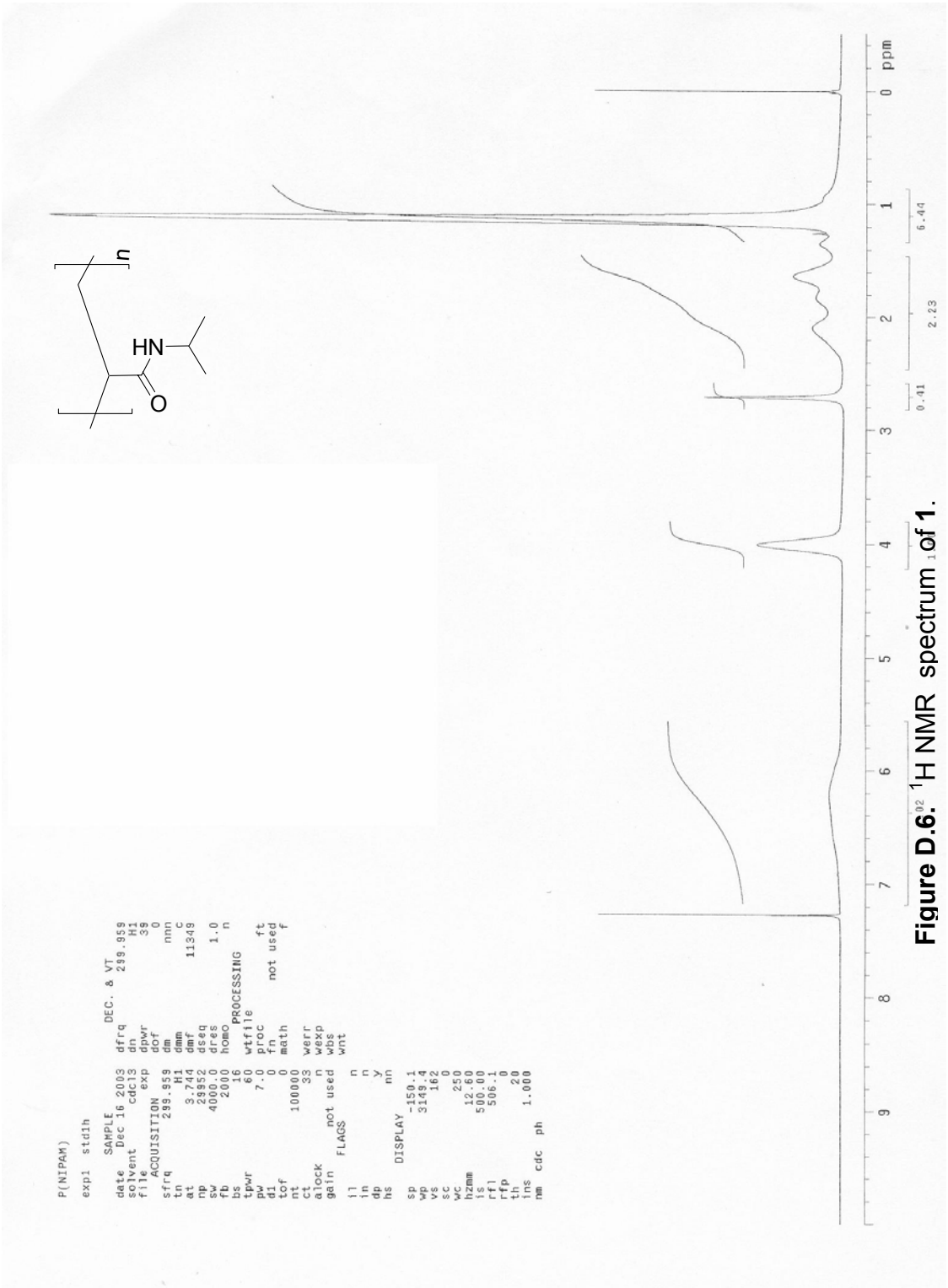

Figure D.6. ^{1}H NMR spectrum of **1**.

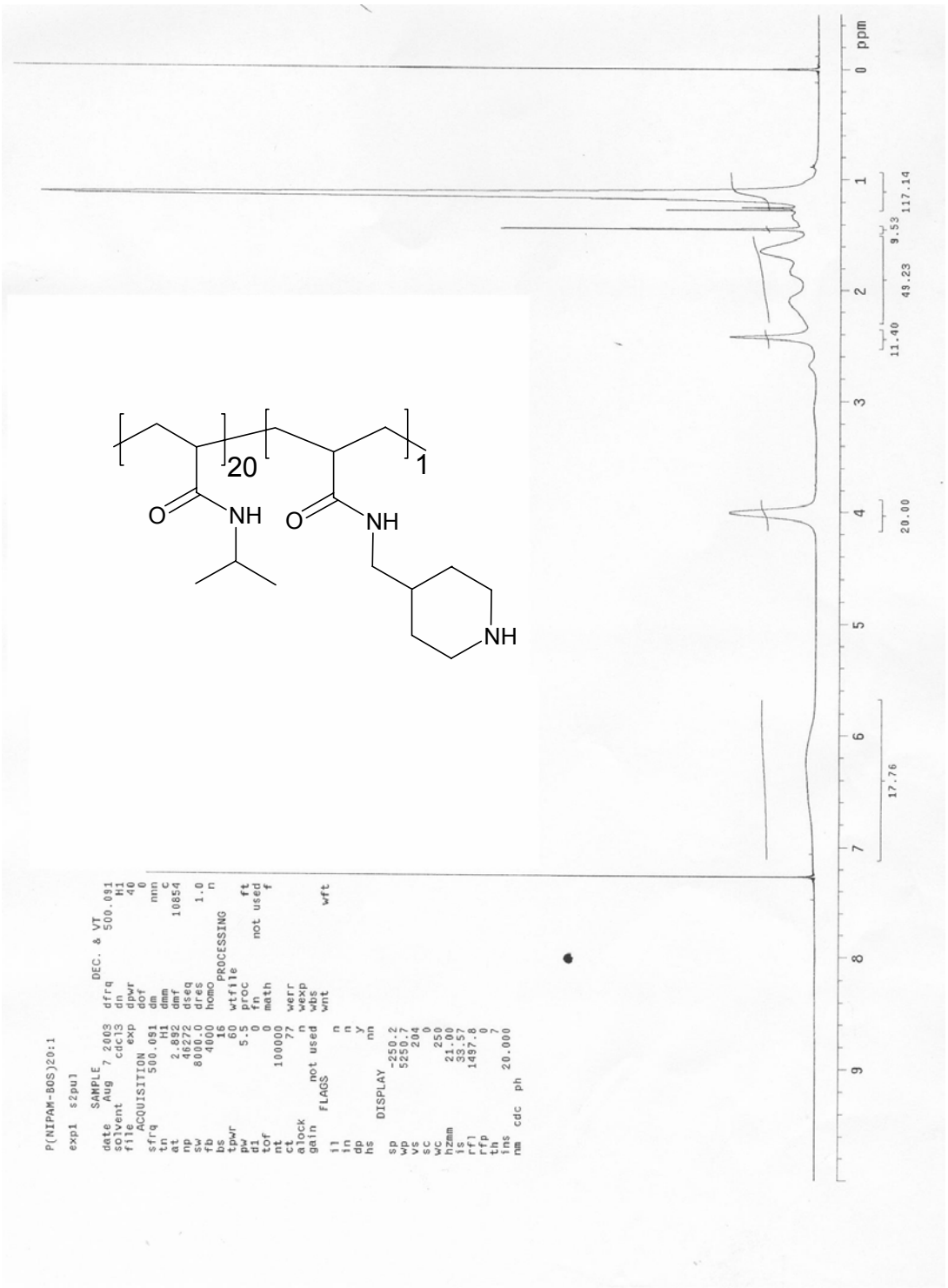

Figure D.7. ^{1}H NMR spectrum of **2**.

