SYNTHESIS OF UNSYMMETRICAL SULFAMIDES AND POLYSULFAMIDES THROUGH SULFUR(VI) FLUORIDE EXCHANGE CHEMISTRY

A Thesis

by

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ABSTRACT

As hydrogen-bond donors and acceptors, *N,N'*-disubstituted sulfamides have been used in a range of applications from medicinal chemistry to anion-binding catalysis. However, compared to ureas or thioureas, the utilization of this unique moiety remains marginal, in part because of a lack of general synthetic methods to access unsymmetrical sulfamides. Specifically, polysulfamides are a virtually unknown type of polymer despite their potential utility in non-covalent dynamic networks, an intense area of research in materials science. This thesis reports a practical and efficient process to prepare unsymmetrical sulfamides via Sulfur(VI)-Fluoride Exchange (SuFEx) click chemistry, which was then applied to synthesize polysulfamides. Additionally, thermal analysis showed that this family of polymers possess high thermal stability and tunable glass transition temperatures. Hydrolysis studies indicated that aromatic polysulfamides could be recycled back to their constituting monomers at the end of their lifecycle. Last, the synthesis and application of AB-type monomers for polysulfamide synthesis will be examined.

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Contributors

This work was supervised by a dissertation committee consisting of Professor Quentin Michaudel (advisor, chair of committee) of the Department Chemistry and Materials Science and Engineering, Professor John A. Gladysz (committee member) of the Department of Chemistry, Professor Emily B. Pentzer (committee member) of the Department of Chemistry and Materials Science and Engineering, and Professor Jodie L. Lutkenhaus (committee member) of the Department of Chemical Engineering and Materials Science and Engineering.

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Initial studies on the syntheses and applications of AISF discussed in Chapter II were performed in collaboration with Dr. Cheoljae Kim. Additionally, studies on the coupling of amines to aliphatic sulfamoyl fluorides, also discussed in chapter II, were performed in collaboration with Dr. Cheoljae Kim and Jiun Wei Wu.

The synthesis and characterization of the bis(sulfamoyl fluoride)s and polysulfamides discussed in Chapter III were performed in collaboration with Jiun Wei

"Alec" Wu. Specifically, Mr. Wu was responsible for the synthesis and characterization of bis(sulfamoyl fluoride)s **3-3** and **3-4**, along with the polymers derived from those two compounds (**3-7**, **3-8**, **3-9**, **3-11**, **3-12**, **3-17**, and **3-18**).

All other work conducted for the thesis was completed by the student independently.

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NOMENCLATURE

AISF	4-(Acetylamino)phenyl]imidodisulfuryl difluoride
Bn	Benzyl
BPA	Bisphenol A
Boc	*tert*-butoxycarbonyl
$Đ$	Dispersity
DCM	Dichloromethane
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
DMAc	*N,N'*-dimethylacetamide
DMF	*N,N'*-dimethylformamide
DMSO	Dimethylsulfoxide
DP	Degree of polymerization
DP_n	Number-average degree of polymerization
DSC	Differential scanning calorimetry
η_{inh}	Inherent viscosity
ESI-MS	Electrospray ionization mass spectrometry
EtOAc	Ethyl acetate
FTIR	Fourier-transform infrared spectroscopy
M_n	Number-average molecular weight
Me	Methyl
MeCN	Acetonitrile

NMP	*N*-methyl-2-pyrrolidone
NMR	Nuclear magnetic resonance
OTf	Trifluoromethylsulfonate
ω	Weight fraction
p	Monomer conversion
Ph	Phenyl
Pyr	Pyridine
PIDA	Phenyliodine(III) diacetate
SEC	Size exclusion chromatography
SuFEx	Sulfur(VI) fluoride exchange
T_d	Decomposition temperature
T_g	Glass transition temperature
TBS	*Tert*-butyldimethylsilyl
t-Bu	*Tert*-butyl
TFA	Trifluoroacetic acid
TGA	Thermogravimetric analysis
THF	Tetrahydrofuran
XRD	X-ray diffraction

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CHAPTER I

INTRODUCTION

Condensation polymerization is at the core of the production of many high-commodity polymers. Polyesters, polyamides, polycarbonates, and polyurethanes all rely upon high-yielding condensation reactions at activated carbonyl groups, the chemistry of which have been refined over many decades of research. However, there is a parallel set of polymer categories that replace the carbonyl group with the more uncommon –SO_2– group that have not received as much study (Figure 1-1).

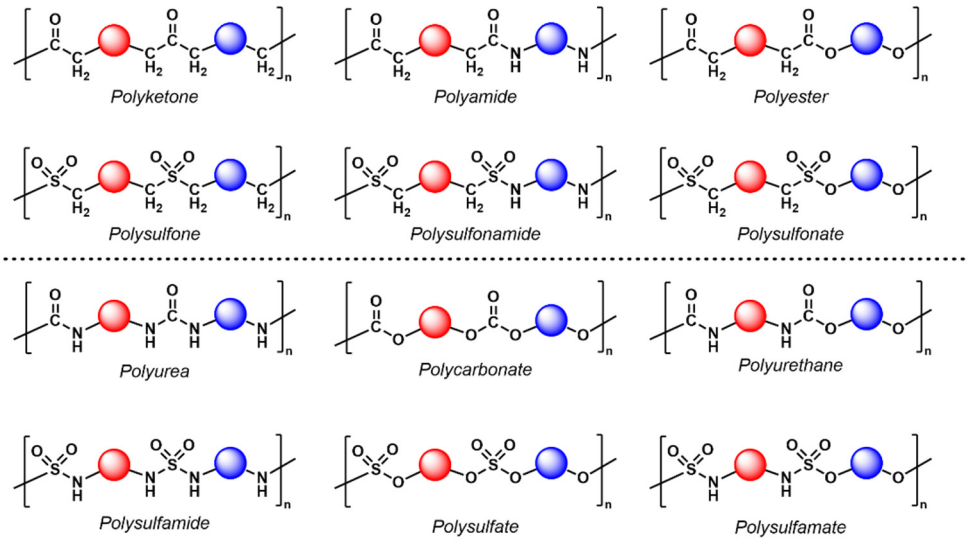

Figure 1-1. Common classes of carbonyl-containing polymers and their –SO_2– analogues.

The most common class of polymers to contain backbones containing sulfur(VI), poly(aryl ether sulfone)s have seen widespread use in industries ranging from medical

equipment to vehicle construction.[1] This class of polymers is notable for their high glass transition temperatures, allowing them to remain durable at temperatures in excess of 150 °C. The inclusion of ether linkages allows for additional chain flexibility, giving the resulting material thermoplastic properties. The glass transition of these materials can be altered using aliphatic comonomers, which provide additional chain flexibility and allow the polymer to be injection molded. The popularity of these materials can be partially explained by the ease with which they can be produced. Historically, these polymers were produced through the condensation of diphenyl ether and bis(arylsulfonyl chloride)s through electrophilic aromatic substitution, usually with the aid of a Lewis acid catalyst (Figure 1-2A).

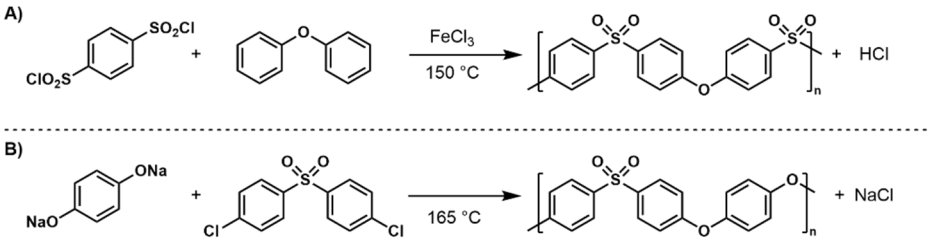

Figure 1-2. Example syntheses of poly(aryl ether sulfones) through A) electrophilic aromatic substitution and B) nucleophilic aromatic substitution.

This method was often complicated by the lack of preference for substitution at the *para* or the *ortho* position of the aryl ether, resulting in both structural irregularities and crosslinking that could greatly affect the mechanical and thermal properties of the resulting polymers. Modern methods for poly(aryl ether sulfone) synthesis typically rely on polycondensation of bis(phenoxide)s and bis(4-chlorophenyl)sulfone (Figure 1-2B).

This method allows for the production of polymers with consistent mechanical and thermal properties due to the enforced regiochemistry inherent to nucleophilic aromatic substitution. Poly(aryl ether sulfone)s are also resistant to acids, bases, and oxidants. The latter is likely due to the aromatic groups as the oxidative stability decreases significantly when aliphatic linkages are introduced to the polymer chain.

When it comes to sulfur(VI) polymers containing heteroatom linked to the $–SO_2–$ moiety, not nearly as much research has been performed. Polysulfates[2], polysulfonates[3-6], and polysulfonamides[7-8] have all been prepared using solution-phase or interfacial chemistry through the use of monomers containing sulfonyl chloride functional groups. Sulfonyl chloride groups differ from acyl chlorides in that they are good chlorinating agents in addition to being good electrophiles. There are also no reasonable alternatives to commonplace carbonyl polymer precursors. Sulfuryl chloride, the sulfur(VI) analogue of phosgene is also a potent chlorinating agent that easily hydrolyzes in the presence of water.[9] Meanwhile isocyanates, the industrial precursor to polyamides and polyurethanes, have no bench-stable sulfur(VI) counterpart. Replacing the carbonyl portion of an isocyanate with a sulfonyl group gives the azasulfene functional group, which is an incredibly potent electrophile that has only been discussed as a short-lived intermediate in sulfur(VI) group exchange reactions.[10-12] The use of sulfonyl chlorides complicates the condensation reactions that were traditionally performed to synthesize sulfur(VI) polymers. These chlorinating side reactions not only lower the reaction yield, and by extension the molecular weight of the obtained polymer, but also lead to structural irregularities and chain degradation.

As an example, consider early studies on the synthesis of polysulfates, the sulfonylated variant of polycarbonates.[2] Initial studies on the synthesis of polysulfates were performed by Firth using aryl chlorosulfates and 2,2-bis(4-hydroxyphenyl)propane, known colloquially as Bisphenol A or BPA (Figure 1-3A). Reacting BPA directly with sulfuryl chloride in the presence of an acid acceptor did not successfully produce any polymer, likely due to side reactions of the chlorosulfate or the sulfuryl chloride itself. The aryl bischlorosulfate monomers were prepared by the slow addition of sulfuryl chloride to a solution of BPA and pyridine in DCM at -64 °C. Higher reaction temperatures were noted to produce chlorinated byproducts that proved difficult to remove from the desired monomer. When the bischlorosulfate was treated with BPA and pyridine at 80 – 120 °C, only chlorinated oligomers could be obtained. These oligomers were hydrolyzed with aqueous sodium hydroxide and treated with phosgene to create a carbonate-sulfate copolymer for further examination. Based on elemental analysis, the number of sulfate groups in the copolymer barely outnumbered the number of carbonate groups, giving the original sulfate oligomers an average degree of polymerization of 2 or less. The copolymer was also heavily chlorinated, further demonstrating the highly unselective reactivity of chlorosulfates towards phenols.

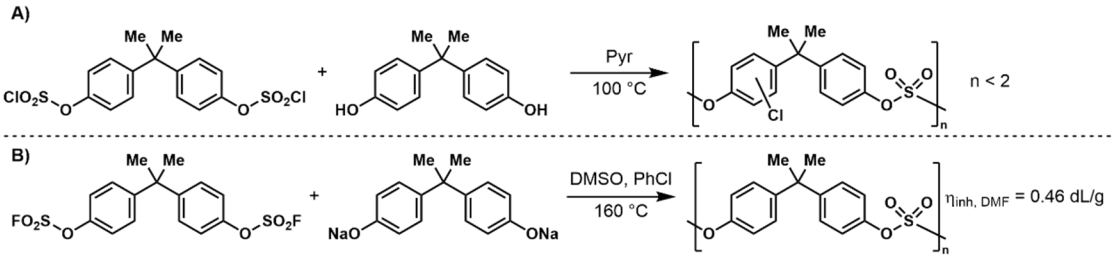

Figure 1-3. Synthesis of BPA polysulfate using A) bis(chlorosulfate) and B) bis(fluorosulfate) monomers.

In the search for a more well-behaved monomer, Firth turned to fluorosulfates; substituting sulfuryl chloride with sulfuryl fluoride. Similar to sulfuryl chloride, reacting sulfuryl fluoride with BPA in pyridine solution at 115 °C yielded no polymer. However, instead of producing halogenated side products like sulfuryl chloride, sulfuryl fluoride formed the bisfluorosulfate of BPA and reacted no further. This indicated the desired lower activity of the fluorosulfate functional group, making it a promising monomer for polycondensation. Reaction of the aforementioned bisfluorosulfate with the disodium salt of BPA in DMSO solution at 150 °C yielded the desired polysulfate polymer in good yield as an amporphous solid. The reaction also produced a crystalline, low molecular weight impurity, which was likely a cyclic oligomer. The polymer obtained from the bisfluorosulfate was of a significantly higher molecular weight than that that obtained from the bischlorosulfate, and with less side reactions based on the NMR and elemental analysis data obtained. The polymer had a T_g of 93 °C and was noted to be strong, rigid, and more resistant to hydrolysis than BPA polycarbonate. In this scenario, sulfur(VI) fluorides were clearly a more effective monomer due to their increased selectivity compared to their respective chlorides.

Seeing the synthetic utility of sulfur(VI) fluorides as more stable alternatives to sulfur(VI) chlorides, Sharpless and coworkers developed SuFEx click chemistry. As outlined in a seminal article in 2014,[13] this chemistry relies on the chemical and thermal stability of sulfonyl fluorides compared to sulfonyl chlorides to create linker molecules that remain bench-stable until they are utilized in a desired coupling reaction with a nucleophilic species. Compared to their respective sulfonyl chloride, sulfonyl fluorides are generally less prone to hydrolysis, do not act as halogenation agents, and can exist at high temperatures for longer periods of time before degrading (Figure 1-4). When reacting with a nucleophile, sulfuryl fluorides react quickly and selectively to form sulfur(VI) containing molecules. The fluoride that is eliminated can be controlled by performing the reaction in basic conditions to prevent the formation of hydrofluoric acid or using silylated nucleophiles. All these factors make sulfonyl fluorides exciting new precursors to sulfur(VI) polymers. Indeed, since its inception, SuFEx has been used to synthesize polysulfates and polysulfonates in high yield with substantial molecular weight.[14-16] While

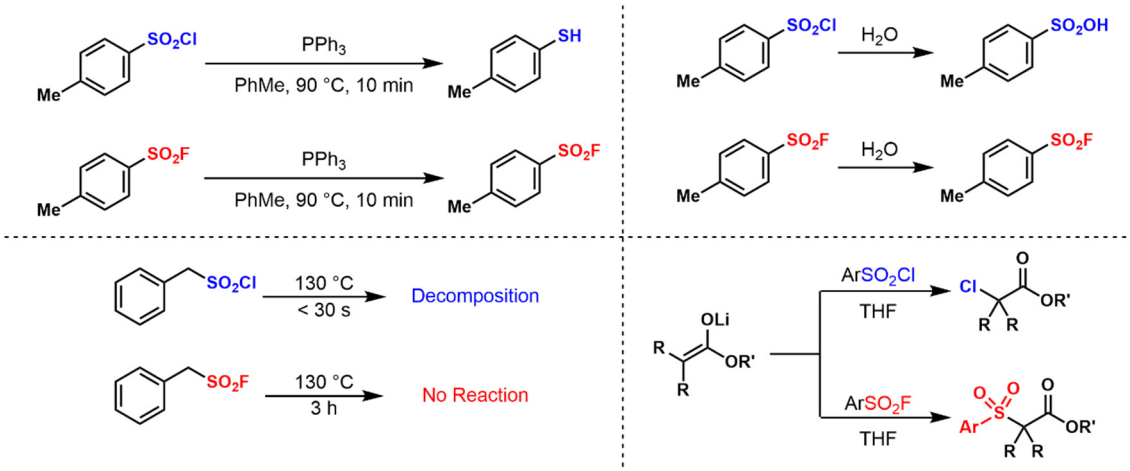

Figure 1-4. Sample reactions showcasing the stability and selectivity of sulfur(VI) fluorides

catalytic amounts of DBU were originally used for these reactions, it was found since then that bifluoride catalysts can provide similar polymers of similar molecular weight at lower catalyst loadings.

As the sulfur(VI) analogue to ureas, sulfamides have a variety of applications as hydrogen bond acceptors and donors, depending on the level of substitution at each nitrogen in the sulfamide functional group, and have received sporadic attention over the years.[17,18] For example, *N,N′*-disubstituted sulfamides have been used as gelators to trigger the assembly of 3D networks and vesicles.[19] In a medicinal chemistry setting, sulfamides can be used as bioisosteres for amides, ureas, and carbamates, and have become more common in the medicinal chemist's arsenal.[20] For example, the broad-spectrum antibiotic doripenem contains a monosubstituted sulfamide pharmacophore.[21] Hydrogen-bonding organocatalysis could become a natural avenue of research for these compounds, but only a handful of useful transformations have been reported with sulfamides thus far. Also of note is that one class of sulfur(VI) polymer that has not been accessed through SuFEx click chemistry is the polysulfamide.

While polyureas are used as a commodity polymer (e.g., spandex), only a few syntheses of polysulfamides have been reported, rendering their properties underexplored. Unlike many of the polymer archetypes discussed previously, polysulfamides cannot be prepared using a sulfur(VI) chlorides starting material, in this case a sulfamoyl chloride. In addition to the chlorinating side reactions that were already a problem present in polymerizations involving sulfur(VI) chlorides, sulfamoyl chlorides easily decompose in the presence of bases. The inherent basicity of diamines makes this a major issue with

using this synthetic route to make polymers. The simplest way to bypass this issue was through the use of unsubstituted sulfamide. One of the first methods used to create polymers using sulfamide was through the condensation of formaldehyde and sulfamide in basic conditions, which led to the formation of a soft, resinous material, but was not further characterized due to the lack of analytical methods at the time.[22] Scott and Smith built on this procedure by adding a crosslinking agent, such as melamine, to create a stronger, more thermally stable polymer (Figure 1-5A). However, the polymers created through both acid and base catalyzed polymerization resulted in the creation of highly crosslinked and highly insoluble materials which were limited in application and processability. The polymers were also found to have inconsistent structure based on elemental analysis. However, these materials had good thermal stability, decomposing at around 225 °C.

Approaching the synthesis from a different direction Vandi, Moeller, and Audrieth claimed to have synthesized a polysulfamide through a bulk melt of hexamethylenediamine and sulfamide at 130 °C (Figure 1-5B).[23] The evolution of ammonia gas from the melt was noted, indicating the condensation of the two monomers. The white solid obtained after the reaction is insoluble in most organic solvents except for boiling DMF and *m*-cresol. This material has a melting point of 236 – 238 °C, much higher than either of the monomers used to synthesize it. Elemental analysis was consistent with a linear structure, with no branching or crosslinking, and the IR spectrum of the material showed the expected N-H and –SO_2– peaks of a symmetrically substituted sulfamide.

With this characterization it was likely that some kind of polymer was produced, but not much else can be inferred about the size or properties of this polymer.

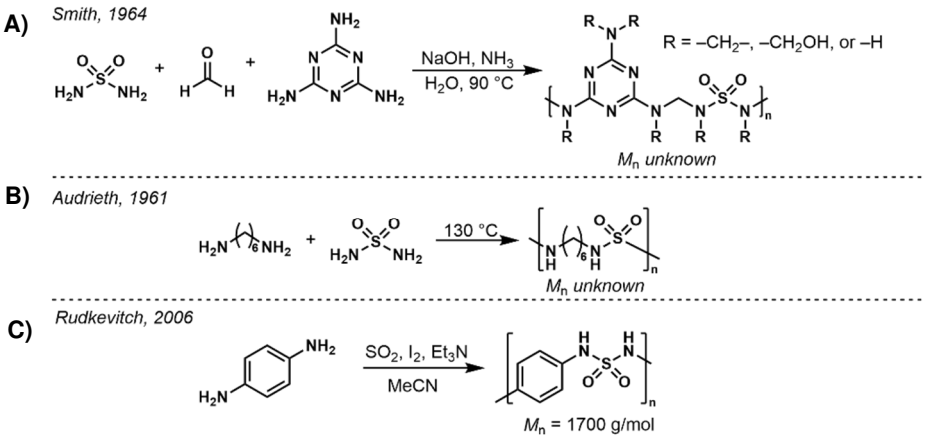

Figure 1-5. Previously reported syntheses of polysulfamides.

More recent forays into the synthesis of polysulfamides focus on the usage of sulfur dioxide as the sulfonylating agent in a one-pot synthesis. Rudkevich first demonstrated the use of iodine and dissolved sulfur dioxide for the formations of symmetrical sulfamides in moderate to good yield, along with one polysulfamide obtained from 1,4-phenylenediamine using a similar procedure (Figure 1-5C).[24] This reaction is very fast, and likely involves multiple sulfur(VI) iodide intermediates. The presence of sulfamides in oxidizing and basic conditions, however, allows for many uncontrolled side reactions, resulting in fairly short polymers (M_n = 1.7 kg/mol), limiting the usefulness of this reaction for the synthesis of functional materials. Tao and Dai were able to utilize this method to develop porous polysulfamides using fluorene and triphenylbenzene based

monomers.[25] These polymers were found to have decent BET surface area (57 and 211 m^2/g) along with good thermal stability (T_d = 300 °C). An advantage of these polymers over more traditional porous organic polymers is that the polysulfamides synthesized are more soluble in organic solvents, making them easier to form into membranes.

Considering the Carothers equation,[26] it was hypothesized that in order to obtain polysulfamides with higher degrees of polymerization (DP), a new synthetic method should be devised that 1) afford control over the stoichiometry of AA/BB type monomers, and 2) avoid potential deleterious oxidative side-reactions that diminish the yield of the coupling reaction. This was the motivation for the development of conditions based on SuFEx click chemistry for the high-yielding preparation of isolable sulfamoyl fluorides, unsymmetrical sulfamides, and polysulfamides. While several methods producing sulfamides have been reported, these methods usually involve the use of highly reactive sulfamoyl chlorides or large leaving groups.[27] SuFEx was an attractive alternative due to its mildness, efficiency, atom-economy, and stability of the fluoride-containing intermediate.

The following reports the examination of polysulfamide formation via SuFEx chemistry (Figure 1-6). The next chapter will discuss the synthesis of primary sulfamoyl fluorides and the optimization of the synthesis of sulfamides through SuFEx chemistry.

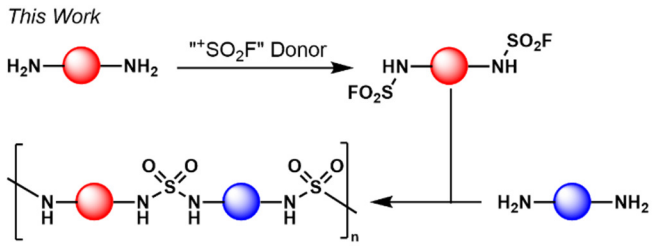

Figure 1-6. The synthesis of polysulfamides through SuFEx.

Chapter III will cover the synthesis of polysulfamides through AA/BB type step-growth polymerization. The basic properties of polysulfamides will then be examined using thermal and spectroscopic techniques. This will be followed by a discussion on the environmentally-friendly degradation of these polymers back to their constituent diamines. Last, chapter IV will discuss the synthesis of an AB-type monomer for SuFEx polycondensation, as well as these monomers viability for polymerization.

Polysulfamides are currently a largely unknown class of polymers, due to the lack of a reliable method to synthesize them. However, there is an increasing demand for the study of molecules containing sulfamides in material and pharmaceutical design. With SuFEx chemistry,an opportunity has been opened for many new sulfur(VI)-containing polymer species, including poly(sulfamide)s, to be studied.

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CHAPTER II

SULFAMOYL FLUORIDE SYNTHESIS AND THE OPTIMIZATION OF SULFAMIDE FORMATION*

2.1 Synthesis of Sulfamoyl Fluorides

Finding the most efficient way to synthesize sulfamoyl fluorides was the logical starting point for synthesizing sulfamides through SuFEx. The most obvious route to sulfamoyl fluorides would be similar to Firth's method, later utilized by Sharpless, to create fluorosulfates from phenols and apply it to primary amines.[1,2] This involves the use of sulfuryl fluoride gas and a base to create the desired fluorosulfate from a phenol through simple substitution. One issue that complicates the usage of this method for the synthesis of primary sulfamoyl fluorides is the intended reactivity of the product toward bases. The proton of a primary sulfamoyl fluoride group is relatively acidic, and will again lead to the formation of a highly reactive azasulfene intermediate when removed (Figure 2-1).

As described by Murthy and coworkers,[3] and confirmed during this work, treating a primary amine with sulfuryl fluoride leads to the production of the desired sulfamoyl fluoride. However, due to the basic nature of the reaction solution, the sulfamoyl fluoride further reacts with the remaining amine in solution, leading to the formation of a symmetrically substituted sulfamide (Figure 2-1). While this proves the high reactivity of primary sulfamoyl fluorides under basic conditions, it is not ideal for the synthesis of the

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desired AA and AB type monomers. In order to produce a bench-stable monomer for polysulfamide formation in decent yield, another synthetic strategy needed to be used.

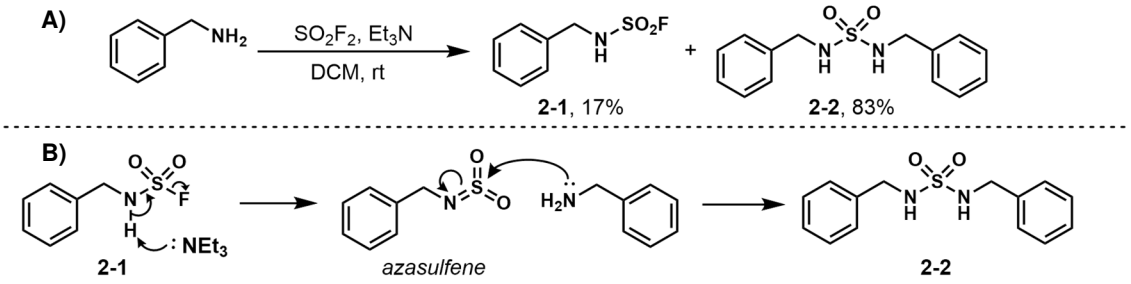


Figure 2-1. A) Experimental result of treating a primary amine with sulfuryl fluoride gas. Yields were determined using ^{1}H NMR B) Mechanism of azasulfene formation, followed by its attack by an amine.

While secondary sulfamoyl fluorides are easier to synthesize directly from sulfuryl fluoride, primary sulfamoyl fluorides would be the ideal monomer due to their significantly higher reactivity. As a representative example, the sulfamoyl fluorides of benzylamine and *N*-methylbenzylamine were subjected to identical conditions in an attempt to form a sulfamide with benzylamine. While the primary sulfamoyl fluoride, **2-1**, undergoes complete conversion within only a couple of hours to form *N,N'*-dibenzylsulfamide, the secondary sulfamoyl fluoride, **2-3**, shows no sign of conversion after 18 hours (Figure 2-2A). This result is consistent with previous studies examining the hydrolysis of sulfamate esters, which proceeds through a similar azasulfene intermediate.[4] This does not mean that secondary sulfamoyl fluorides are completely inert. On the contrary, there have been two sets of conditions previously published on the synthesis of sulfamides from secondary sulfamoyl fluorides (Figure 2-2B). The first, described by Sharpless and coworkers,[5] involves treatment with magnesium oxide and the use of an

aqueous solvent system. The presence of a base and water in the reaction mixture may cause solvolysis of the polymer chain over the course of the reaction, as will be discussed in chapter 3. Meanwhile, during the writing of this thesis, Ball and coworkers demonstrated that calcium triflimide could activate the sulfamoyl fluoride group and allow the coupling to another amine.[6] This synthesis was shown to have the best yields in THF, which is a solvent that polysulfamides are not soluble in. The lack of solubility could hinder polymer growth.

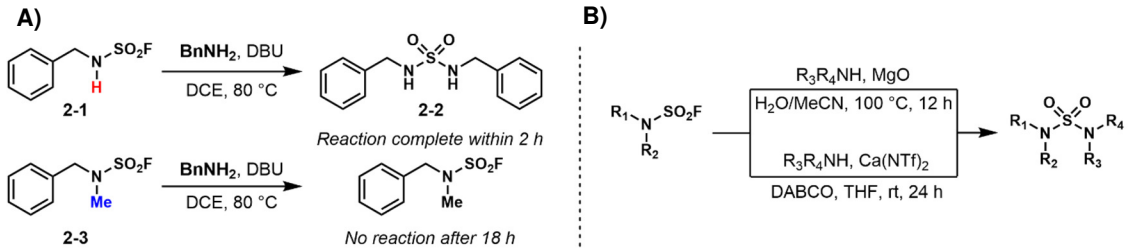


Figure 2-2. A) Observed difference in reactivity between primary and secondary sulfamoyl fluorides. B) Previously published conditions for secondary sulfamoyl fluoride coupling.[5,6]

Many synthetic methods have been devised to form primary sulfamoyl fluorides. The simplest, reported by Weiß and Schulze, involves the halide exchange of a sulfamoyl chloride with a fluoride salt.[7] This can be achieved through the treatment of a sulfamic acid, obtained through the reaction of a primary amine with chlorosulfonic acid, and phosphorous pentachloride to produce the sulfamoyl chloride, as reported by Kloek and Leschinsky (Figure 2-3A).[8] The sulfamoyl chloride is then treated with an inorganic fluoride salt to transform it to a sulfamoyl fluoride.

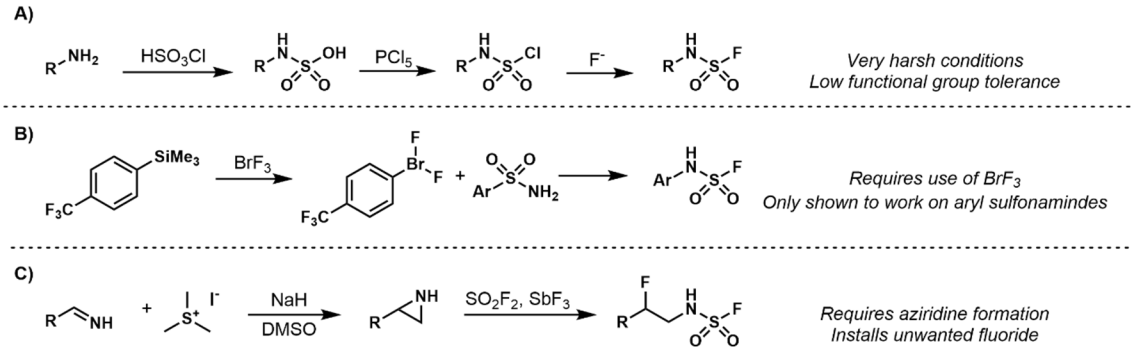


Figure 2-3. Previously published methods of primary sulfamoyl fluoride formation.

While these synthetic methodologies work well with simple alkylamines, there is no literature describing such a synthesis working on diamines. This is likely due to the incredibly harsh conditions a molecule needs to be subjected to in order to complete these reactions, along with the high reactivity of sulfamoyl chlorides leading to unwanted oligomerization. Higher yielding conditions more tolerant of a variety of functional groups would be desirable. Ochiai and coworkers demonstrated the utility of a difluoro-λ_3-bromane in the Hoffmann rearrangement of aryl sulfonamides to form primary aryl sulfamides in good yield (Figure 2-3B).[9] It stands to reason that this reaction could potentially work on dianilines, however the synthesis of the bromane reagent requires the use of bromine trifluoride.[8] This is an strongly oxidizing liquid that easily hydrolyzes to form hydrofluoric acid, and is corrosive to many metals as well. So, overall this method was found to be undesirable. Last, a patent by Hamprect describes a method for producing primary sulfamoyl fluorides through the treatment of aziridines with sulfuyl fluoride and antimony trifuoride (Figure 2-3C).[10] This method also installs a fluoride at the beta position of the resulting sulfamoyl fluoride. So, overall, this method requires the

installment of an aziridine, which can prove difficult, and installs an undesired halide. The ideal reagent would be able to directly transform a primary amine to its sulfamoyl fluoride in good yield.

Therefore, more recent studies into the synthesis of "$^{+}SO_2F$" donors were examined. Two such candidates were featured in recent published works due to the renewed interest in sulfonyl fluorides with the rise of SuFEx chemistry. The first, AISF (**2-4**) was of particular interest due to its synthesis requiring no sulfuryl fluoride gas (Figure 2-4).[11] Instead, this reagent is prepared from acetanilide and lithium bis(fluorosulfonyl)imide using PIDA. Similar in structure and function to Comins' reagent, AISF is an arylbis(fluorosulfon)imide that transfers a fluorosulfonyl group to a nucleophilic functional group. Interestingly, while the reagent was shown to work with secondary amines and phenols, its utility with primary amines was not discussed. Demonstrating the utility of this reagent in the context of primary amines would be incredibly useful. Since sulfuryl fluoride is a toxic gas, avoiding its use would be beneficial.

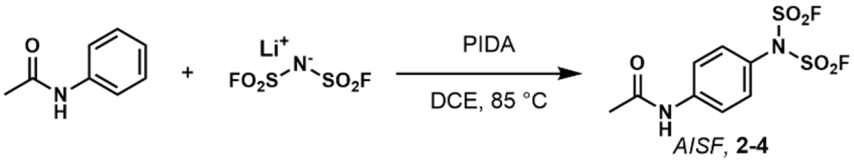


Figure 2-4. Synthesis of AISF (**2-4**).

Using benzylamine and aniline as model substrates, the conditions for fluorosulfanation were optimized (Table 1). It was found that aromatic amines generally performed poorly

with AISF, showing no sign of reaction after multiple days. We hypothesized that this reaction is not thermodynamic favorable based on the similar nucleofugality of aniline and 4-acetylaminoaniline. Additionally, the poor nucleophilicity of aniline should also be considered a factor for its lack of reactivity. When the reaction was attempted in the absence of base, the yield of the reaction was lowered. Aliphatic amines fared better with this reagent, producing the desired sulfamoyl fluoride in yields considerably higher than sulfuryl fluoride gas. It can be inferred that, after transferring one "$^{+}SO_2F$" group to an amine, AISF is transformed to an aryl sulfamoyl fluoride species that acts as a sort of sacrificial species. This byproduct preferentially reacts with the base instead of the desired aliphatic sulfamoyl fluoride product. This also means that the AISF byproduct will undergo unwanted coupling reactions with the remaining free amine, leading to reduced yields when compared to reactions performed with secondary amines and phenols. Overall, AISF is a useful reagent for synthesizing primary sulfamoyl fluorides from aliphatic amines, especially if one is not equipped with or wishes to avoid the use of sulfuryl fluoride gas.

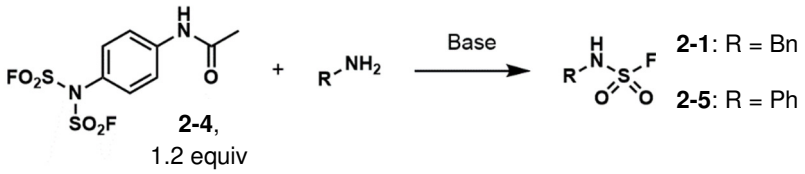


Table 2-1. Optimization of fluorosulfonylation with AISF

R	Base (equiv)	Solvent	Yield (%)[a]
Bn	None	DCM	6
Bn	DBU (2.2)	DCM	54
Bn	None	THF	46
Bn	DBU (2.2)	THF	39
Bn	None	MeCN	36
Bn	DBU (2.2)	MeCN	65
Bn	DBU (2.2)	MeCN	19[b]
Bn	DMAP (2.2)	MeCN	33
Bn	Cs_2CO_3 (2.2)	MeCN	65
Bn	K_2CO_3 (2.2)	MeCN	45
Ph	DBU (2.2)	MeCN	<10

[a]Yields were determined through crude ^{1}H NMR using an internal standard. [b]Reaction conducted with 0.6 equivalents of **2-4**.