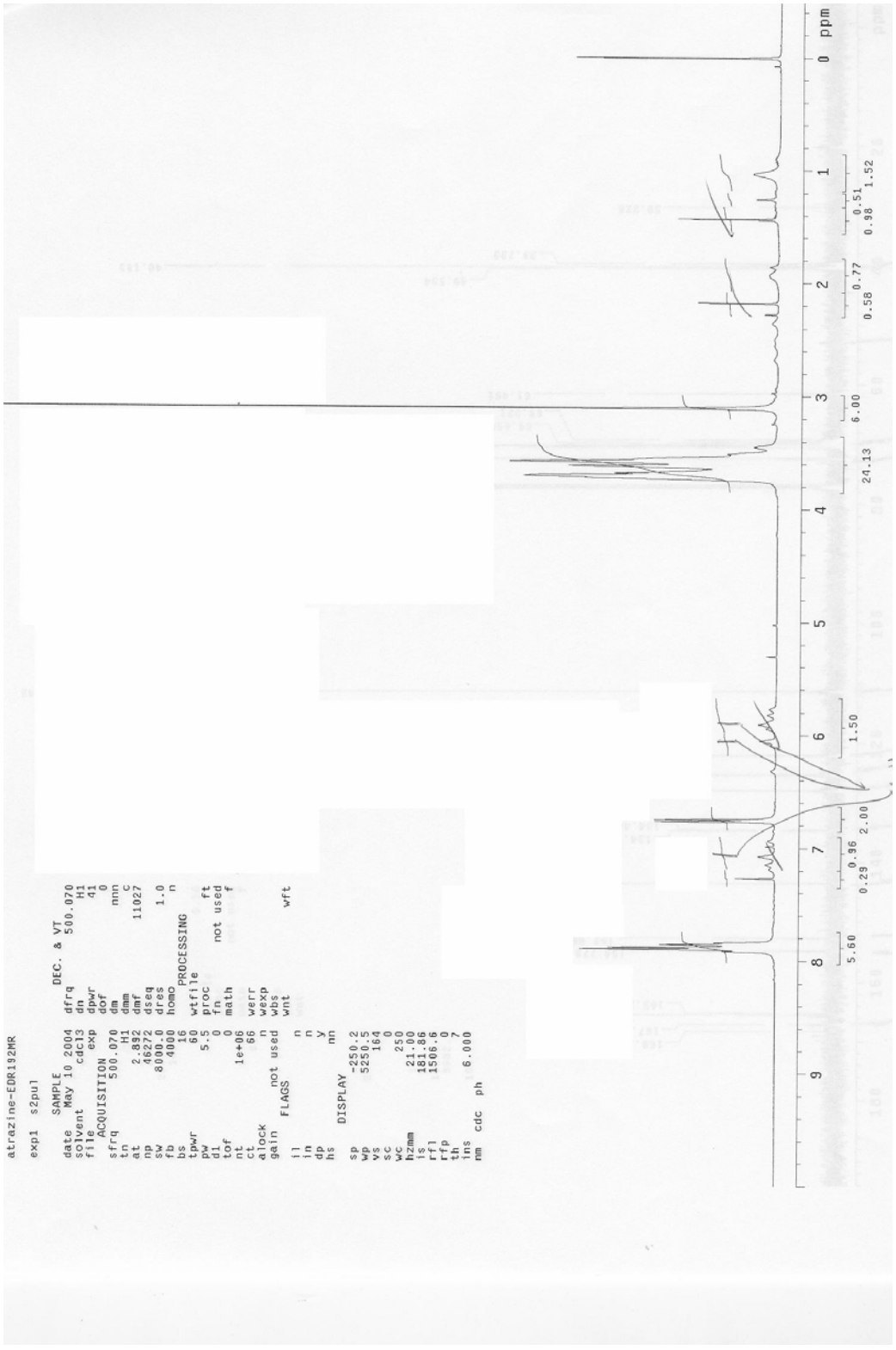

Figure D.8. ^{1}H NMR spectrum of **4**.