However, in order to produce bis(sulfamoyl fluoride)s with good yields, the conversion of the fluorosulfonylation reaction needed to be increased, and any side reactions needed to be eliminated. If a disubstitution can be essentially be considered as the same reaction being performed twice, a 60% yield on a monoamine would translate to a 36% yield on a diamine of similar structure. This poor yield is far from ideal, especially when using a reagent that is expensive and time-consuming to synthesize like AISF. Additionally, the lack of applicability to anilines barred access to the study of a broad and important class of molecules. Fortunately, a second, bench-stable, crystalline fluorosulfonating reagent was disclosed by Dong and Sharpless before the beginning of

this work, a *N*-methylimidazolium triflate (Figure 2-7).[12] Alkylated imidazolium triflates have been utilized as sulfonylating reagents for alcohols and amines in the past, and while high temperatures were often required for these reactions, in most cases no base was needed. This is key for creating primary sulfamoyl fluorides since it reduces the likehood of the azasulfene intermediate forming and prematurely reacting to create a sulfamide. This imidazolium reagent was used to transform primary amines into the corresponding sulfamoyl fluorides in yields ranging from 60–99%.

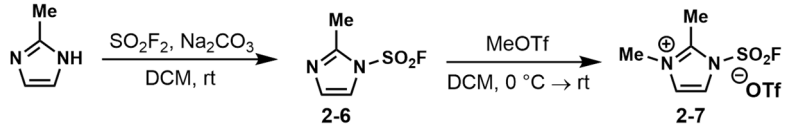


Figure 2-5. Synthesis of imidazolium triflate **2-7**

Similar to AISF, the imidazolium triflate is a white, bench-stable solid, maximizing its utility as a fluorosulfonating agent. Additionally, the isolation of this reagent is incredibly simple compared to AISF, requiring no column chromatography. The only caveat to this reagent is that sulfuryl fluoride is required to synthesize it. However, with yields up to 95% for the fluorosulfonation of primary amines, the use of sulfuryl fluoride was considered an acceptable downside.

The imidazolium triflate reagent was synthesized according to the published procedure, with some occasional issues. While the intended product is described as a white solid, sometimes it condenses as a viscous brown oil. It was determined that the formation of this oil is likely the result of excess methyl triflate coagulating with the intended product. Vigorous stirring of this oil in methyl tert-butyl ether at 0 °C was found to

separate the product from any excess methyl triflate, generating the intended white solid product. Once the imidazolium reagent was produced, multiple aromatic and aliphatic sulfamoyl fluorides were synthesized in good yield (Figure 2-6A).

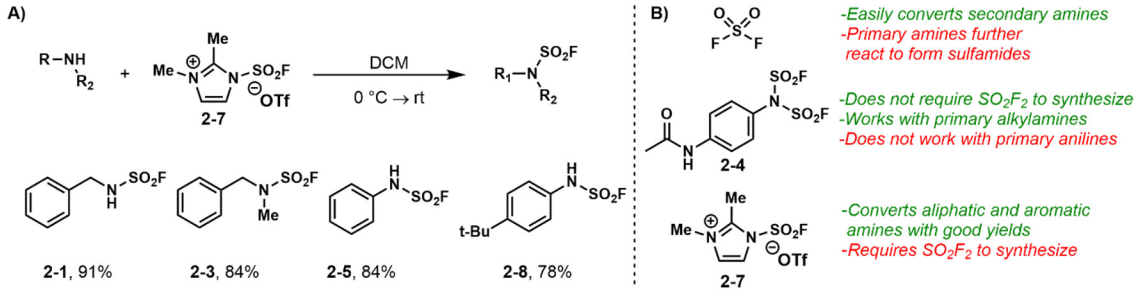


Figure 2-6. A) Results of synthesizing sulfamoyl fluorides using reagent **2-7**. B) Summary of the three fluorosulfonylating reagents tested.

2.2 Optimization of Sulfamide Synthesis

With facile access to primary sulfamoyl fluorides obtained, work was then done on the optimization of the coupling reaction to form sulfamides. This is the key reaction to optimize for the purposes of polymerization due to the Carothers equation,[12] which states:

Equation 2-1. $DP_n = 1/(1 - p)$

Based on this equation, in order to obtain polymers with the highest molecular weight possible, the monomer coupling reaction needs to be as high-yielding as possible, maximizing the value of p. Temperatures, bases, and solvents were all screened in order to maximize the yield of the SuFEx coupling reaction.

Initially, silylated and free amines were tested for the coupling reaction (Tables 2 and 3). Sharpless and coworkers offered the TBS group as a "goldilocks" protecting group for the polymerization of bis(fluorosulfate)s and bisphenols, providing polymers of high

molecular weight at low catalyst loadings.[2] However, with the coupling of sulfamoyl fluorides and amines, this was not found to be the case. Silylated aliphatic and aromatic amines were both probed as potential improvements over unprotected amines, but the silylation of the amine only provided a marginal benefit to the yield of the coupling reaction. In the case of aromatic amines, the addition of a silyl group consistently lowered the yield of the reaction. The reason for this may lie in the differing modes of reactivity between sulfamoyl fluorides and fluorosulfates. The addition of a silyl group to a phenol is said to increase its reactivity due to the high Si-F bond energy. This affinity of silicon to fluorine lowers the energy of the transition state of the reaction, allowing it to proceed more quickly. However, the mechanism proposed for primary sulfamoyl fluorides relies instead on the formation of an azasulfene intermediate, which immediately reacts with a nucleophile to complete the coupling reaction. Since performing the reaction with unprotected amines was found to produce sulfamides in high yield, the silyl protection step was deemed unnecessary.

Table 2-2. Optimization of the SuFEx coupling of aliphatic amines*

Equiv Amine	R	Base (equiv)	Solvent	Temperature (°C)	Yield (%)
1.5	H	Et_3N (1.5)	MeCN	80	91
1.5	H	Et_3N (1.5)	DMF	80	68
1.5	H	Et_3N (1.5)	DCE	80	79
1.5	H	Et_3N (1.5)	THF	80	74
1.5	H	Et_3N (1.5)	DME	80	<10
1.5	H	Et_3N (1.5)	Toluene	80	95
1.5	H	Et_3N (1.5)	Benzene	80	89
1.5	H	Et_3N (1.5)	NMP	80	73
1.5	H	DBU (1.5)	MeCN	80	96
1.5	H	Cs_2CO_3 (1.5)	MeCN	80	97
1	H	DBU (1.0)	MeCN	80	97
1	H	DBU (0.1)	MeCN	80	78
1	TBS	DBU (1.0)	MeCN	80	85
1	TBS	DBU (0.1)	MeCN	80	96
1	TBS	DBU (2.5)	MeCN	80	59
1	H	DBU (2.5)	MeCN	80	99
1	H	DBU (2.5)	MeCN	50	92
1	H	DBU (2.5)	MeCN	20	76

*Modified with permission from the Royal Society of Chemistry (*Ibid.*)

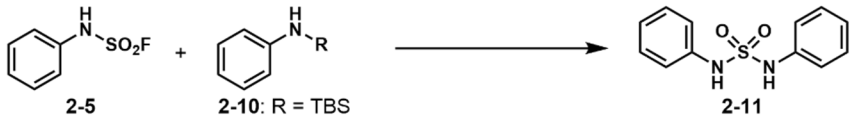


Table 2-3. Optimization of the SuFEx coupling of aromatic amines

Base (equiv)	R	Solvent	Temperature (°C)	Yield (%)
DBU (2.5)	H	MeCN	80	44
DBU (2.5)	TBS	MeCN	80	51
DBU (2.5)	H	DMF	80	11
DBU (2.5)	H	NMP	80	7
DBU (2.5)	H	Benzene	80	58
DBU (2.5)	TBS	Benzene	80	33
DBU (2.5)	H	DCE	80	42
DBU (2.5)	TBS	DCE	80	34
DBU (2.5)	H	1,4-Dioxane	80	31
DBU (5.0)	H	MeCN	80	58
DBU (1.25)	H	MeCN	80	42
Et_3N (2.5)	H	MeCN	80	77
Pyridine (2.5)	H	MeCN	80	85

The base and solvent used in the reaction was screened to maximize the yield of the sulfamide coupling reaction. Overall, for aliphatic sulfamoyl fluorides it was found that stronger bases, such as DBU and triethylamine produced better yields, which is consistent with the hypothesis that the formation of the azasulfene intermediate triggered by proton abstraction is the slow step of the reaction mechanism. On the contrary, pyridine was found to be the more effective in the case of the aromatic sulfamoyl fluorides. It could be the case that there is a certain "sweet spot" that needs to be met in the difference

between the pKa of the sulfamoyl fluoride and that of the base. Aromatic sulfamoyl fluorides are expected to have significantly lower pK_a values than aliphatic ones, so it may be the case that a less powerful base is needed to drive the coupling reaction for the former. Since proton exchange is required to complete the formation of the sulfamide, it may also be beneficial to use less powerful bases when forming sulfamides of higher acidities. In terms of solvent, the sulfamide coupling prefers polar, aprotic solvents with the exception of DMF and NMP. Strangely, toluene was also found to be a fair solvent for the coupling reaction. The success of toluene may be due to the aromatic character of the substrates used. However, it was decided that acetonitrile would be a preferable solvent for polymerization due to solubility concerns for polymerization. Even the small molecules used for optimizing the reaction precipitated from solution almost immediately when toluene was used as the solvent. Using the best conditions found for aromatic and aliphatic amines, larger scale reactions were conducted to confirm that these results were consistent for all potential amines.

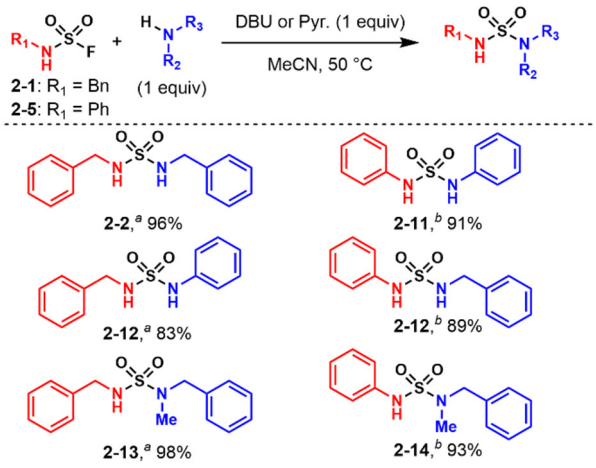


Figure 2-7. Synthesis of a variety of sulfamides via SuFEx with isolated yields (0.5-0.6 mmol scale). [a]DBU; [b]pyridine. Adapted with permission from the Royal Society of Chemistry (*Ibid.*)

Following the optimization of the reaction conditions, kinetic studies were also performed to ascertain the amount of time needed to complete the SuFEx coupling between a primary sulfamoyl fluoride and an amine. This is due to concerns that were raised over the potential degradation of the polymer over time. Recent work by Lu, Xu and coworkers has shown that, when using DBU to synthesize polysulfonates through SuFEx, the molecular weight of the resulting polymer plateaus, then steadily decreases as the reaction progresses.[13] It was found that, through base-promoted sulfonate ester exchange, the polymer was being broken apart until an equilibrium molecular weight was reached. Therefore, to avoid possible side reactions, the reaction must be stopped and quenched as soon as total conversion is reached. Additionally, since the mechanism of amine exchange likely resembles that of sulfamate ester[14] and proceeds through a highly

electrophilic azasulfene intermediate, protic solvents should be avoided for polymerization at the risk of chain scission and termination. Time scale experiments were run on a model aromatic and aliphatic amine, taking aliquots at designated times to determine the reaction yield at that time. The current yield of the reaction was determined using an internal NMR standard. The results of these time scale experiments are shown in Figure 2-8.

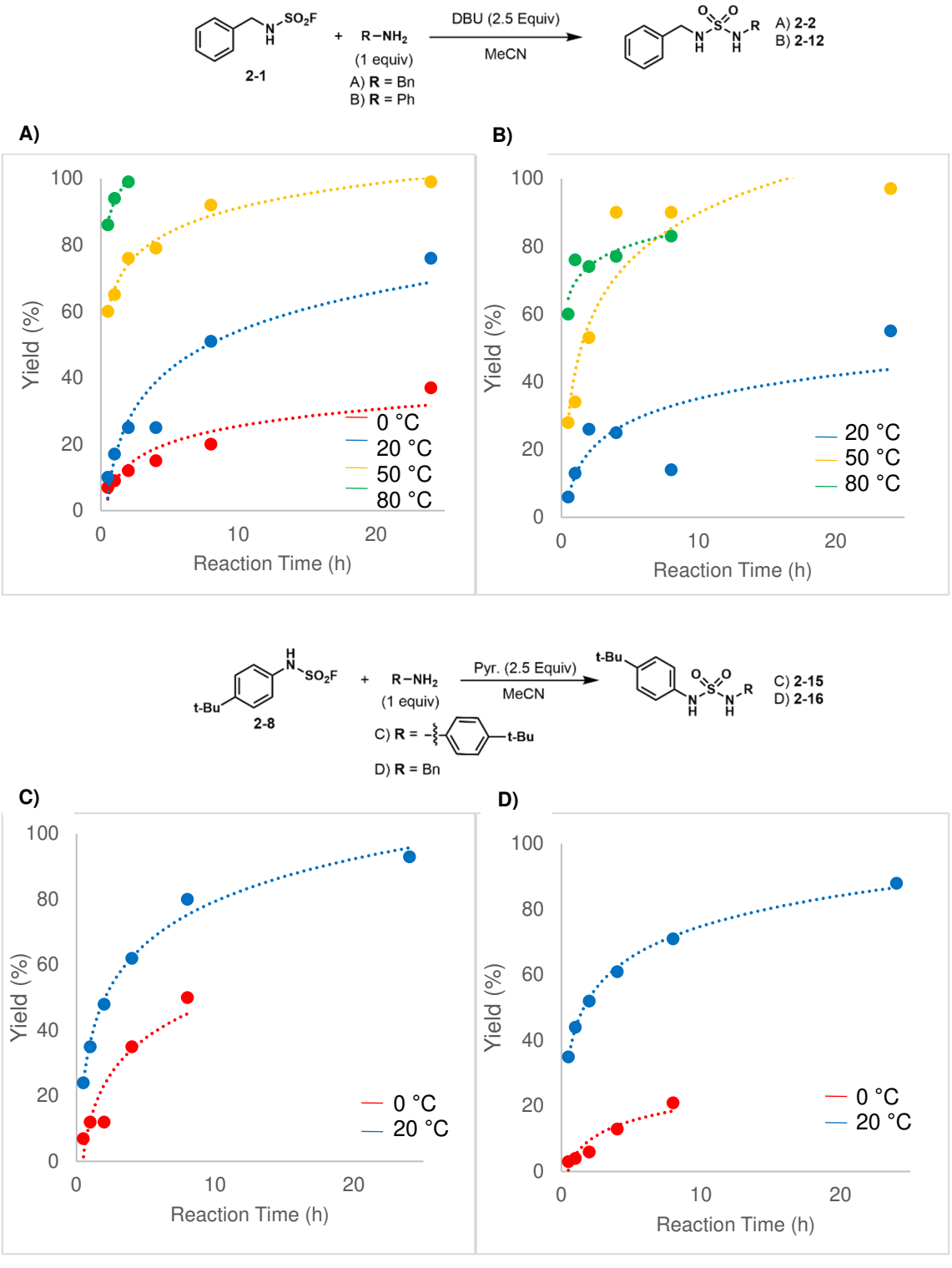
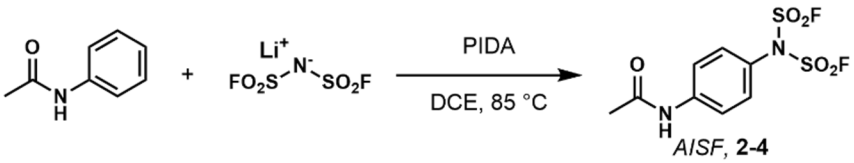


Figure 2-8. Results of kinetic experiments for sulfamide formation. Calculated yields based on ^{1}H NMR data. Trendlines added to aid in the visualization of the data.

Based on the yields observed at the same temperature, benzylamine was faster to react with the sulfamoyl fluoride than either of the aromatic amines used. These findings are consistent with the assumed reaction mechanism, which proceeds through a nucleophilic attack from the amine. At 80 °C, the temperature the sulfamide coupling was normally run until this point, it was found that the reaction between a sulfamoyl fluoride and an amine was complete in under an hour, which was much shorter than expected. At 50 °C, the reaction was found to be complete within 4 hours, and at room temperature the reaction takes about 24 hours to reach completion. The yield in each case was about equivalent, with the reactions performed at 20 °C and 50 °C occasionally producing higher yields. For small molecules, it was decided that running the coupling reaction at 50 °C would be ideal, giving higher yields while not having to be run overnight. The reaction could be monitored by TLC and stopped when the sulfamoyl fluoride-containing starting material is no longer present.

2.3 Experimental

2.3.1 Synthesis of [4-(acetylamino)phenyl]imidodisulfuryl difluoride (AISF, 2-4)



Compound **2-4** was prepared following a previously reported procedure[11] with slight modifications. A solution of (diacetoxyiodo)benzene (8.24 g, 25.6 mmol, 1.5 equiv) and lithium bis(fluorosulfonyl)imide (6.38 g, 34.1 mmol, 2.0 equiv) in DCE (30 mL) was stirred at 100 °C in a flame-dried 3-necked round bottom flask adapted with a condenser.

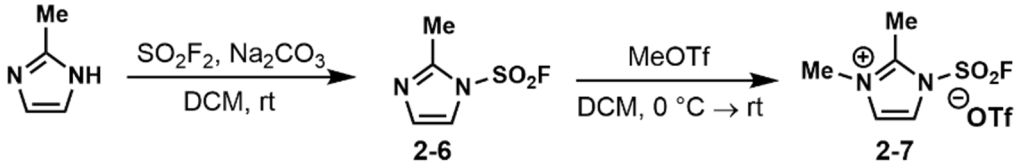
A solution of acetanilide (2.31 g, 17.1 mmol, 1.0 equiv) in DCE (35 mL) was slowly added to the refluxing mixture over 25 min. After stirring for an additional 15 min, the mixture was cooled to room temperature and activated carbon (4 g) was added. The mixture was stirred for 18 h at room temperature, then filtered through a short silica plug and washed with EtOAc. The filtrate was concentrated in vacuo. Column chromatography (SiO_2, 10:90 to 30:70 EtOAc:hexanes) allowed to remove most of the impurities. Recrystallization of the resulting brown solid with the minimum of EtOAc and slow addition of hexanes afforded 9 as crystalline white needles (3.42 g, 65%). The spectroscopic data for this compound were identical to those reported in the literature.