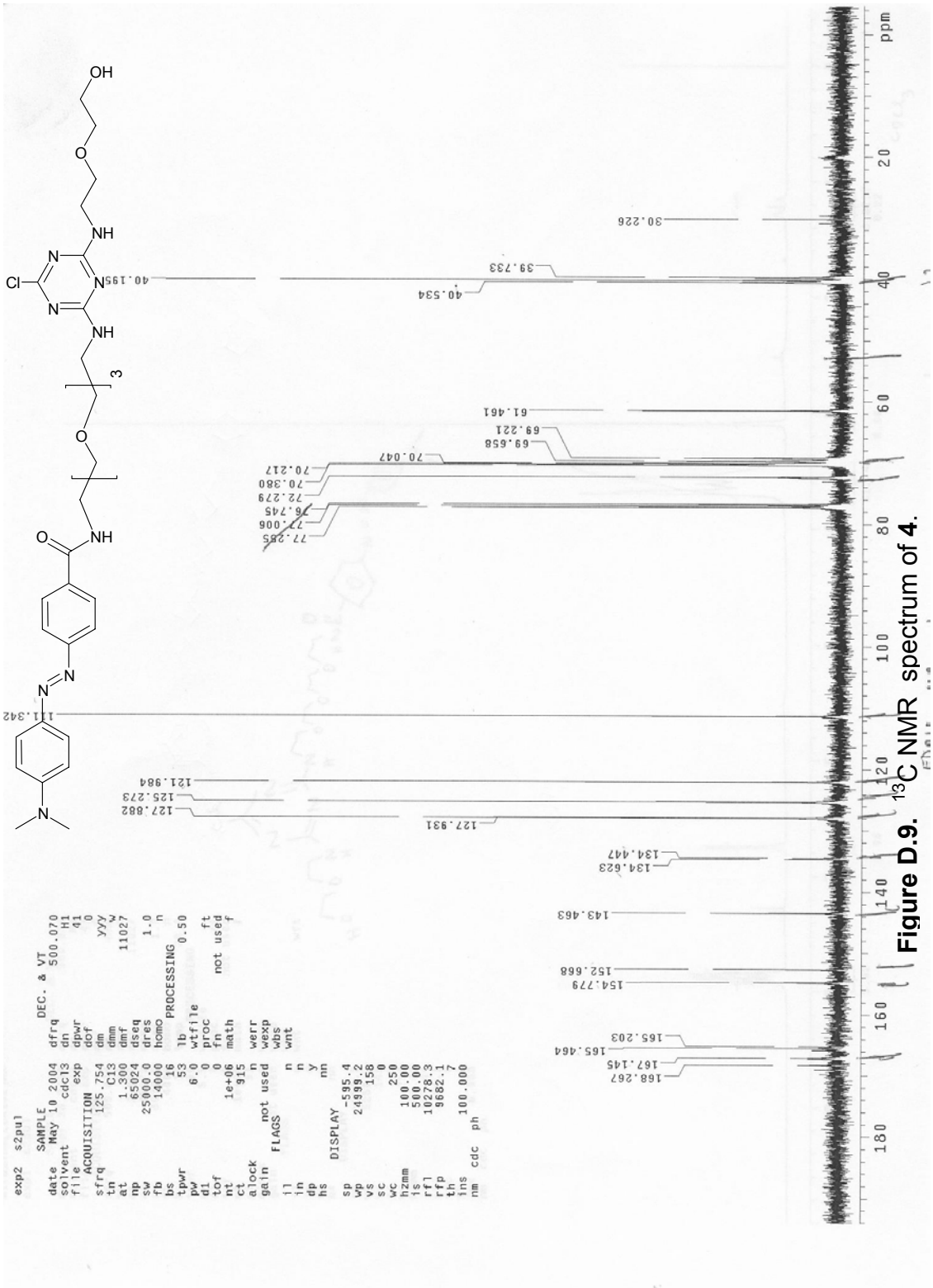

Figure D.9. ^{13}C NMR spectrum of **4**.

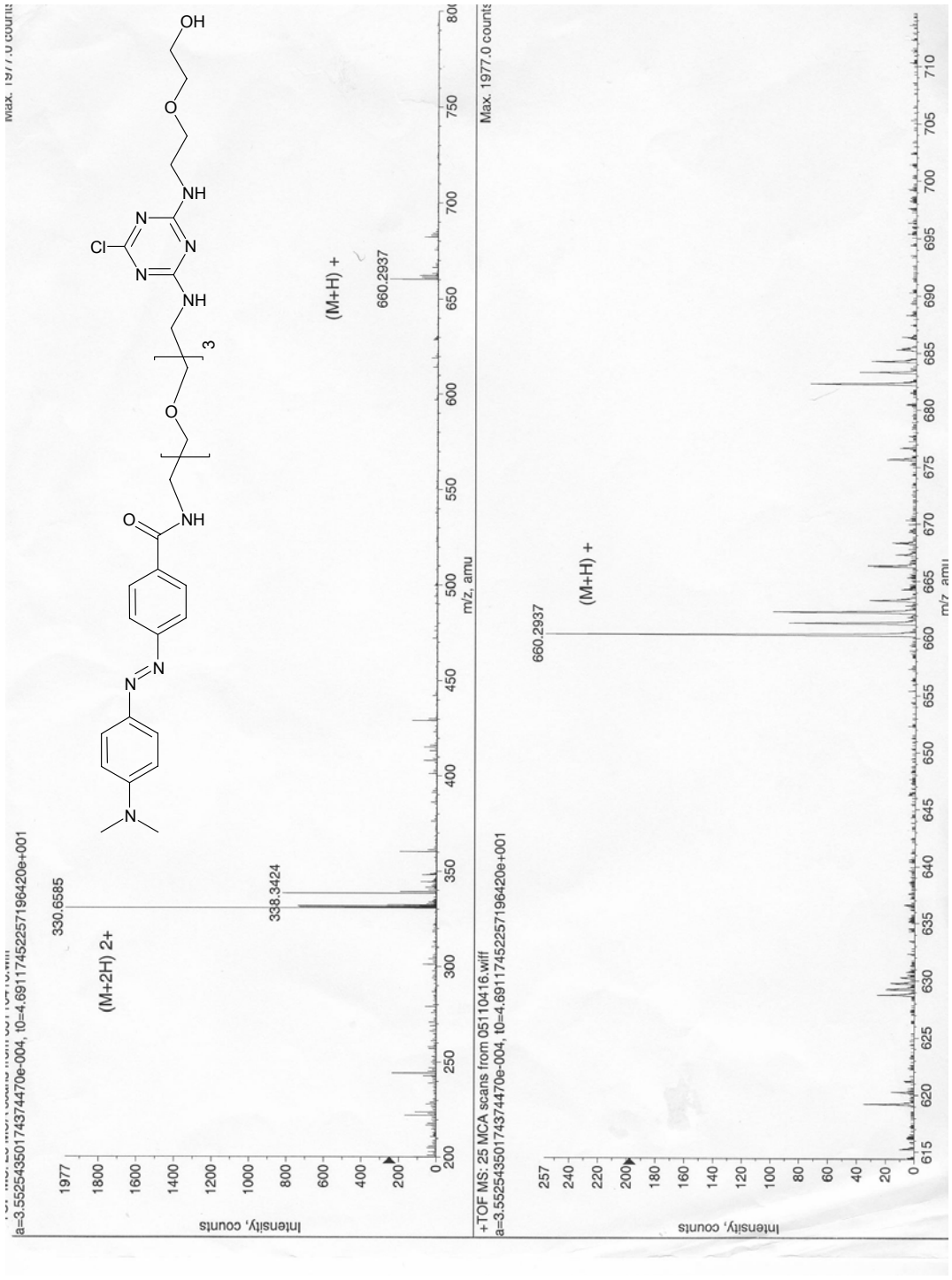

Figure D.10. ESI mass spectrum of **4**.