^{1}H NMR: (d_6-DMSO, 400 MHz) δ : 10.37 (s, 1 H), 7.90–7.63 (m, 4 H), 2.09 (s, 3 H) ppm.

^{13}C NMR: (d_6-DMSO, 126 MHz) δ : 169.1, 142.9, 130.3, 126.1, 120.3, 24.1 ppm.

^{19}F NMR: (d_6-DMSO, 470 MHz) δ : 56.8 (s, 2 F) ppm.

2.3.2 Synthesis of 1-(fluorosulfonyl)-2,3-dimethyl-1H-imidazol-3-ium triflate (2-7)



Caution: sulfuryl fluoride is a highly toxic gas. As such, all reactions using sulfuryl fluoride should be carried out in a well-ventilated fume hood to avoid exposure and inhalation.

Compound **2-7** was prepared following a previously reported procedure[12] with some slight modifications. In a flame-dried flask containing a suspension of 2-methylimidazole (4.93 g, 60.0 mmol, 1.0 equiv) and sodium carbonate (15.9 g, 150 mmol, 2.5 equiv) in anhydrous DCM (60 mL) the pressure was reduced using a Schlenck line until the DCM began boiling, and a balloon containing sulfuryl fluoride gas (approx. 1.5 L) was introduced. The mixture was stirred until full conversion of the imidazole was confirmed by NMR. If full conversion was not reached after 18 hours, a second balloon of sulfuryl fluoride was added. Solid residues were removed by filtration over a silica plug eluted with DCM. The filtrate was washed with distilled water (3 x 50 mL). The aqueous fractions were then combined and extracted with DCM (50 mL). The organic fractions were combined and washed with brine (50 mL) before drying over $MgSO_4$. The solvent was evaporated in vacuo using a 20 °C bath and a pressure of 200 mbar to avoid distilling away volatile sulfamoyl fluoride **2-6**. When a volume of roughly 60 mL of solution was reached, the solution was cooled to 0 °C. Methyl trifluoromethanesulfonate (9.85 g, 60 mmol, 1.0 equiv) was then added to the mixture over 15 min using a syringe pump with vigorous stirring. The mixture was then warmed to room temperature and allowed to stir for 2 h, during which time the product precipitated from the solution. 8 was collected by vacuum filtration as a white solid (15.7 g, 79% over 2 steps) and washed thoroughly with MTBE. Note: Likely due to the presence of residual methyl trifluoromethylsulfonate, the product sometimes collects as a dense brown oil rather than a white solid. Here, the DCM can be removed first in vacuo, then upon addition of MTBE (50 mL) and stirring the

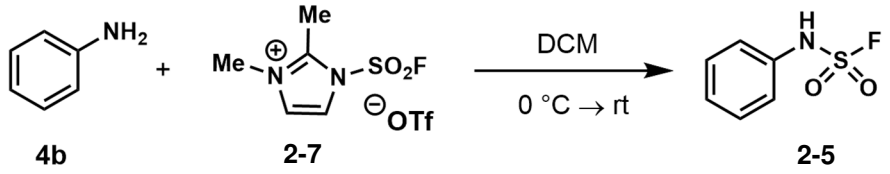
mixture vigorously at 0 ºC, the desired solid precipitates. The spectroscopic data for this compound were identical to those reported in the literature.

^{1}H NMR (CD_3CN, 400 MHz) δ: 7.87 (d, 1 H, J = 2.5 Hz), 7.54 (d, 1 H, J = 2.5 Hz), 3.85 (s, 3 H), 2.86 (s, 3 H) ppm.

^{13}C NMR (CD_3CN, 126 MHz) δ: 151.4, 125.5, 122.1, 122.0 (q, J = 318 Hz), 37.5, 12.9 ppm.

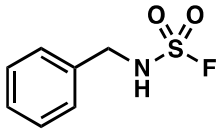
^{19}F NMR δ: (CD_3CN, 470 MHz) δ: 61.4 (s, 1 F), –78.1 (s, 3 F) ppm.

2.3.3 General Procedure for the Synthesis of Sulfamoyl Fluorides using reagent 2-7 (Using 2-5 as an Example)



To aniline (900 mg, 9.66 mmol, 1.0 equiv) in dry DCM (30 mL) stirring in an ice bath Compound **2-7** (3.18 g, 9.66 mmol, 1.0 equiv) was added. The reaction was brought to room temperature and stirred for 2–4 h, until the starting amine was seen to be fully consumed by TLC.

After completion, the resulting mixture was diluted with DCM (10 mL) and washed with 0.1M HCl (3 x 15 mL) and brine (20 mL). The organic layer was dried over $MgSO_4$ and concentrated *in vacuo* to afford the product as an orange oil (1.42 g, 84%) without further purification.



2-1

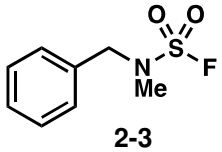
Sulfamoyl Fluoride **2-1** was prepared following the general procedure. Starting with benzylamine (0.11 mL, 0.107 g, 1.0 mmol) to afford the product as a yellow oil (0.173 g, 91%). The spectroscopic data for this compound were identical to those reported in the literature.[12]

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.42 - 7.33 (m, 5 H), 5.15 (br, 1 H), 4.45 (d, J = 5.6 Hz, 2 H) ppm.

^{13}C NMR ($CDCl_3$, 126 MHz) δ: 134.8, 129.2, 128.8, 128.1, 48.5 ppm.

^{19}F NMR ($CDCl_3$, 470 MHz) δ: 50.4 ppm.

Alternatively, **2-1** can be prepared using AISF (**2-4)** as the fluorosulfonation reagent. To a solution of benzylamine (107 mg, 1.0 mmol, 1.0 equiv) and AISF (**2-4)** (377 mg, 1.2 mmol, 1.2 equiv) in acetonitrile (3.5 mL), DBU (335 mg, 0.33 mL, 2.2 mmol, 2.2 equiv) was added dropwise at room temperature. The mixture was stirred and monitored by TLC until benzylamine was fully a consumed (about 3 h). The mixture was diluted with EtOAc (5 mL) and washed with HCl (0.5 M, 10 mL x 2) and brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. Column chromatography (SiO_2, 10:90 EtOAc:hexanes) afforded **2-1** as a yellow oil (123 mg, 65%).



2-3

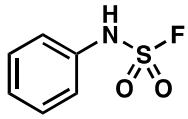
Sulfamoyl Fluoride 2-3 was prepared following the general procedure. Starting with N-benzylmethylamine (0.13 mL, 1.0 mmol), using MeCN as solvent to afford the product as colorless oil (171.2 mg, 0.84 mmol, 84%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.32 - 7.43 (m, 5 H), 4.48 (s, 2 H), 2.90 (d, 3 H, *J* = 2.2 Hz) ppm.

^{13}C NMR ($CDCl_3$, 126 MHz) δ: 133.8, 129.1, 128.8, 128.7, 55.2, 35.3 ppm.

^{19}F NMR ($CDCl_3$, 470 MHz) δ: 42.0 ppm.

HRMS-ESI: calc'd. for $C_8H_{10}NO_2SNa$ $[M+Na]^+$ 226.0308, found 226.0302.



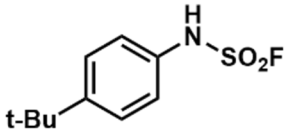
2-5

Sulfamoyl fluoride 2-5 was prepared following the general procedure. Starting with aniline (4b) (900 mg, 9.66 mmol) to afford the product as an orange oil (1.42 g, 84%). The spectroscopic data for this compound were identical to those reported in the literature.[12]

^{1}H NMR (CD_3CN, 400 MHz) δ: 8.85 (br, 1 H), 7.44 (m, 2 H), 7.33 (m, 3 H) ppm.

^{13}C NMR (CD_3CN, 126 MHz) δ: 135.6, 130.7, 128.1, 123.9 ppm.

^{19}F NMR (CD_3CN, 470 MHz) δ: 50.1 ppm.



2-8

Sulfamoyl fluoride 2-8 was prepared following the general procedure. Starting with 4-*tert*-butylaniline (750 mg, 5.03 mmol) to afford the product as a yellow solid (884 mg, 78%).

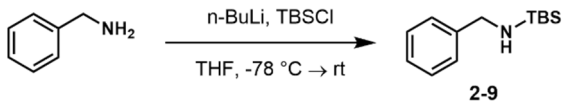
^{1}H NMR ($CDCl_3$, 500 MHz) δ: 7.43 (d, 2 H, *J* = 8.7 Hz), 7.22 (d, 2 H, *J* = 8.7 Hz), 6.82 (br, 1 H), 1.33 (s, 9 H) ppm.

^{13}C NMR ($CDCl_3$, 126 MHz) δ: 151.2, 131.1, 126.9, 123.4, 34.77, 31.38 ppm.

^{19}F NMR ($CDCl_3$, 470 MHz) δ: 50.6 ppm.

2.3.4 Preparation of Silylated Amines

Synthesis of N-(tert-Butyldimethylsilyl)benzylamine (2-9)

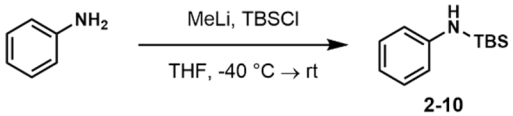


2-9

To a flame dried flask containing anhydrous THF (15 mL), benzylamine (500 mg, 4.67 mmol, 1 equiv) was added. The reaction mixture was placed in a cooling bath (CO_2(s)/Acetone) and allowed to cool to -78 ºC. A solution of *n*-butyllithium (1.6 M in THF, 3.21 mL, 5.14 mmol, 1.1 equiv) was added dropwise over 10 min. The reaction mixture was stirred at -78 ºC for 90 min. In a separate, flame dried flask, TBS chloride (740 mg, 4.90 mmol, 1.05 equiv) was dissolved in anhydrous THF (15 mL). This solution was added to the reaction mixture dropwise over 5 min. The mixture was allowed to warm to room temperature, and was stirred for 15 h. The reaction mixture was diluted to 250 mL with hexanes, causing a white solid to precipitate. The resulting heterogeneous mixture was filtered three times over Celite to remove the white solid completely. The filtrate was concentrated *in vacuo* to obtain the title compound as a yellow oil (1.06 g, 97%). The spectroscopic data for this compound were identical to those reported in the literature.[15]

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.34–7.28 (m, 4 H), 7.23–7.18 (m, 1 H), 3.99 (d, 2 H, J = 7.5 Hz), 0.94 (s, 9 H), 0.68 (br, 1 H), 0.07 (s, 6 H)

Synthesis of N-(tert-Butyldimethylsilyl)aniline (2-10)



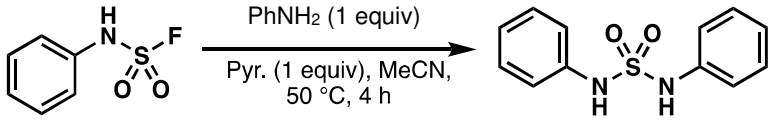
2-10

To a flame dried flask containing anhydrous THF (15 mL), aniline (750 mg, 8.05 mmol, 1 equiv) was added. The reaction mixture was placed in a cooling bath (CO_2(s)/MeCN) and allowed to cool to -40 ºC. A solution of methyllithium (1.6 M in Et_2O, 5.53 mL, 8.86 mmol, 1.1 equiv) was added dropwise over 5 min. In a separate, flame dried flask, TBS chloride (1.34 g, 8.86 mmol, 1.1 equiv) was dissolved in anhydrous THF (15 mL). This solution was added to the reaction mixture dropwise over 5 min. The mixture was allowed to warm to room temperature, and was stirred for 17 h. The reaction mixture was diluted to 250 mL with hexanes, causing a white solid to precipitate. The resulting heterogeneous mixture was filtered three times over Celite to remove the white solid completely. The filtrate was concentrated *in vacuo* to obtain the title compound as an orange oil (1.65 g, 98% yield). The spectroscopic data for this compound were identical to those reported in the literature.[16]

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.20–7.09 (m, 2 H), 6.62–6.77 (m, 3 H), 3.34 (br, 1 H), 0.98 (s, 9 H), 0.27 (s, 6 H) ppm.

^{13}C NMR ($CDCl_3$, 101 MHz) δ: 147.7, 129.1, 117.5, 116.5, 26.4, 18.0, -4.23 ppm.

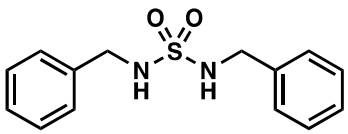
2.3.5 General Procedure for the Synthesis of Sulfamides through SuFEx (using 2-11 as an example)



2-5 **2-11**

To the sulfamoyl fluoride **2-5** (100 mg, 570 μmol, 1.0 equiv) in acetonitrile (5 mL) the aniline (62 mg, 570 μmol,1.0 equiv) and pyridine (45 mg, 570 μmol, 1.0 equiv; DBU for

compound **2-1**, pyridine for compounds **2-5** and **2-8**) were added. The reaction mixture was heated to 50 ºC and stirred for 4–5 h, until none of the sulfamoyl fluoride could be observed by TLC. After all the sulfamoyl fluoride was consumed, 1M HCl (10 mL) was added into residue to stop the reaction. The mixture was extracted with ethyl acetate (3 x 5 mL). The organic fractions were combined, dried over $MgSO_4$ and concentrated in vacuo to yield product **2-11** as a white crystalline solid (128 mg, 91%).



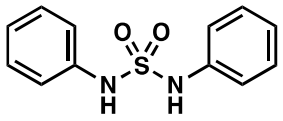
2-2

Sulfamide 2-2 was prepared by starting with sulfamoyl fluoride **2-1** (102.7 mg, 0.543 mmol), coupling with benzylamine and following the general procedure to afford a white solid (144.3 mg, 96%), without further purification.

^{1}H NMR (d_6-DMSO, 400 MHz) δ: 7.45 (t, 2 H, J = 6.2 Hz), 7.32 (m, 8 H), 7.26 (m, 2 H), 4.01 (d, 2 H, J = 6.3 Hz) ppm.

^{13}C NMR (d_6-DMSO, 126 MHz) δ: 138.4, 128.2, 127.7, 127.0, 45.8 ppm.

IR (neat): $\tilde{\upsilon}$= 3269, 3062, 1453, 1414, 1313, 1142, 908 cm–1. The spectroscopic data for this compound were identical to those reported in the literature.[17]



2-11

Sulfamide 2-11 was prepared by starting with sulfamoyl fluoride **2-5** (100 mg, 0.570 mmol), coupling with aniline and following the general procedure to afford the product as white crystals (128 mg, 91%).

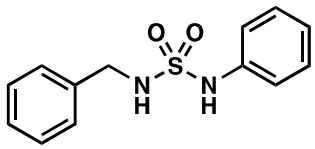
^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.26 (t, J = 7.5 Hz, 4 H), 7.13 (t, J = 7.5 Hz, 2 H),

7.07 (d, J = 7.5 Hz, 4 H), 6.83 (br, 1 H) ppm.

^{13}C NMR ($CDCl_3$, 126 MHz) δ = 136.5, 129.6, 125.6, 121.4 ppm.

FTIR: $\tilde{\upsilon}$ = 3217, 3051, 1598, 1481, 1419, 1337, 1294, 1147, 1032, 938 cm^{-1}

The spectroscopic data for this compound were identical to those reported in the literature.[17]

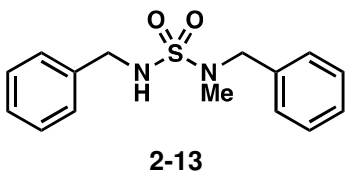


2-12

Sulfamide 2-12 was prepared by starting with sulfamoyl fluoride **2-1** (99.6 mg, 0.526 mmol), coupling with aniline and following the general procedure. Crude mixture was purified column chromatography (20 % EtOAc in hexanes) to afford a white solid (114.0 mg, 83%). Alteratively, starting with sulfamoyl fluoride **2-5** (100 mg, 0.570 mmol), coupling with benzylamine to yield the same product without further purification (133 mg, 89%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.29 (t, J = 7.5 Hz, 2 H), 7.27–7.23 (m, 3 H), 7.17–7.10 (m, 5 H), 6.93 (br, 1 H), 4.95 (t, J = 6.0, 1 H), 4.18 (d, J = 6.0 Hz, 2 H) ppm.

^{13}C NMR ($CDCl_3$, 126 MHz) δ = 137.1, 136.2, 129.6, 129.0, 128.3, 128.2, 124.8, 120.1, 47.6 ppm. The spectroscopic data for this compound were identical to those reported in the literature.[17]



2-13

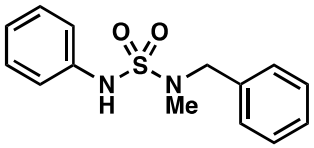
Sulfamide 2-13 was prepared by starting with sulfamoyl fluoride **2-1** (100.1 mg, 0.529 mmol), coupling with N-benzylmethylamine and following the general procedure to afford white to yellow solid (151 mg, 98%)

^{1}H NMR (CD_3CN, 400 MHz) δ = 7.39–7.29 (m, 10 H), 5.72 (br, 1 H, NH), 4.24 (s, 2 H), 4.21– 4.20 (d, 2 H, J = 6.4 Hz), 2.61 (s, 3 H) ppm.

^{13}C NMR (CD_3CN, 126 MHz) δ = 139.2, 138.1, 129.6, 129.5, 129.2, 128.9,128.6,128,5, 54.9, 47.8, 35.1 ppm.

HRMS-ESI: calc'd. for $C_{15}H_{19}N_2O_2S$ $[M+H]^+$ 291.1162, found 291.1156.

mp: 72–74 ºC.

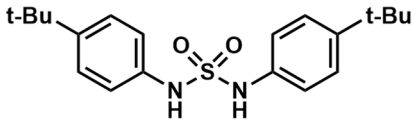


2-14

Sulfamide 2-14 was prepared by starting with sulfamoyl fluoride **2-5** (100 mg, 0.570 mmol), coupling with N-benzylmethylamine and following the general procedure to afford the product as an off-white solid (146 mg, 93%). ^{1}H NMR ($CDCl_3$, 500 MHz) δ = 7.35–7.27 (m, 5 H), 7.22–7.09 (m, 5 H), 7.01 (br, 1 H) 4.32 (s, 2 H), 2.71 (s, 3 H) ppm.

^{13}C NMR ($CDCl_3$, 126 MHz) δ = 137.3, 135.8, 129.6, 129.5, 128.8, 128.4, 128.0, 124.8, 120.5 ppm. HRMS-ESI: calc'd. for $C_{14}H_{17}N_2O_2S$ $[M+H]^+$ 277.1005, found 277.0998.

mp: 64–66 °C.

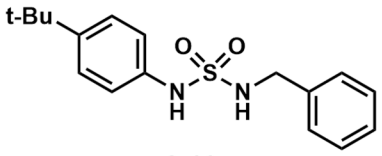


2-15

Sulfamide 2-15 was prepared by starting with sulfamoyl fluoride **2-8** (46 mg, 0.2 mmol), coupling with 4-*tert*-butylaniline and following the general procedure to afford the product as a tan solid (63 mg, 87%).

^{1}H NMR ($CDCl_3$, 500 MHz) δ = 7.30 (d, 4 H, *J* = 8.8 Hz), 7.04 (d, 4 H, *J* = 8.8 Hz), 6.69 (br, 2 H), 1.29 (s, 18 H) ppm.

^{13}C NMR ($CDCl_3$, 126 MHz) δ = 148.7, 133.8, 126.4, 121.6, 34.5, 31.5



2-16

Sulfamide 2-16 was prepared by starting with sulfamoyl fluoride **2-8** (46 mg, 0.2 mmol), coupling with benzylamine and following the general procedure to afford the product as an off white solid (57 mg, 89%).

^{1}H NMR (CD_3CN, 500 MHz) δ = 7.53 (br, 1 H), 7.37 (d, 2 H, *J* = 8.8 Hz), 7.30–7.18 (m, 5 H), 7.12 (d, 2 H, *J* = 8.8 Hz), 5.86 (t, 1 H. *J* = 6.4 Hz), 4.15 (d, 2 H, *J* = 6.4 Hz), 1.31 (s, 9 H) ppm.

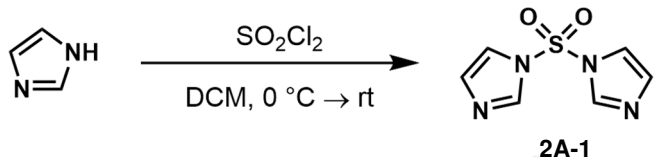
^{13}C NMR (CD_3CN, 126 MHz) δ = 148.0, 138.5, 136.5, 129.4, 128.9, 128.4, 127.0, 120.7, 47.5, 34.9, 31.7 ppm.

2.3.6 Monitoring the Sulfamide Synthesis

To a flame-dried vial under a nitrogen atmosphere, sulfamoyl fluoride **2-1** or **2-8** (0.20 mmol, 1.0 equiv) was dissolved in anhydrous MeCN (2 mL). The amine (0.20 mmol, 1.0 equiv) and base (0.20 mmol, 1.0 equiv) were added. The mixture was stirred at the indicated temperature for 24 h. For each time point, an aliquot of the reaction mixture (0.25 mL) was collected with a syringe. Each aliquot was immediately quenched with HCl (1 M, 1 mL). The aqueous mixture was then extracted with EtOAc (2 x 1 mL). The organic fractions were combined, dried over $MgSO_4$, and concentrated in vacuo. The progress of the reaction was determined by 1H NMR using 1,3,5trimethoxybenzene (4.2 mg, 25 μmol, 0.125 equiv) as an internal standard.

2.3.7 Application of ex situ generated sulfuryl fluoride to a primary amine

Preparation of 1,1'-Sulfonyldiimidazole (2A-1)

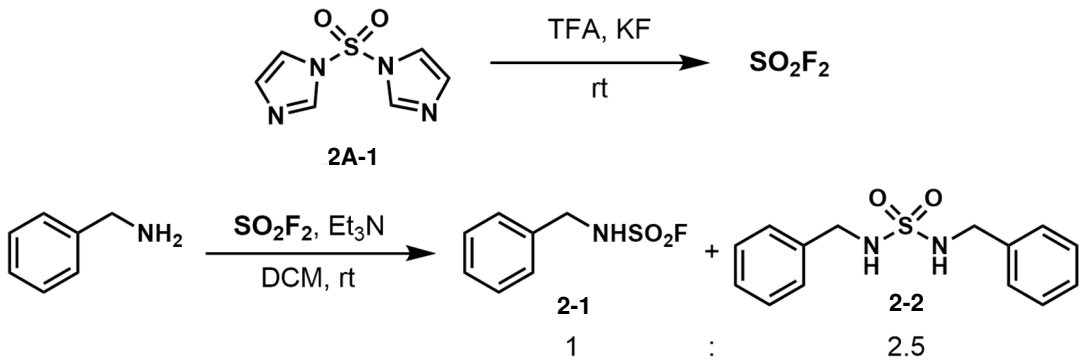


2A-1

2A-1 was prepared according to a literature procedure.[18] In a flame-dried flask under nitrogen, imidazole (5.00 g, 73 mmol, 4.6 equiv) was suspended in anhydrous DCM (30 mL) and cooled to 0 °C. A solution of sulfuryl chloride (2.15 g, 16 mmol, 1.0 equiv) in DCM (6 mL) was added dropwise over 15 min. The reaction mixture was allowed to warm to room temperature and stirred for 18 h. The resulting heterogenous mixture was filtered using a fritted funnel, and the remaining solid was washed several times with DCM. The filtrate was concentrated *in vacuo* to yield a bright yellow solid. The solid was recrystallized in boiling isopropanol, isolated via vacuum filtration, and washed with cold isopropanol to obtain the title compound as a white crystalline solid (2.25 g, 71%). The spectroscopic data for this compound were identical to those reported in the literature.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.03 (s, 1 H), 7.30 (s, 1 H), 7.14 (s, 1 H) ppm.

^{13}C NMR ($CDCl_3$, 101 MHz) δ: 136.7, 132.5, 117.5 ppm.



SO_2F_2 was generated *ex situ* according to a literature procedure.[18] To one chamber of a small two-chamber reactor (Figure 2-9) benzylamine (107 mg, 1.0 mmol, 1.0 equiv) and triethylamine (204 mg, 2.0 mmol, 2.0 equiv) were dissolved in DCM (4 mL). In the second chamber, **2A-1** (279 mg, 1.5 mmol, 1.5 equiv) and potassium fluoride (232 mg, 4.0 mmol, 4.0 equiv) were combined. A stir bar was added to each chamber, and the reactor was sealed with phenolic caps fitted with PTFE septa. To the second chamber, trifluoroacetic acid (1 mL, excess) was added via syringe. The contents of each chamber were stirred at room temperature for 18 h. The contents of the first chamber were transferred to a separatory funnel and diluted with EtOAc (4 mL). The organic layer was washed with HCl (0.1 M, 2 x 5 mL) and brine (5 mL), then dried over MgSO4 and concentrated *in vacuo*. ^{1}H NMR analysis of the crude product revealed a 2.5:1 ratio in favor to **2-2** compared to the desired **2-1** (Figure 2-10).

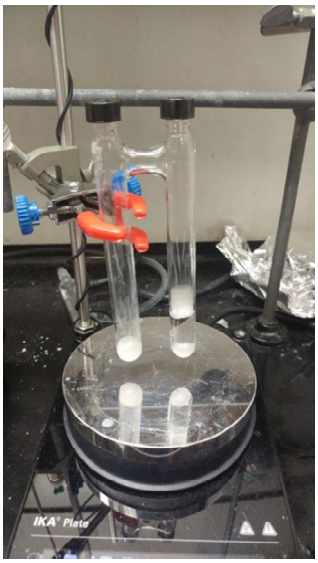


Figure 2-9. Two chamber reactor for *ex situ* generation of SO_2F_2. Reprinted with permission from the Royal Society of Chemistry (*Ibid.*)

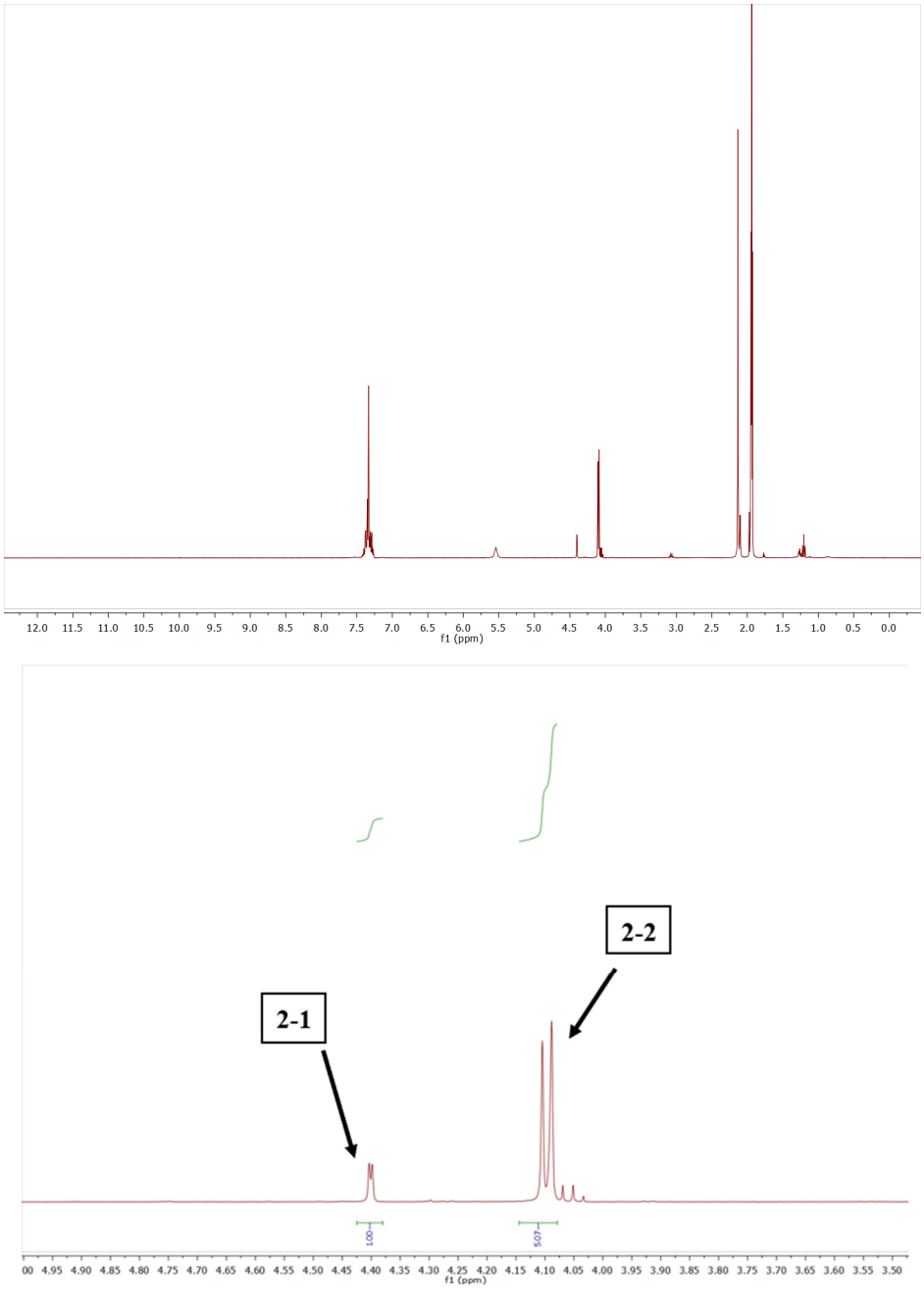
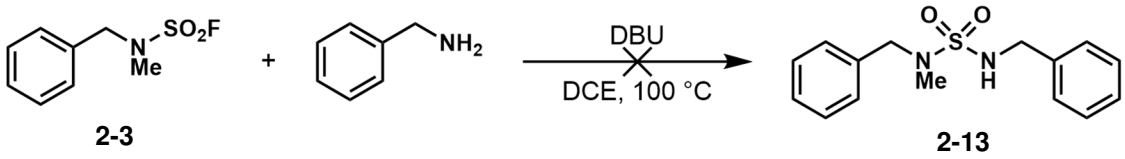


Figure 2-10. ^{1}H NMR (CD_3CN, 400 MHz) of the crude product obtained after treating benzylamine with SO_2F_2, and the integrations of the respective benzylic signals of **2-1** and **2-2** (bottom). Adapted with permission from the Royal Society of Chemistry (*Ibid.*)

2.3.8 Attempt to Couple a Secondary Sulfamoyl Fluoride with a Primary Amine



2-3 **2-13**

To a solution of compound **2-3** (7.0 mg, 34 μmol, 1.0 equiv) in 1,2-dichloroethane (0.4 mL), DBU (8 mg, 52 μmol, 1.5 equiv) and benzylamine (5.5 mg, 52 μmol, 1.5 equiv) were added. The mixture was stirred at 80 °C for 18 h. The mixture was diluted with 1 mL EtOAc and washed with HCl (0.1 M, 1 mL) followed by brine (1 mL). The organic layer was dried over $MgSO_4$ and concentrated in vacuo. 1H NMR analysis of the crude product showed no trace of **2-13**, but only unreacted **2-3** (Figure 2-11).

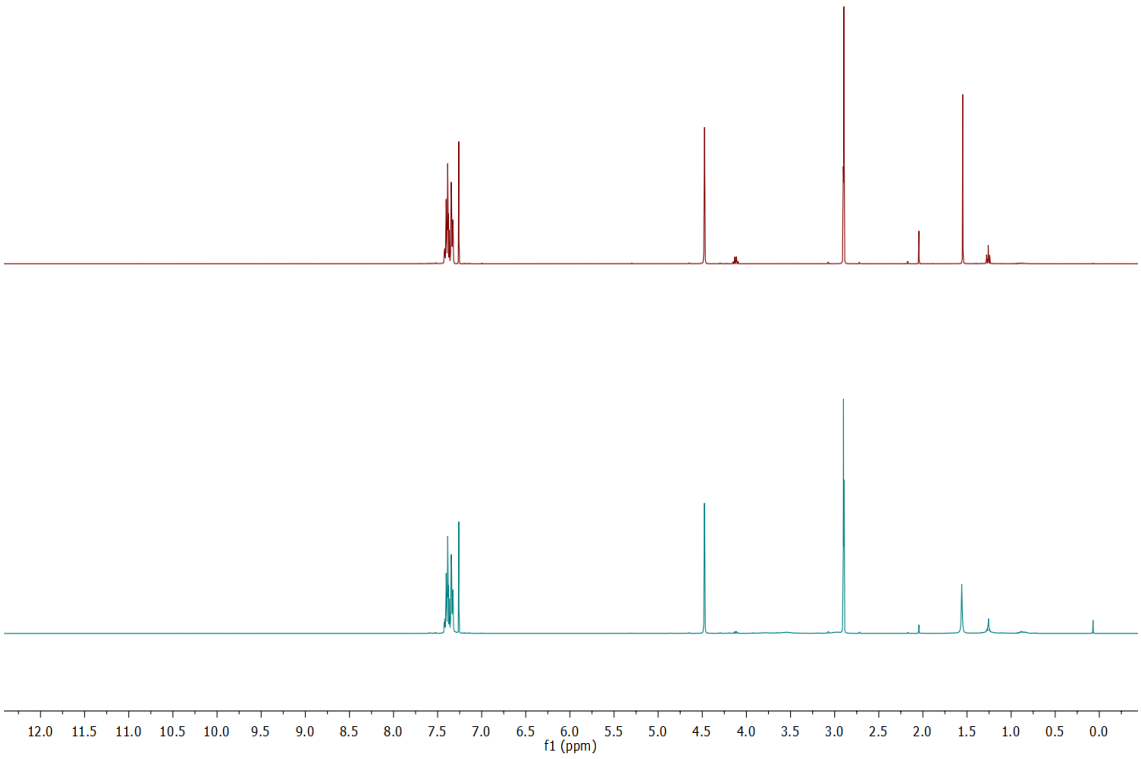
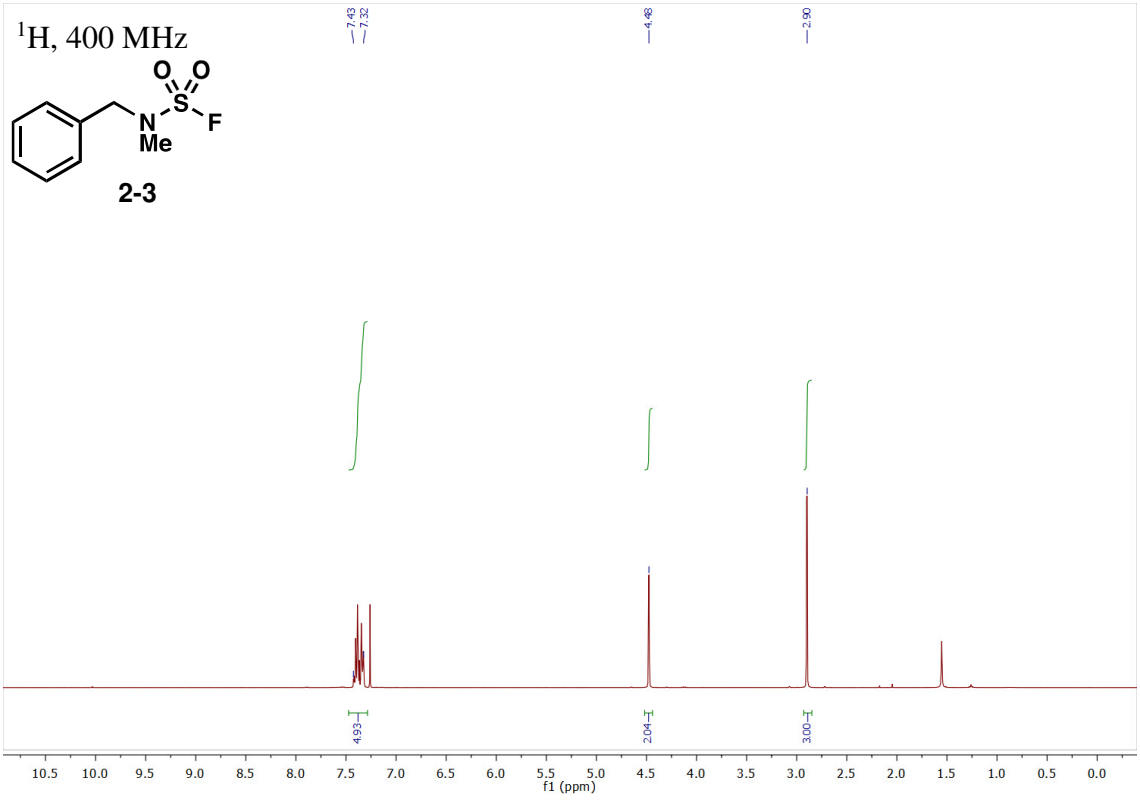