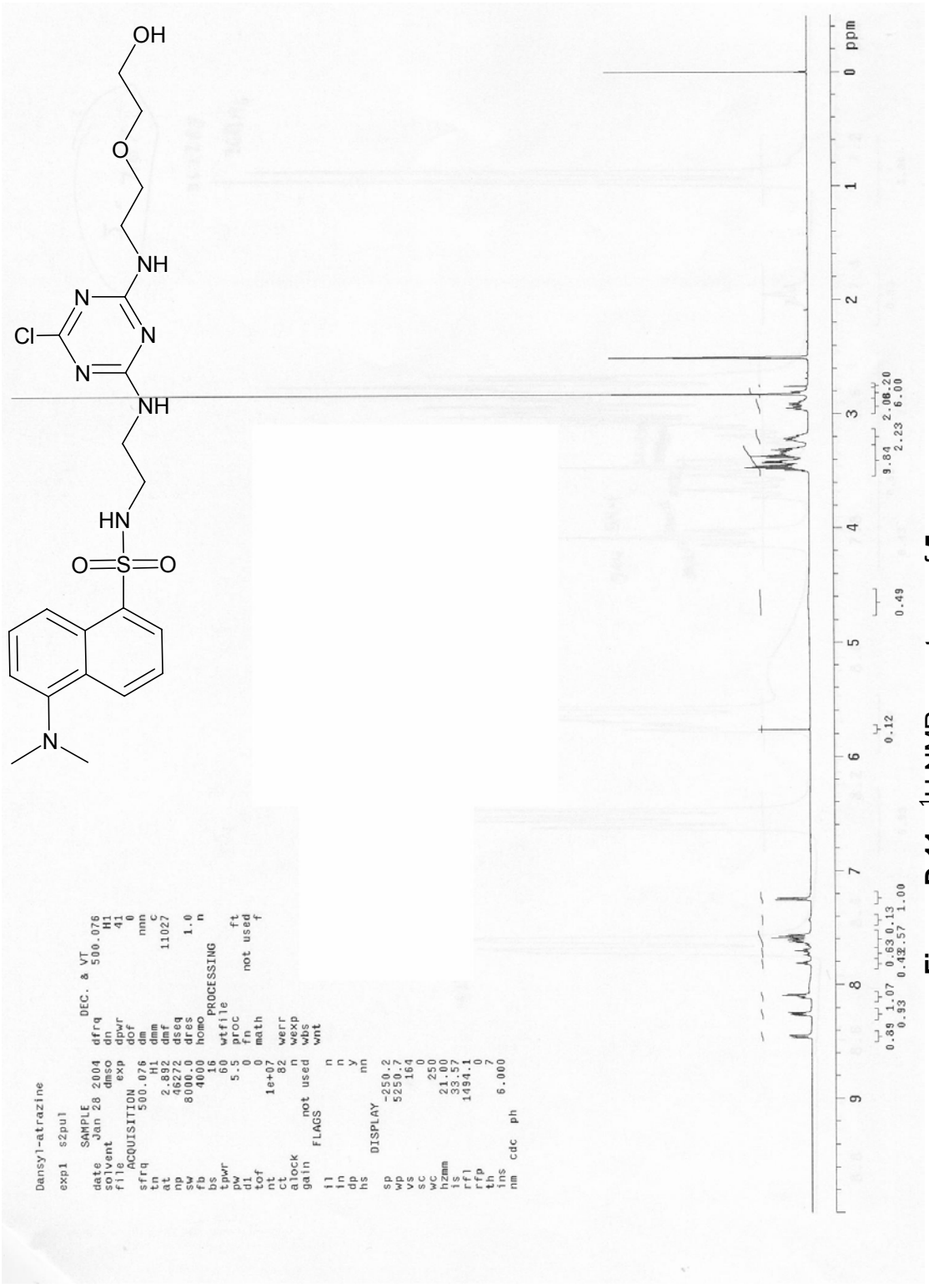

Figure D.11. ^{1}H NMR spectrum of **5**.

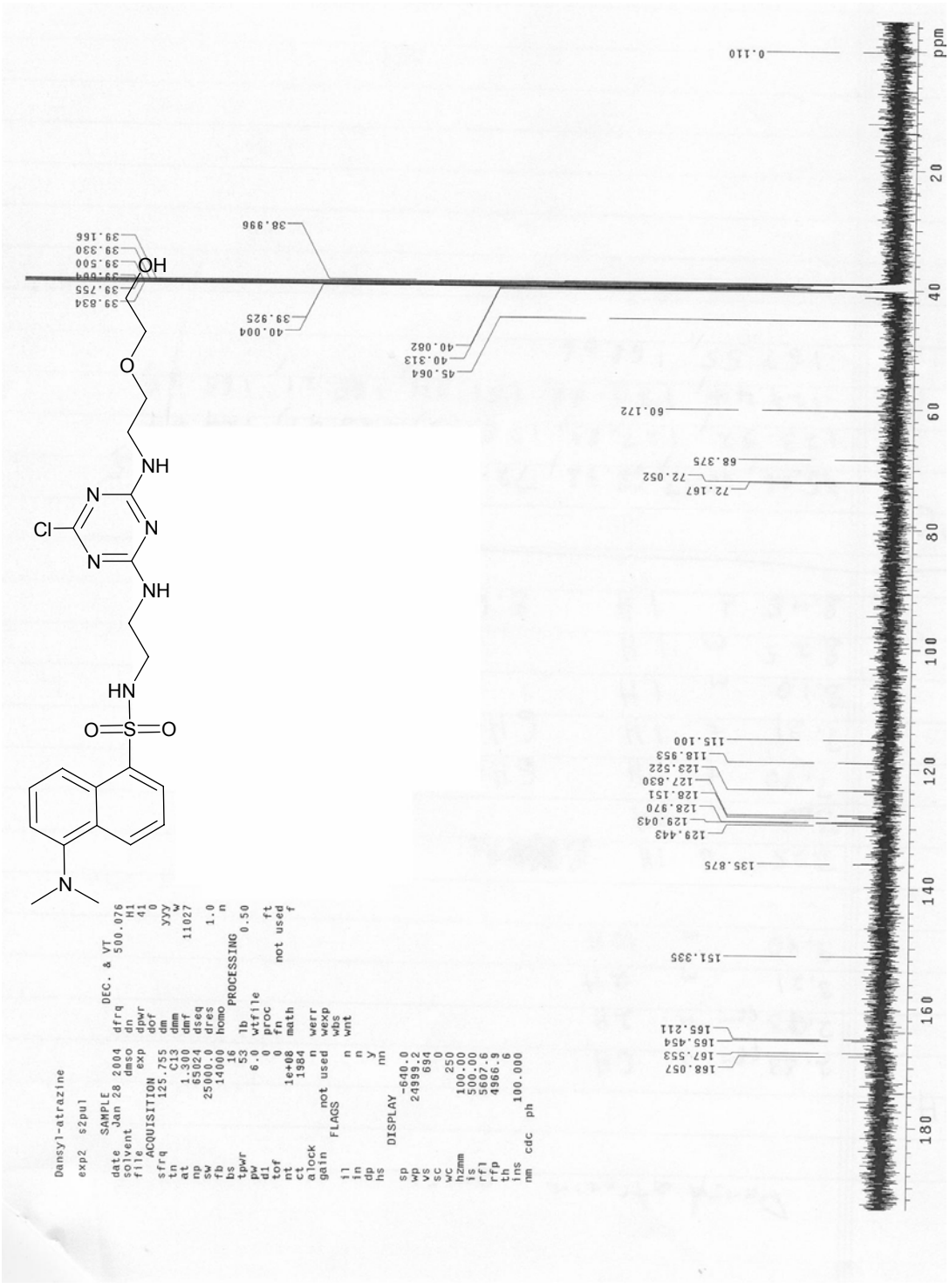

Figure D.12. ^{13}C NMR spectrum of **5**.