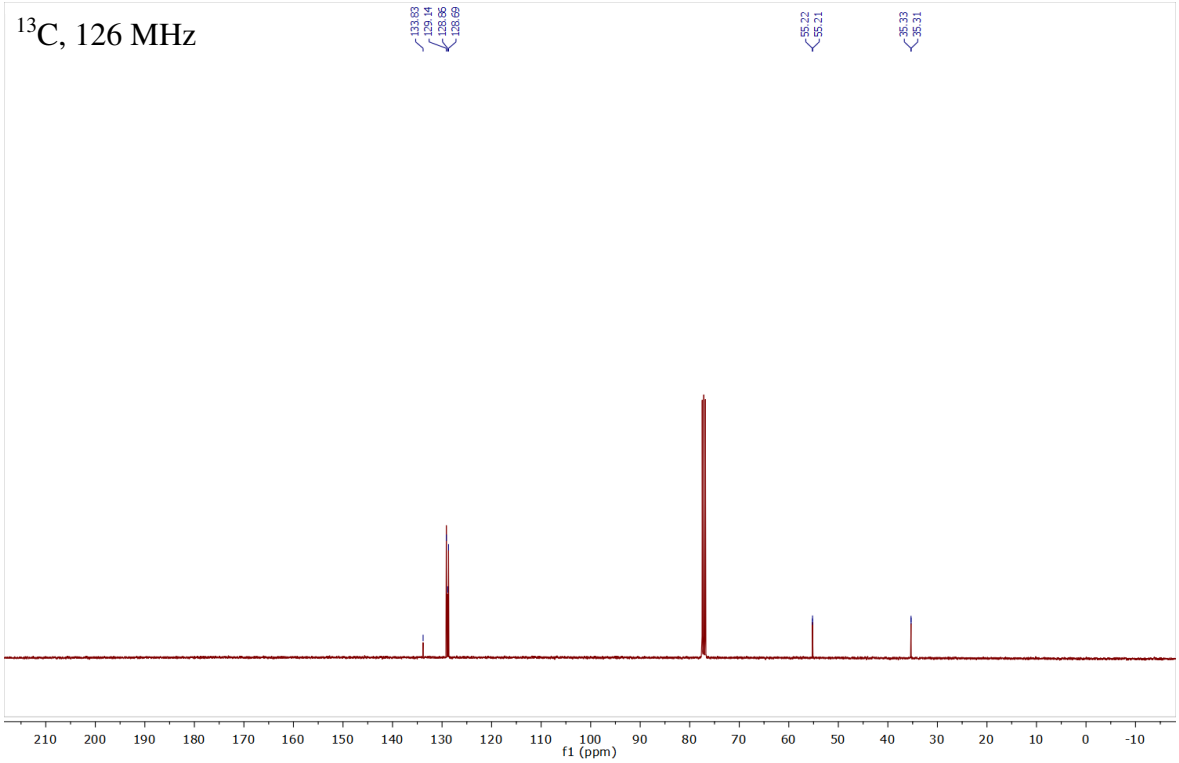
Figure 2-11. Top: ^{1}H NMR spectra of compound **2-3** ($CDCl_3$, 400 MHz), Bottom: ^{1}H NMR ($CDCl_3$, 400 MHz) of material obtained after attempting to react compound **2-3** with benzylamine. Reprinted with permission from the Royal Society of Chemistry (*Ibid.*)

2.3.9 NMR Spectra of Novel Compounds

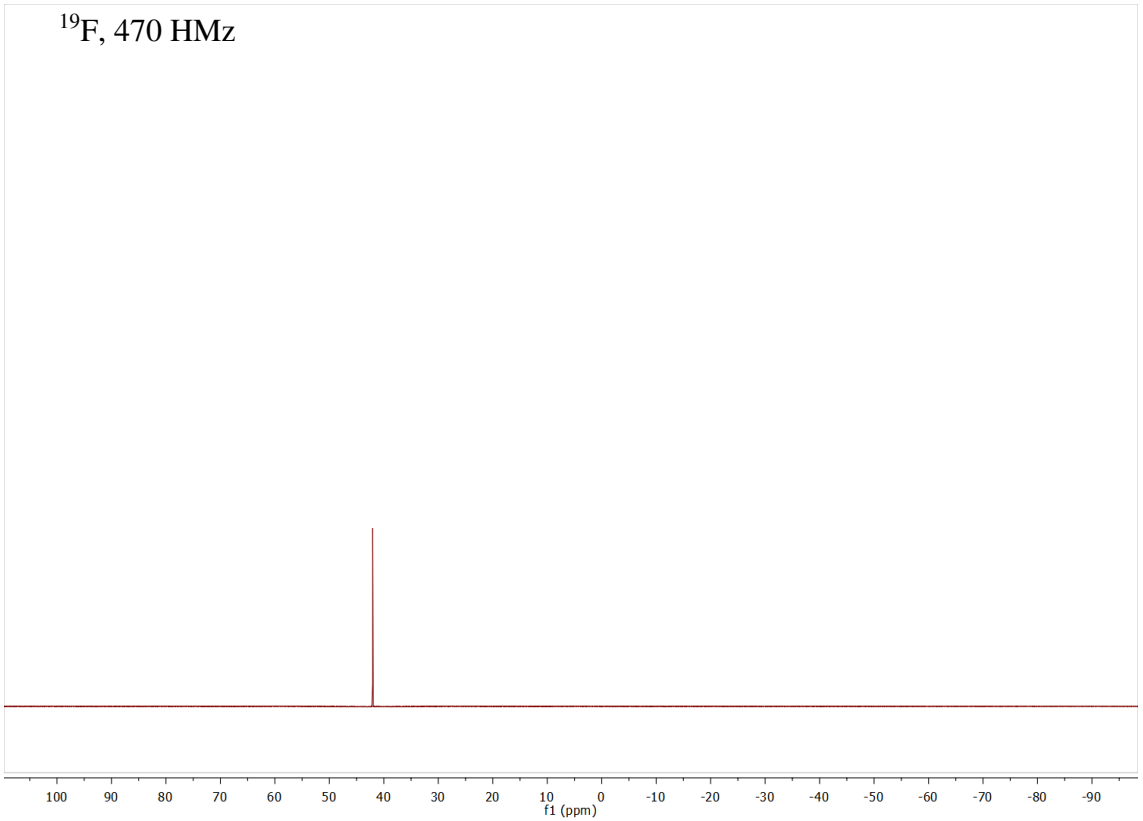
NMR Spectra of *N*-Methylbenzylsulfamoyl Fluoride (**2-3**) ($CDCl_3$)



^{13}C, 126 MHz

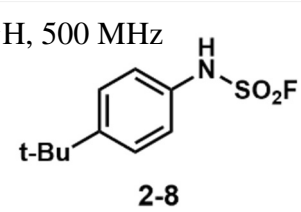


^{19}F, 470 HMz



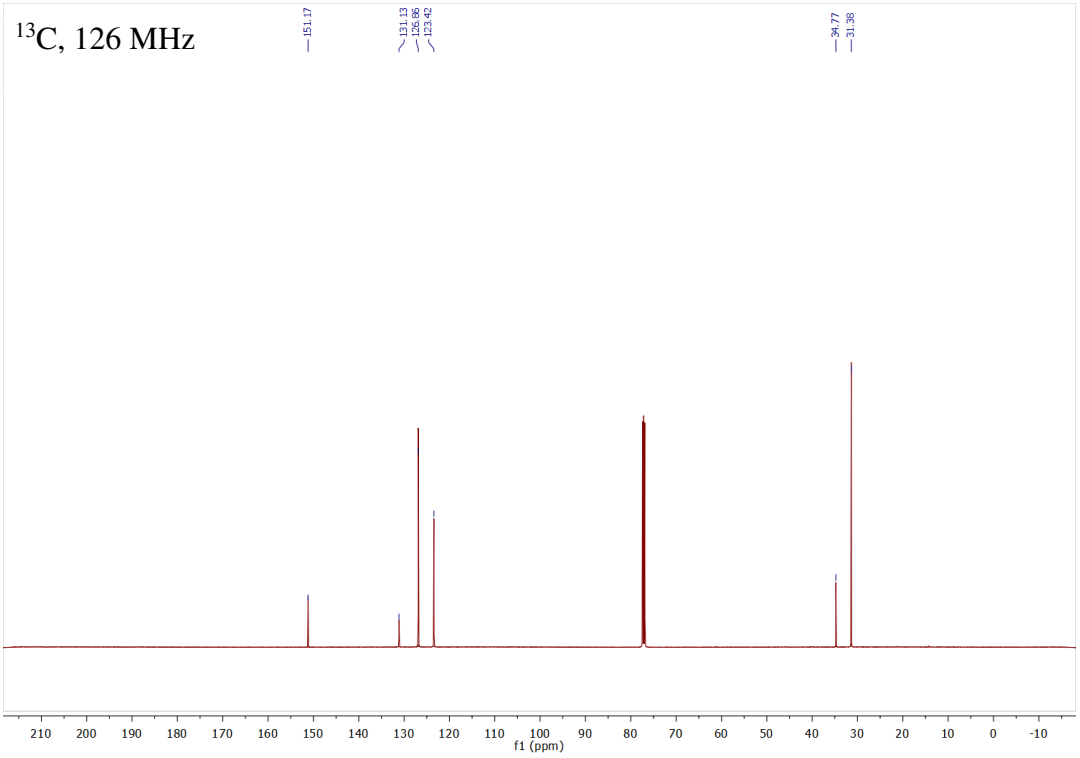
NMR Spectra of 4-*tert*-butylphenylsulfamoyl Fluoride (**2-8**) ($CDCl_3$)

^{1}H, 500 MHz

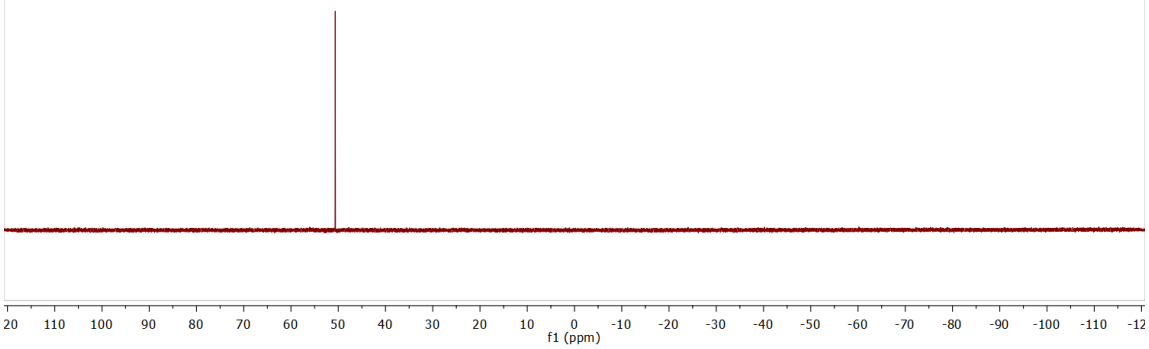


2-8

^{13}C, 126 MHz

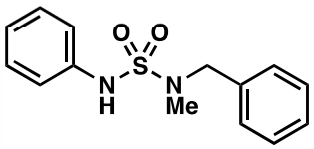


^{19}F, 470 HMz


20 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -12
f1 (ppm)

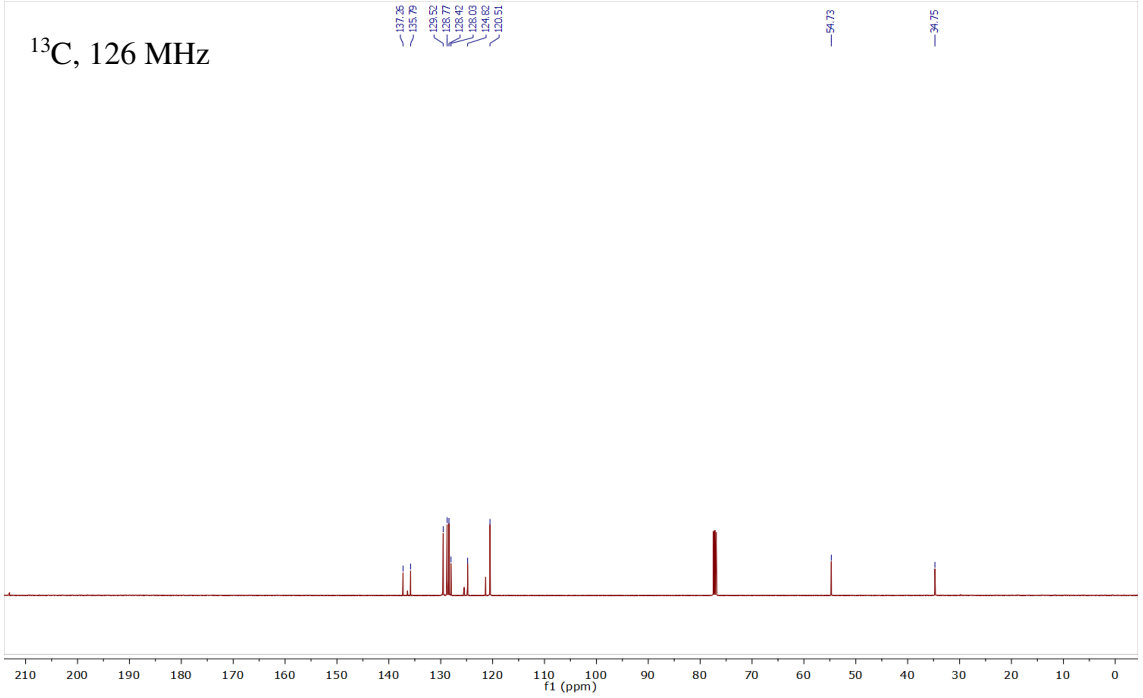
NMR Spectra of *N*-Benzyl-*N*-methyl-*N'*-phenylsulfamide (**2-12**) ($CDCl_3$)

^1H, 400 MHz



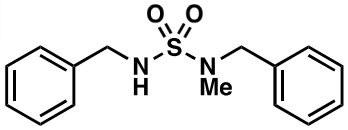
2-12

^{13}C, 126 MHz



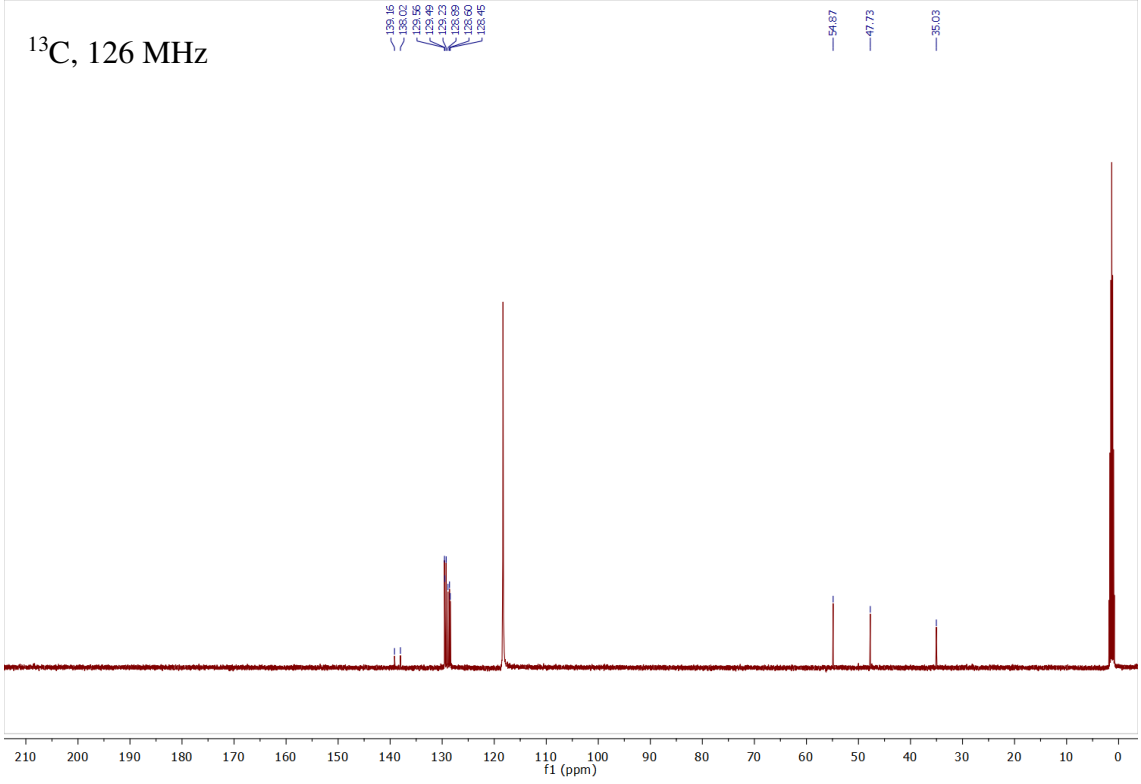
NMR Spectra of *N,N'*-Dibenzyl-*N*-methylsulfamide (**2-13**) (CD_3CN)

^{1}H, 400 MHz



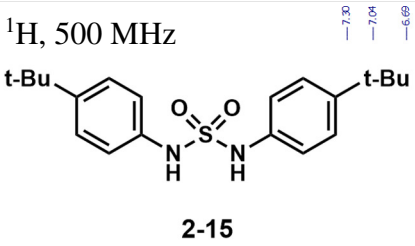
2-13

^{13}C, 126 MHz



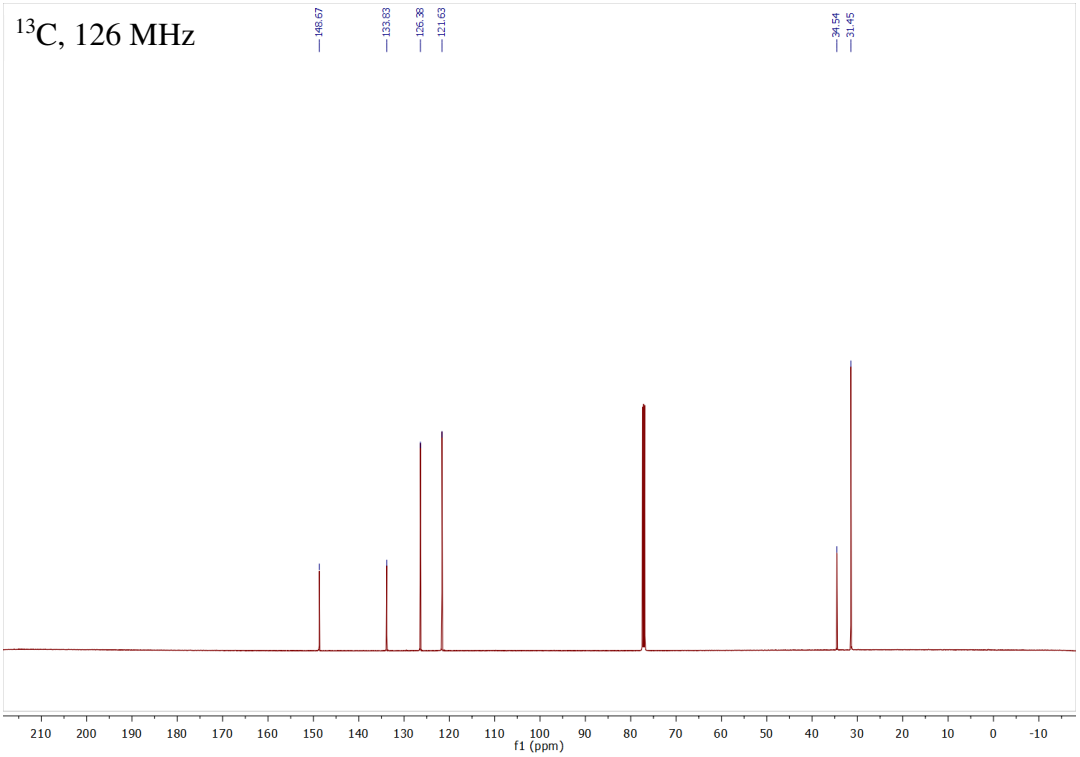
NMR Spectra of *N,N'*-bis(4-*tert*-butylphenyl)sulfamide (**2-15**) ($CDCl_3$)

^1H, 500 MHz



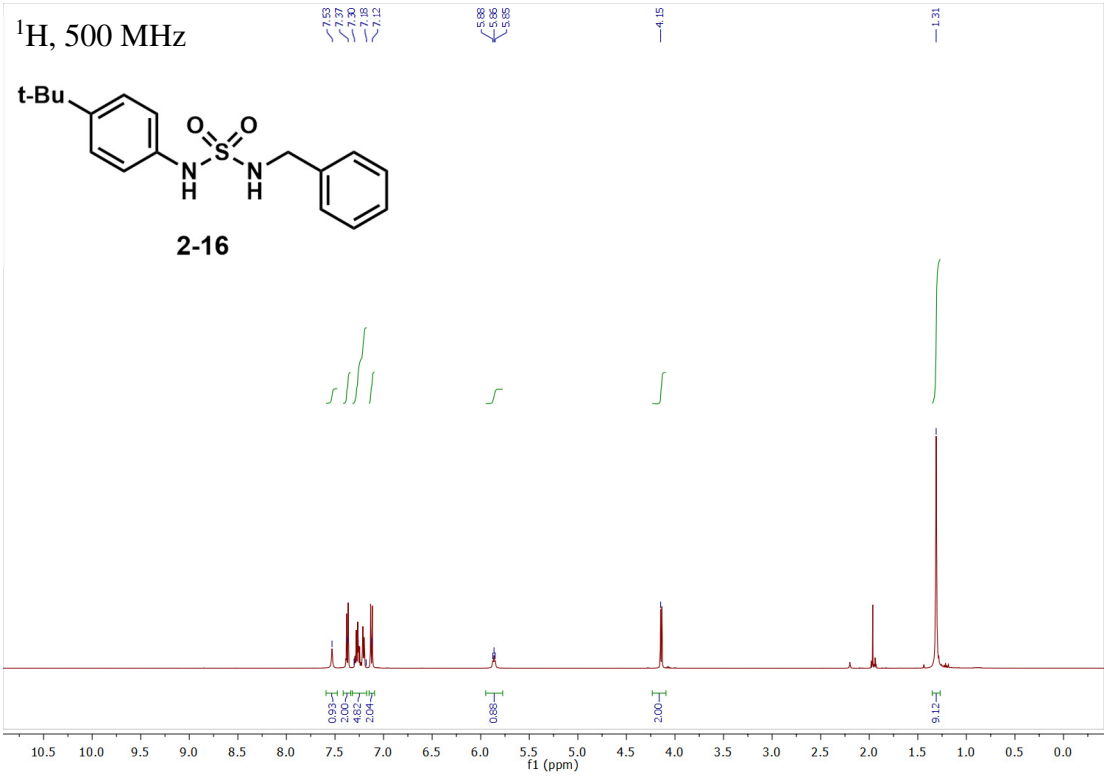
2-15

^{13}C, 126 MHz

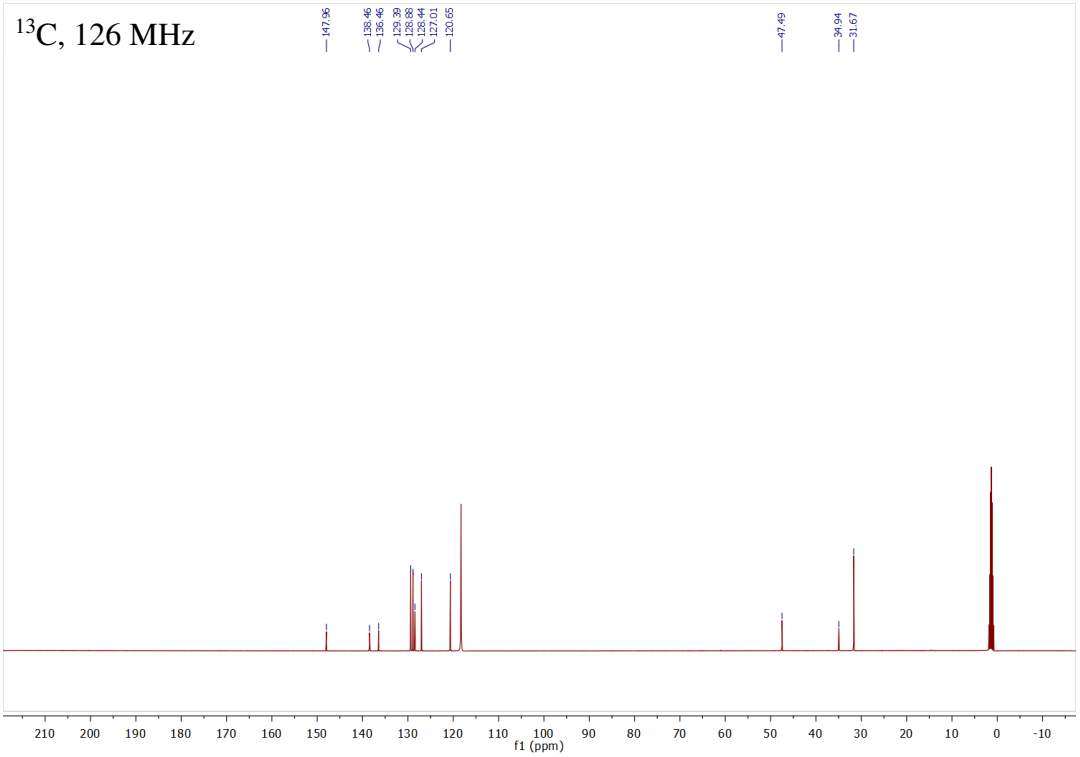


NMR Spectra of *N*-Benzyl-*N'*-(4-*tert*-butylphenyl)sulfamide (**2-16**) (CD_3CN)

^1H, 500 MHz



^{13}C, 126 MHz



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CHAPTER III

POLYSULFAMIDE SYNTHESIS AND CHARACTERIZATION*

3.1 Polysulfamide Synthesis

Once the proper conditions were established for sulfamide formation, the work on polysulfamide synthesis could begin. The bis(sulfamoyl fluoride) monomers **3-1**, **3-2**, **3-3**, and **3-4** were synthesized using a similar procedure to that used on the monoamines discussed in the previous chapter (Figure 3-1). Monomers **3-1** and **3-2** were both aromatic, but **3-1**, having both sulfamoyl fluoride groups attached to the same aromatic ring, was a much more highly activated aromatic species. On the other hand, monomers **3-3** and **3-4** were both aliphatic, but one contained an aromatic group.

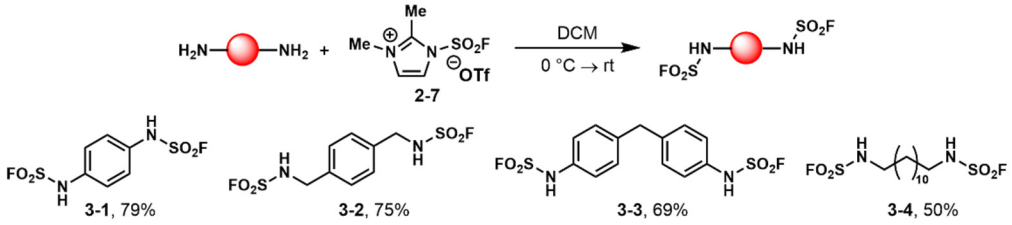


Figure 3-1. Synthesis of AA-type monomers. [a]Synthesized using MeCN as solvent. Adapted with permission from the Royal Society of Chemistry (*Ibid.*)

The purification of these monomers was generally simple in most cases. For all monomers, the bis(sulfamoyl fluoride)s synthesized were initially purified through an aqueous workup. From there, the monomers, with the exception of **3-1**, could be obtained

*Parts of this chapter have been adapted with permission from the Royal Society of Chemistry from *Chem. Sci.* **2020**, *11*, 7807–7812. (https://doi.org/10.1039/D0SC03606D)

in a pure form after column chromatography. The monomers could then be stored as bench-stable solids, though storing them at –20 °C was preferable due to the likelihood of these monomers hydrolyzing over time. Storing them at room temperature led to the formation of impurities observable on ^{1}H NMR within two weeks. As established in chapter 2, maintaining the purity of the monomers is crucial to get high molecular weight polymers from a step-growth polymerization. The outlier in terms of purification, monomer **3-1**, was found to decompose on silica, reforming *p*-phenylenediamine. This could be observed visually by the silica turning dark purple as chromatography was performed. Due to the base sensitivity of the primary sulfamoyl fluoride group, deactivating the silica with a base such as triethylamine was not attempted. Similar results occurred when neutral, acidic, and basic alumina was used in place of silica. Attempts at recrystallizing this monomer did not fare well. In most cases, when subjected to solvents it is insoluble in, this monomer would form a dense, solvent-saturated oil instead of the initial brown solid. Indeed, this occurs during the synthesis of this monomer as well, since it is not soluble in DCM. In order to obtain pure monomer **3-1**, it was instead decided to use 1.8 equivalents of reagent **2-7** instead of the 2 equivalents used for all other monomers. This would mean that the minor products of the reaction, anticipated to be unsubstituted and monosubstituted diamine, would be removed by the initial acidic workup. This strategy succeeded, producing monomer **3-1** in relatively good yield without the need for further purification.

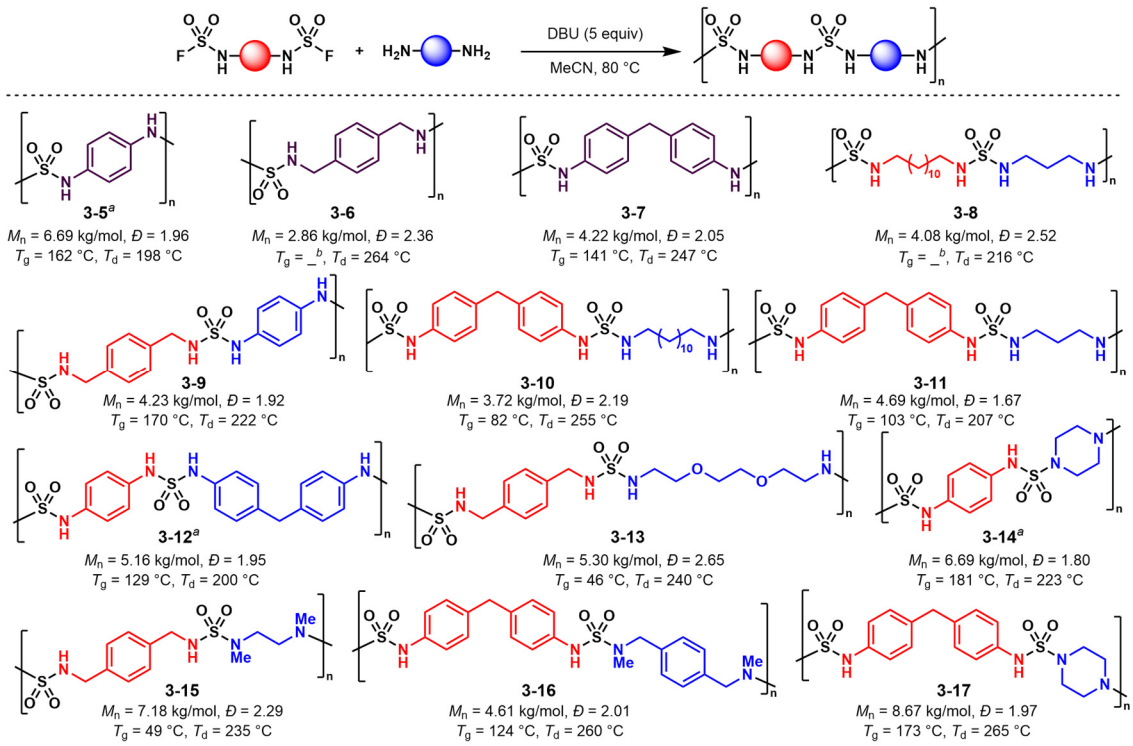


Figure 3-2. Synthesis of polysulfamides using AA/BB polymerization. [a]Synthesized using pyridine (5.0 equiv); [b]no T_g observed by DSC. Modified with permission from the Royal Society of Chemistry (*Ibid.*)

Using these AA-type monomers, and the optimized reaction conditions discussed in Chapter 2, a variety of polysulfamides were synthesized (Figure 3-2). When performed at 50 °C, the reaction mixture quickly became turbid, indicating that oligomers were precipitating from solution. Performing the polymerization at 80 °C with an excess of base allows the polymer to be soluble for most, if not all, of the reaction time. The synthesized polysulfamides include homopolymers as well as alternating copolymers, depending on the diamine comonomer used. For the polymers made using monomer **3-1**, pyridine was used as a base instead of DBU. This is based both on the earlier optimization indicating

that aryl sulfamoyl fluorides favor the use of pyridine, as well as the difficulty experienced with removing DBU from the polymer during purification, as will be discussed later. The molecular weights of these polymers were found to be a marked improvement over those obtained by the method outlined by Rudkevitch and coworkers.[1]

The purification of these polymers proved to be quite challenging, and was the first subject of inquiry after establishing that polysulfamides were being produced. Initially, the only method of purification we attempted was the repeated reprecipitation of the polymer from DMF into either methanol or ethyl ether. This led to some issues involving the removal of base from the reaction. Due to the high acidity of the sulfamide protons in the polymer, the base used in the reaction could not be dissociated from the polymer through reprecipitation. The base contaminated polymer would be isolated as an incredibly viscous oil or resin rather than the powders we now know the purified polymers to be. This problem worsened in the case of polymers derived from monomer **3-1**. Since the polymers it was used to create contain highly acidic sulfamide protons, due to the highly activated *p*-phenylene aromatic system, stronger bases such as DBU were incredibly difficult to remove with acidic washes. Knowing that the two primary contaminants of the polymer would be the excess base, along with the dissolving solvent used for reprecipitation (either DMF or DMAc), work began to find a method for the purification of polysulfamides. The initial precipitation in ethyl ether was kept, since it would remove the acetonitrile and any small molecule impurities from the desired polymer. From there, various acidic workups were tested for their efficacy in the removal of both aforementioned impurities. It was found that stirring the polymer in a saturated

aqueous solution of ammonium chloride could be used to remove the majority of the base. The slightly acidic nature of the solution removed the basic impurities form the polymer backbone and did not dissolve the polymer itself. Reprecipitating the polymer in the ammonium chloride solution seemed to be equally effective in removing the base impurities. Since ammonium chloride would be left behind in the polymer after decanting the solution off, the polymer would then be washed multiple times with distilled water. After drying in a vacuum oven, a powdery solid would be all that remained, which is not only easier to handle but considerably purer as well.

3.2 Properties of Polysulfamides

The thermal properties of these polymers were examined first with thermogravimetric analysis, then through differential scanning calorimetry. TGA revealed that these polymers were thermally stable, with most of the polysulfamides synthesized decomposing at temperatures in excess of 200 °C. The temperature of decomposition is likely dependent on a combination of the stability of the sulfamide linkages in the polymer along with the lability of the polymer backbone. Polymers with low decomposition temperatures include **3-5**, which contains only the highly activated *p*-phenylene monomer and **3-8**, which contains only highly flexible aliphatic monomer groups. This is further evidenced by the effect of adding more or less rigid monomers on the decomposition temperature. For example, forming an alternating copolymer with piperazine and *p*-phenylenediamine creates a material with a decomposition temperature 20 °C higher than that of polymer **3-5**. On the other hand, linking a short, but very flexible, polyethylene

glycol chain to *p*-xylylenediamine results in a material that decomposes at a temperature 20°C lower than the *p*-xylenediamine homopolymer, **3-6**.

Performing DSC on these polymers revealed the expected relationship between chain flexibility and glass transition temperature. The polymer with the lowest observed T_g, **3-6**, contains the aforementioned polyether chain, whereas the polymers with the highest glass transition temperatures contain rigid aromatic and heterocyclic monomers, such as polysulfamides **3-9**, **3-14**, and **3-17**. In order to demonstrate the tunability of the glass transition temperature, two additional polymers were synthesized using bis(sulfamoyl fluoride) monomer **3-2** and combinations of *p*-phenylenediamine and 2,2'-(ethylenedioxy)bis(ethylamine) adding up to one equivalent (Figure 3-3). These two polymers, which had similar M_n's to the other polymers synthesized, were found to have T_g's between those of polymers **3-9** and **3-13**, with the T_g increasing as the amount of the phenylene monomer increased.