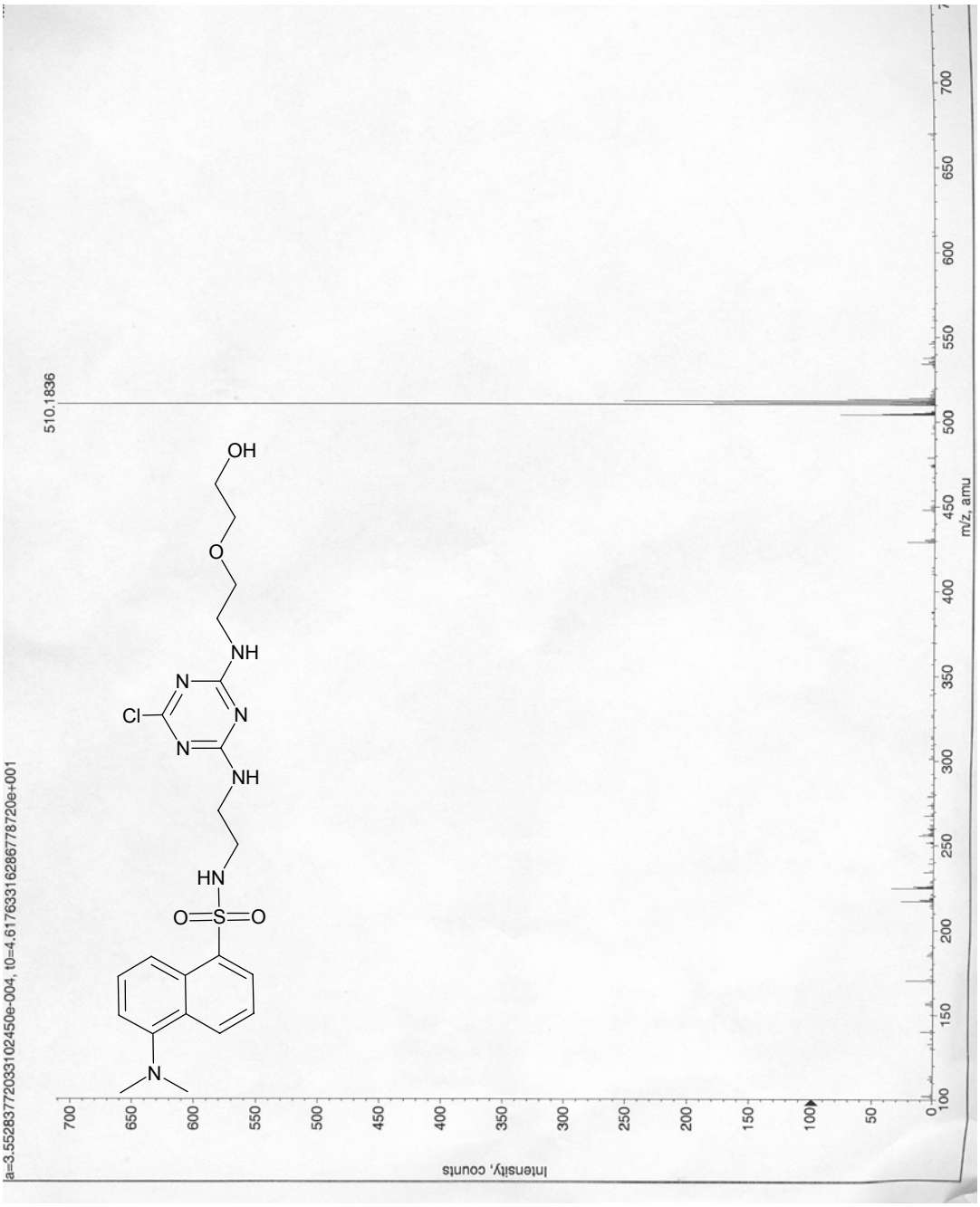

Figure D.13. ESI mass spectrum of **5**.

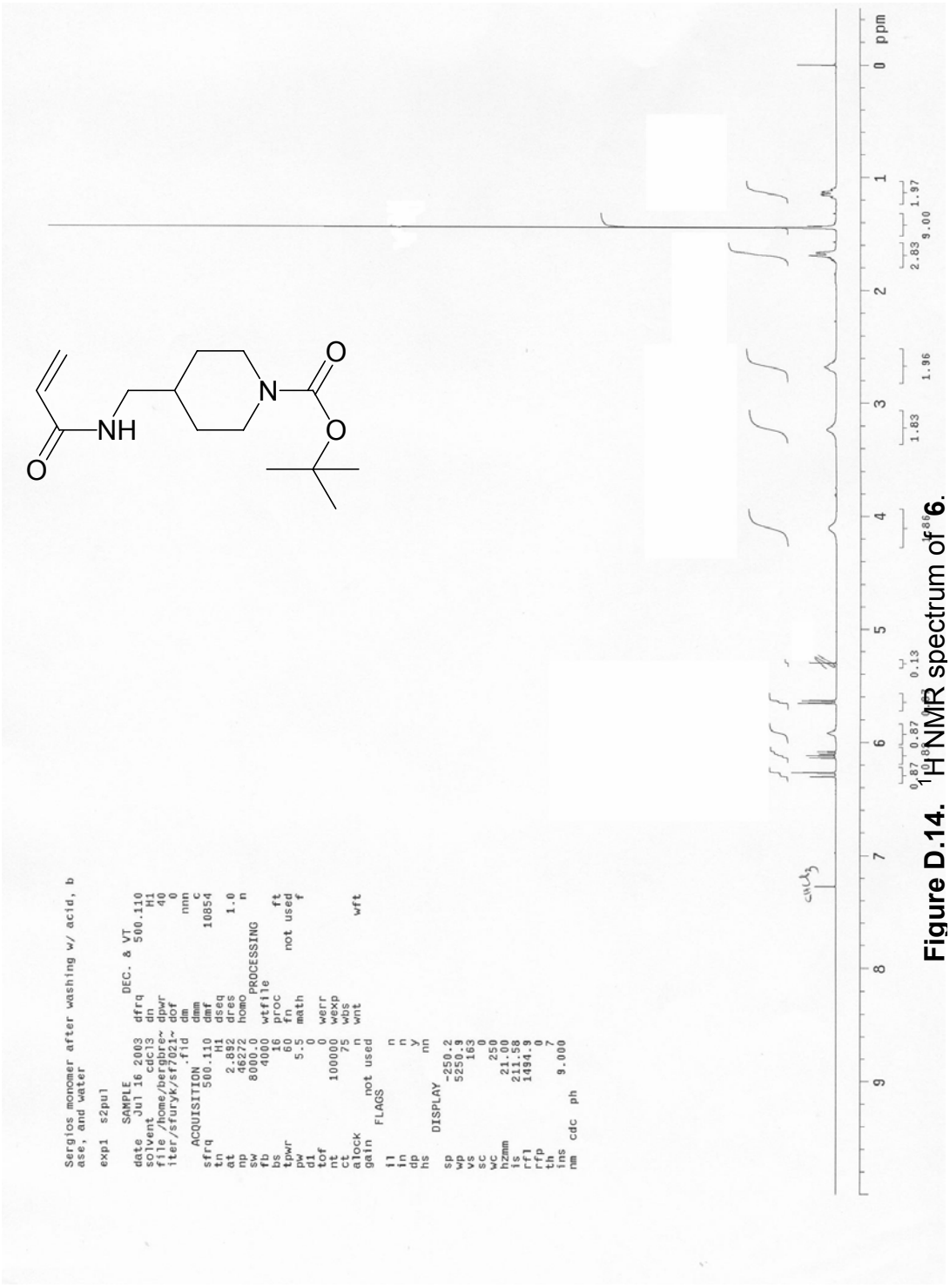

Figure D.14. ^{1}H NMR spectrum of ^{86}**6**.

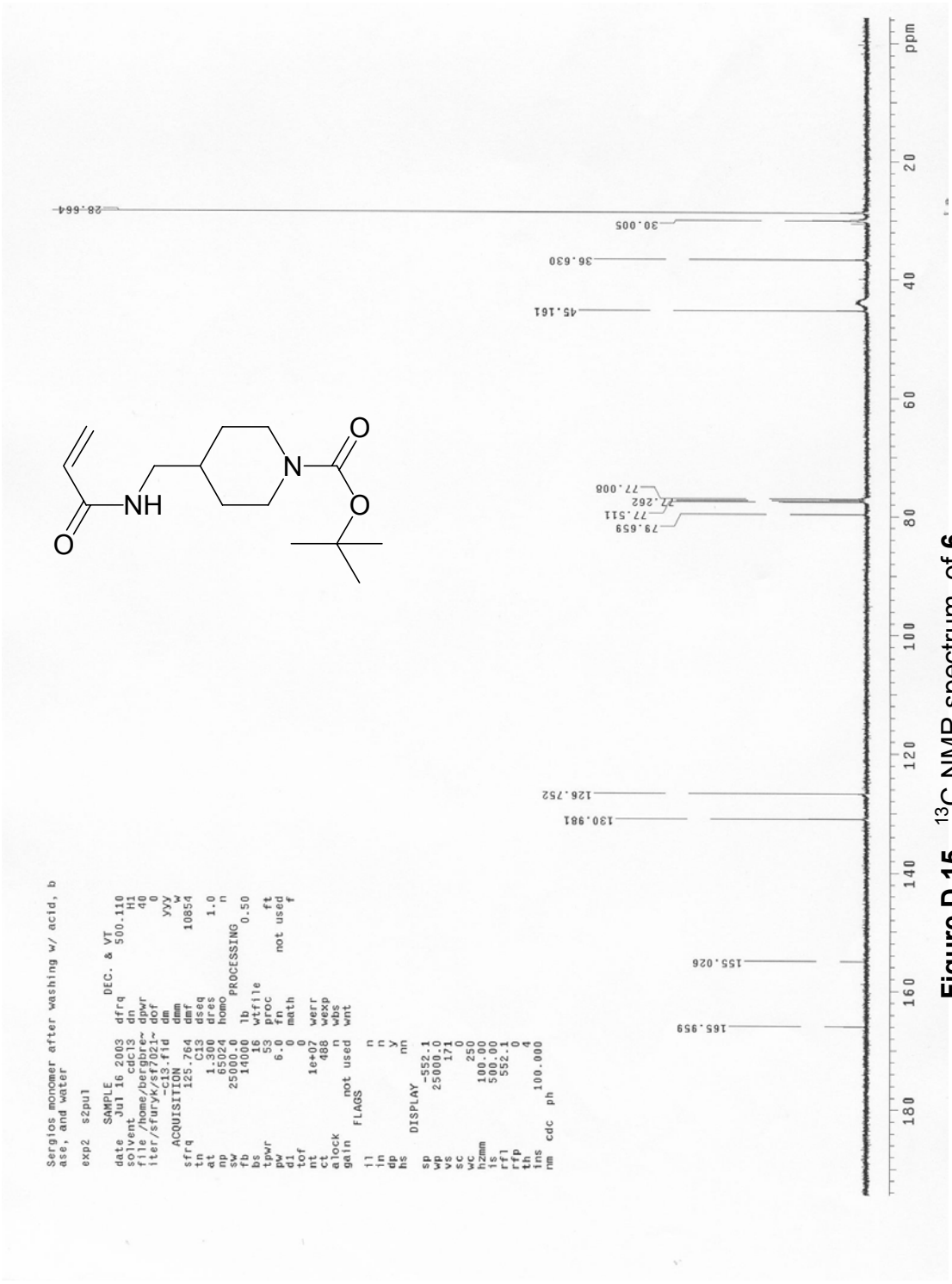

Figure D.15. ^{13}C NMR spectrum of **6**.

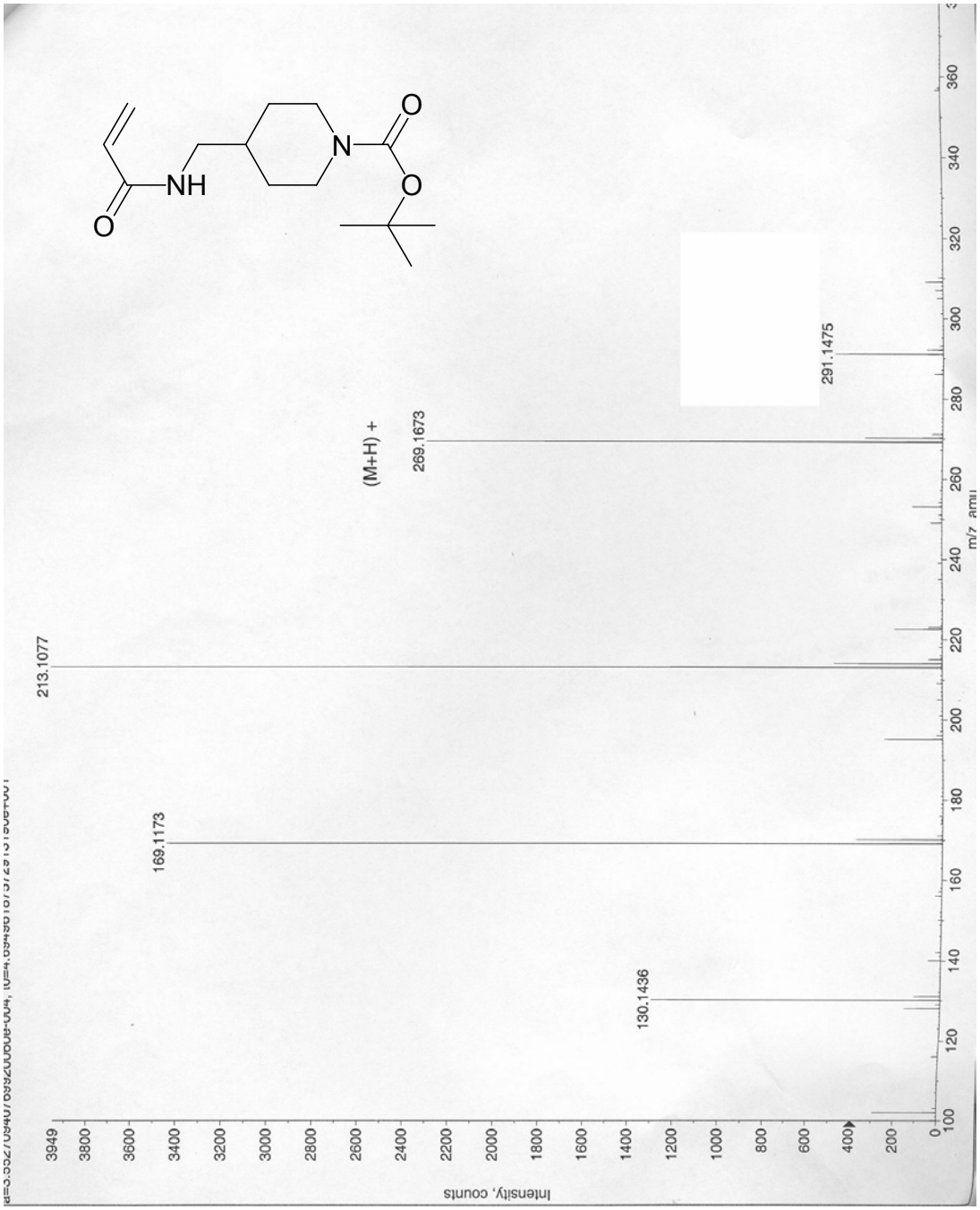

Figure D.16. ESI mass spectrum of **6**.

Figure D.17. ^{1}H NMR spectrum of **7**.

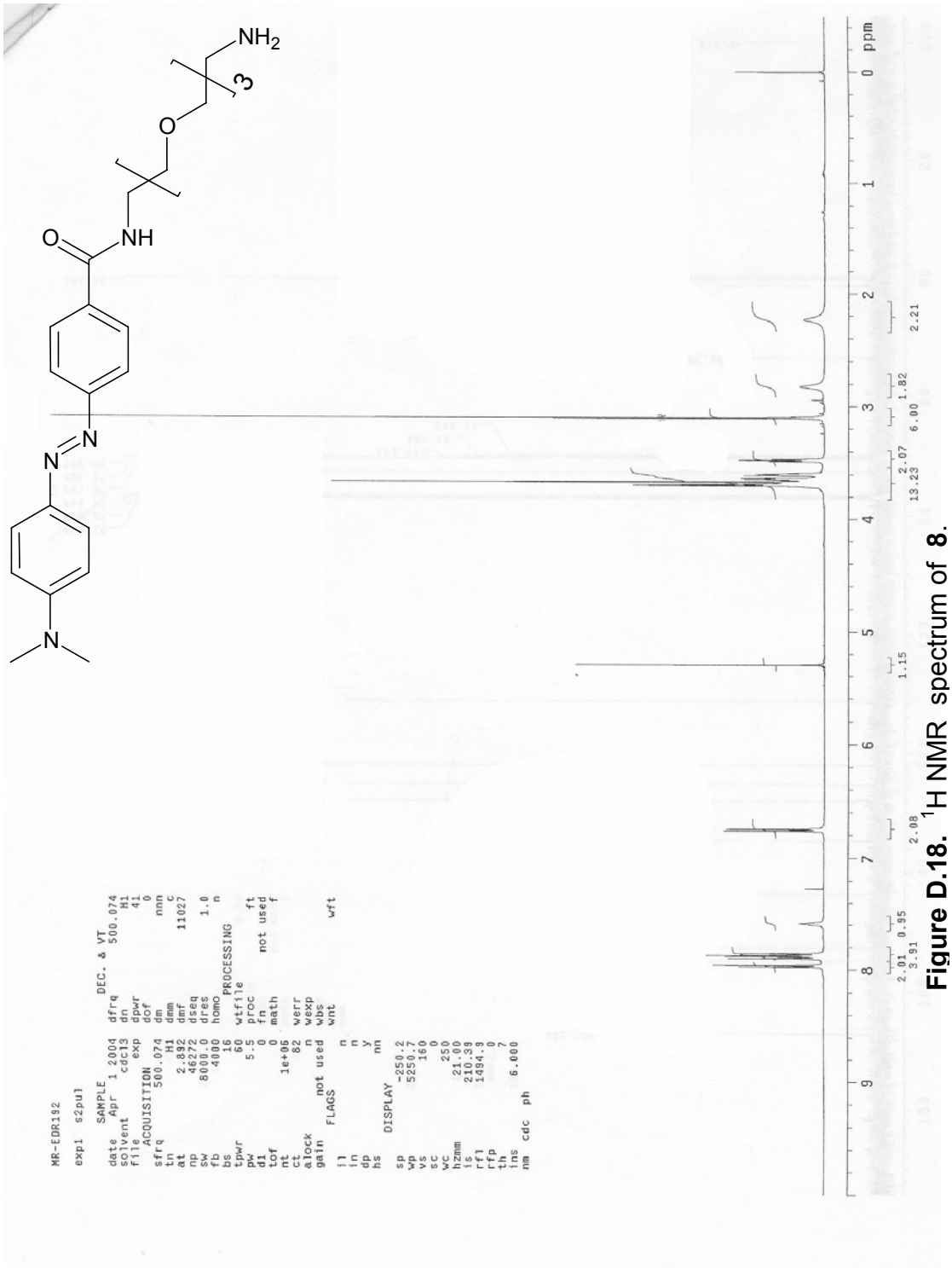

Figure D.18. ^{1}H NMR spectrum of **8**.

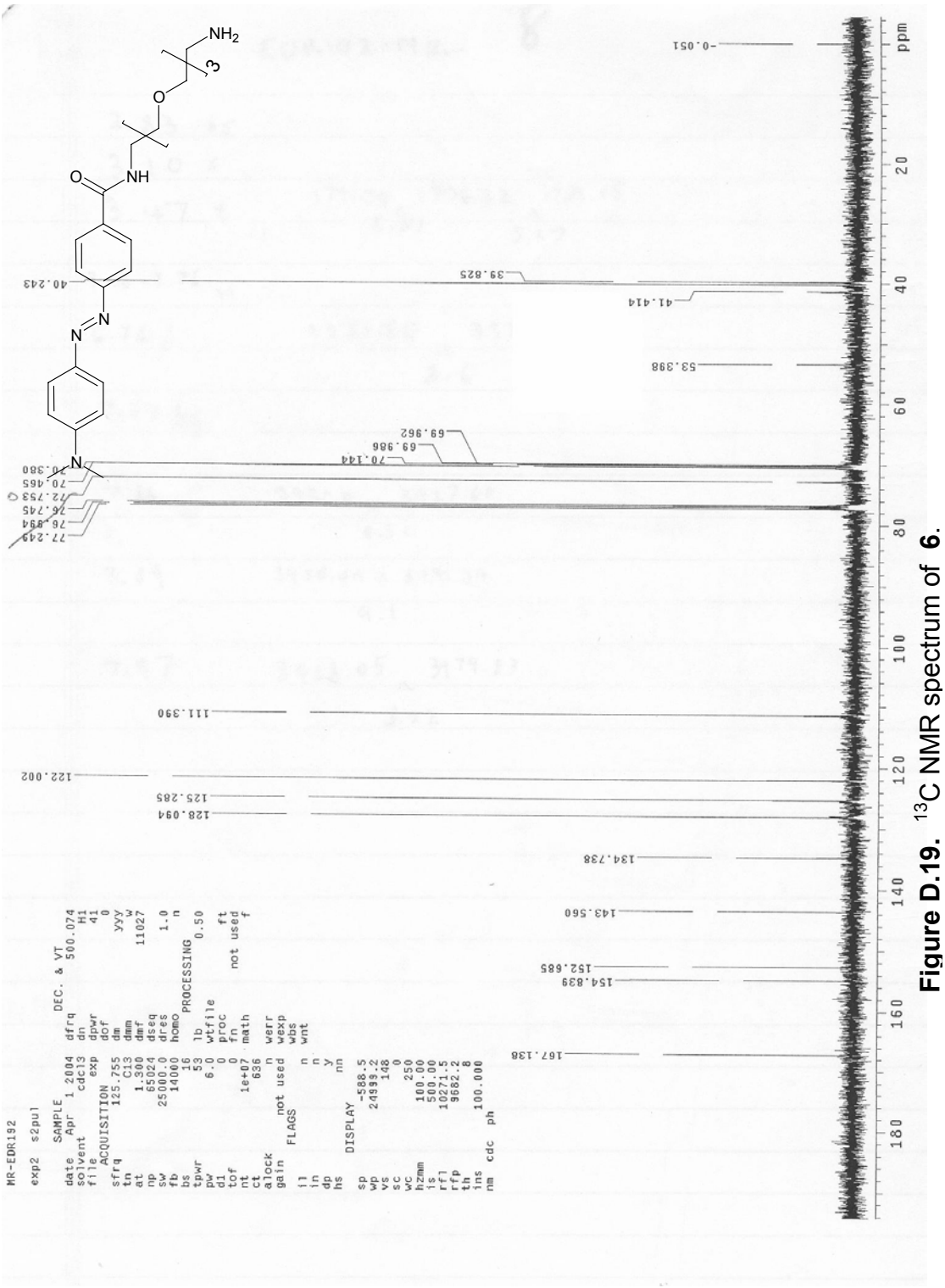

Figure D.19. ^{13}C NMR spectrum of **6**.

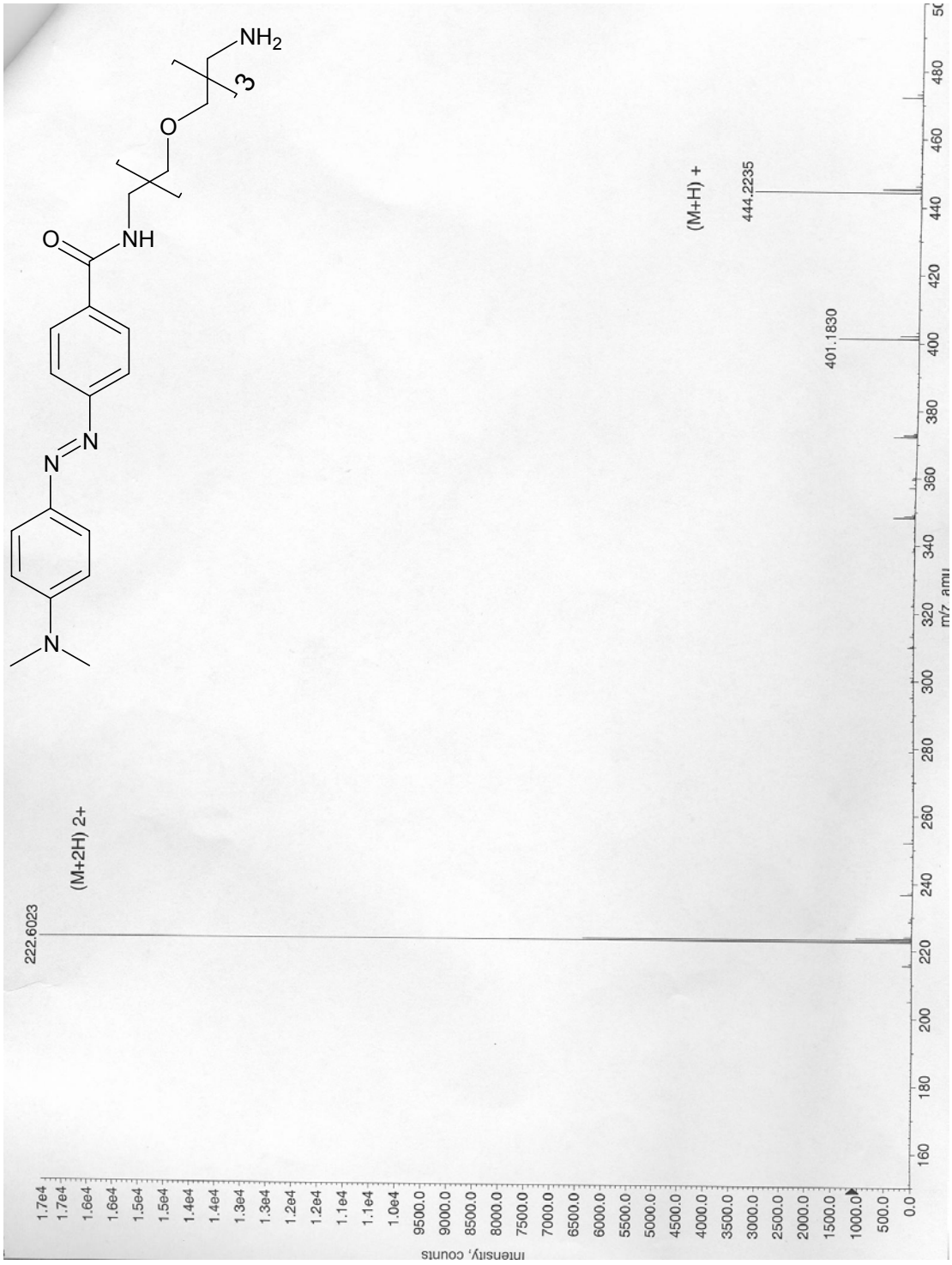

Figure D.20. ESI mass spectrum of **8**.

VITA

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