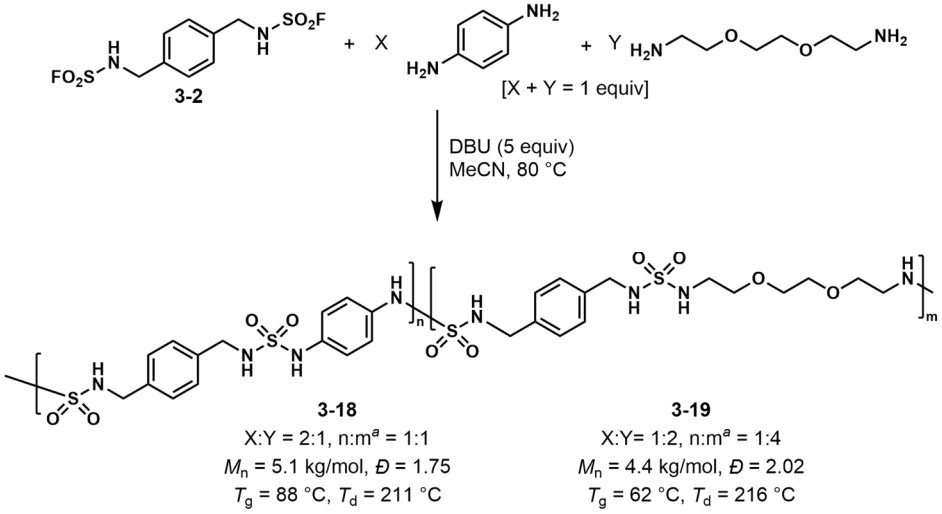


Figure 3-3. Synthesis of a terpolymer using two diamine monomers. [a]Monomer incorporation estimated using HNMR

Interestingly, the T_g of the copolymers differs from the value predicted using the Fox equation.[2] These discrepancies are likely the result of intermolecular interactions such as hydrogen bonding (see section 3.4.9 for more information). The ratio of each monomer determined through NMR skewed in favor of the aliphatic polyether monomer in both cases. This preference confirms the observation from the kinetic study discussed in Chapter 2 that aliphatic amines generally react with aliphatic sulfamoyl fluorides more quickly at the same temperature. Interestingly, DSC analysis revealed an absence of crystallization and melting temperatures for all these materials, suggesting that these materials are all amorphous in structure. This thermal response contrasts with the melting temperatures measured in low-molecular-weight sulfamide films[3] and the high crystallinity observed with these small molecules.[4-7] Powder X-ray diffraction performed on polysulfamides provided a more precise depiction of their structural order. Polysulfamides exhibited various degrees of crystallinity from amorphous to semicrystalline. This behavior is reminiscent of that of work by Aida and coworkers,[8] which demonstrated that polythioureas with low M_n's are amorphous, mechanically robust, and self-healable due to a zig-zag arrangement of the hydrogen-bond network. Polyureas, on the other hand, are generally characterized by a linear array of hydrogen-bond networks, rendering them semicrystalline and brittle. IR spectroscopy was used to probe the hydrogen-bond interactions in the solid state. Strong N-H peaks at approximately 3290 cm^{-1} were found in both **3-6** and sulfamide **2-2** (Figure 3-4) and are consistent with N–H bonds engaged in hydrogen-bonding based on prior studies.[3,6-7] By

contrast, the IR spectrum of **3-5** displayed a much broader N–H peak, suggesting that the structure of the backbone strongly affects the hydrogen bonding ability of the repeating sulfamide groups. More in-depth characterization of the hydrogen-bonding architecture is needed to determine its effect on the thermal and mechanical properties of polysulfamides.

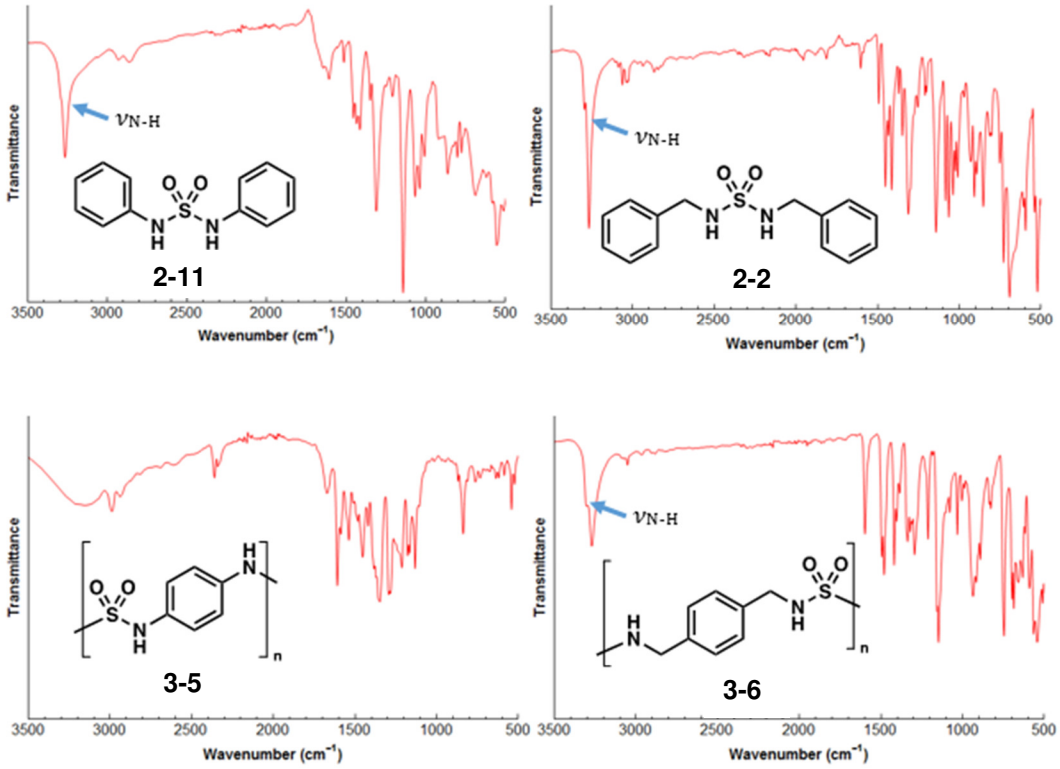


Figure 3-4. Evidence of hydrogen bonding in polys□lfamides Adapted with permission from the Royal Society of Chemistry (*Ibid.*)

3.3 Degradation Studies

The synthesized polysulfamides showcased high thermal stability, a desirable feature for many applications. However, the global accumulation of plastic waste has created a dire environmental crisis that must be addressed by the development of recyclable polymers. Knowing the hydrolytic stability of polyureas,[9] the depolymerization of the synthesized polysulfamides was investigated.

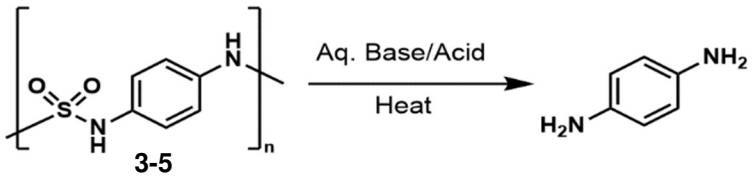


Table 3-1. Hydrolytic degradation of polysulfamide **3-5***

Aq. Base/Acid	Temp. (°C)	Monomer Recovery (%)
NaOH (4 M)	80	32
NaOH (4 M)	130	42
NH4OH (18 M)	80	53
HCl (4 M)	80	63
HCl (4 M)	130	74
HCl (conc.)	20	0
HBr (4 M)	130	70
H_2SO_4 (conc.)	20	0
H_2SO_4 (2 M)	20	0

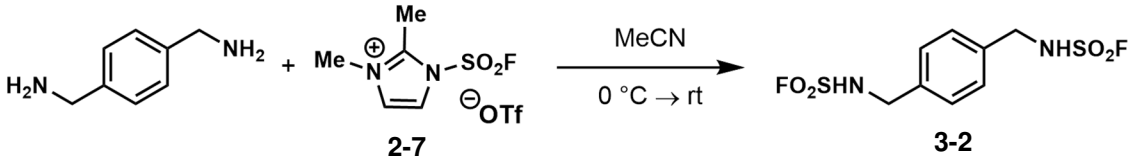
*Modified with permission from the Royal Society of Chemistry (*Ibid.*)

Following the work done on small molecules,[10-11] it appeared that hydrolytic cleavage to form the component amines of a sulfamide was possible. While most studies employ acidic conditions to perform this transformation, basic media including solutions

of ammonium hydroxide were tested as well. While alkyl polysulfamide **3-15** displayed remarkable stability in acidic or basic media at elevated temperatures, aryl polysulfamide **3-5** could be hydrolyzed in a variety of aqueous conditions. The polymer was typically suspended in an aqueous solution and heated for 40 h. The resulting aqueous solution was then extracted at pH~14 with EtOAc and the amount of bis(amine) monomer was determined by mass. After treatment with a basic solution containing NaOH or NH_4OH for 40 h, up to 53% of pure *p*-phenylenediamine was isolated. In the case of the ammonium hydroxide solutions, temperatures were not tested above 80 °C due to concerns over the structural integrity of the sealed reaction container. In HCl at 125 °C for the same amount of time, the recovery of *p*-phenylenediamine was improved to 74%. In both basic and acidic conditions, it can be inferred that the byproduct of this reaction is a sulfate anion generated from the hydrolysis of the sulfamide group. When aqueous ammonium hydroxide is used, sulfamide and sulfamic acid may also be formed through the partial or complete ammonolysis of the sulfamide group, but this cannot be confirmed at this time due to these species being washed out in the aqueous workup. This initial study will serve as a blueprint to investigate the recyclability potential of aromatic polysulfamides.

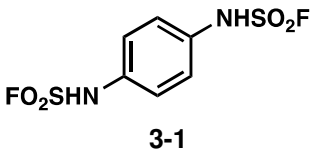
3.4 Experimental

3.4.1 General Procedure for the Synthesis of Bis(sulfamoyl fluoride) Monomers (Using 3-2 as an Example)



2-7 **3-2**

Reagent **2-7** (2.41g, 7.33 mmol, 2.0 equiv) was added to a mixture of *p*-xylylenediamine (500 mg, 3.67 mmol, 1.0 equiv) in MeCN (15 mL) at 0 °C. The mixture was brought to room temperature and stirred for 2 h, subsequently diluted with ethyl acetate (10 mL), and washed with HCl (0.1 M, 2 x 10 mL) and brine (10 mL). The organic phase was dried over $MgSO_4$ and concentrated *in vacuo* to yield the crude product. When required, the product was then purified through column chromatography.



3-1

Bis(sulfamoyl fluoride) 3-1 was obtained as a brown solid using 1,4-phenylenediamine (100 mg, 0.925 mmol), **2-7** (546 mg, 1.67 mmol, 1.8 equiv), and DCM as the solvent. The product was noted to decompose during column chromatography using silica gel (deactivated or not). Using only 1.8 equiv of **2-7** prevented the formation of undesired side products and delivered pure **3-1** as a brown solid without further purification (180 mg, 79%).

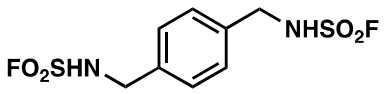
^{1}H NMR (CD_3CN, 400 MHz) δ: 8.88 (br, 2 H), 7.37 (s, 4 H) ppm.

^{13}C NMR (CD_3CN, 126 MHz) δ: 134.3, 125.1 ppm.

^{19}F NMR (CD_3CN, 470 MHz) δ: 49.5 ppm.

HRMS-ESI: calc'd. for $C_6H_5N_2O_4S_2F_2$ $[M–H]^-$ 270.9664, found 270.9662.

mp: Decomposed before melting.



3-2

Bis(sulfamoyl fluoride) 3-2 was obtained as a white solid using *p*-xylylenediamine (500 mg, 3.67 mmol) and MeCN as the solvent. Column chromatography (SiO_2, 5:95 to 10:90 EtOAc:hexanes) provided **3-2** as a white solid (824 mg, 75%).

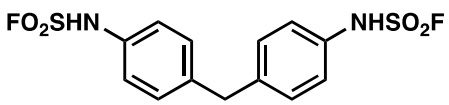
^{1}H NMR (CD_3CN, 500 MHz) δ: 7.39 (s, 4 H), 7.06 (br, 2 H), 4.41 (d, 4 H) ppm.

^{13}C NMR (CD_3CN, 126 MHz) δ: 137.1, 129.4, 48.2 ppm.

^{19}F NMR (CD_3CN, 470 MHz) δ: 50.3 ppm.

HRMS-ESI: calc'd. for $C_6H_9N_2O_4S_2F_2$ $[M–H]^-$ 298.9977, found 298.9973.

mp: 145–146 °C.



3-3

Bis(sulfamoyl fluoride) 3-3 was obtained using 4,4'-diaminodiphenylmethane (793 mg, 4.0 mmol) and DCM as the solvent. Column chromatography (SiO_2, 10:90 to 20:80 EtOAc:hexanes) provided **3-3** as a yellowish solid (1.00g, 2.76 mmol, 69%).

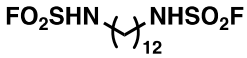
^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.22 (m, 8 H), 6.78 (br, 2 H, NH), 3.99 (s, 2 H) ppm.

^{13}C NMR ($CDCl_3$, 126 MHz) δ: 140.2, 132.2, 130.4, 123.8, 40.8 ppm.

^{19}F NMR ($CDCl_3$, 470 MHz) δ: 50.8 ppm.

HRMS-ESI: calc'd. for $C_{13}H_{11}N_2O_4S_2F_2$ $[M–H]^-$ 361.0123, found 361.0132.

mp: 96–99 ºC



3-4

Bis(sulfamoyl fluoride) 3-4 was obtained using 1,12-diaminododecane (200 mg, 1.0 mmol) as the starting bis(amine) and DCM as the solvent. Column chromatography (SiO_2, 5:95 to 10:90 EtOAc:hexanes) provided **3-4** as a white solid (183 mg, 0.502 mmol, 50%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 4.86 (br, 2 H, NH), 3.28 – 3.32 (ddd, J = 5.2, 5.2, 1.9 Hz, 4 H), 1.62 (m, 4 H), 1.23 – 1.40 (m, 16 H) ppm.

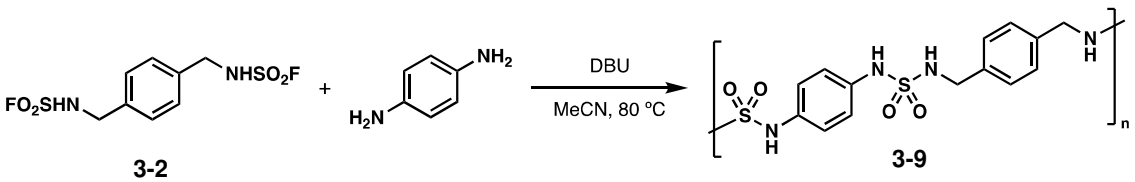
^{13}C NMR ($CDCl_3$, 126 MHz) δ: 44.9, 29.5, 29.4, 29.4, 29.0, 26.3 ppm.

^{19}F NMR ($CDCl_3$, 470 MHz) δ: 50.7 ppm.

HRMS-ESI: calc'd. for $C_{12}H_{25}N_2O_4S_2F_2$ $[M–H]^-$ 363.1218, found 363.1228.

mp: 64–66 ºC.

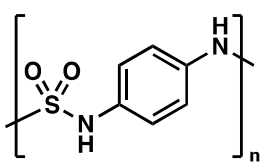
3.4.2 General Procedure for the Synthesis of Polysulfamides (Using 3-9 as an Example)



3-2 3-9

To a solution of bis(sulfamoyl fluoride) **3-2** (150 mg, 0.500 mmol, 1.0 equiv) in MeCN (1.0 mL), DBU (380 mg, 2.50 mmol, 5.0 equiv) and *p*-phenylenediamine (54 mg, 0.500 mmol, 1.0 equiv) were added. The mixture was stirred at 80 ºC for 90 min. The resulting mixture was dissolved in DMF (1 mL), then precipitated in a centrifuge tube through the addition of Et_2O, until a volume of 50 mL was reached. After centrifuging and removing the supernatant liquid, the resulting dark orange solid was re-dissolved in DMF (1 mL)

and re-precipitated through the addition of saturated NH_4Cl (aq) until a volume of 50 mL was reached. The solid was then washed with distilled water (2 x 50 mL) and once with isopropanol (50 mL). The polymer was dried *in vacuo* (< 1 mmHg) at 100 ºC for 18 hours to obtain the final polymer as a dark orange solid (150 mg). Molecular weight and polymer distribution were determined through SEC. All diamines were commercially available, unless otherwise noted.



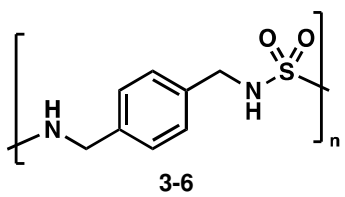
3-5

Polysulfamide 3-5 was obtained as a purple solid through the general procedure using compound **3-1** (200 mg, 0.733 mmol), 1,4-phenylenediamine, and pyridine as a base.

^{1}H NMR (d_6-DMSO, 500 MHz) δ = 9.87 (2 H), 7.01 (4 H) ppm.

^{13}C NMR (d_6-DMSO, 126 MHz) δ = 133.6, 120.1 ppm.

FTIR: $\tilde{\upsilon}$ = 3187, 2992, 2938, 2360, 1609, 1538, 1454, 1351, 1294, 1177, 1132, 837 cm^{-1}



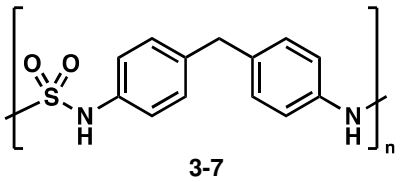
3-6

Polysulfamide 3-6 was obtained as an off-white solid by the general procedure using compound **3-2** (150 mg, 0.500 mmol) and *p*-xylylenediamine. *N,N'*-Dimethylacetamide was used as the solvent for reprecipitation due to poor solubility in DMF.

^{1}H NMR (d_6-DMSO, 500 MHz) δ = 7.44 (4 H), 7.29 (4 H), 4.01 (4 H) ppm.

^{13}C NMR (d_6-DMSO, 126 MHz) δ = 137.7, 128.1, 46.0 ppm.

FTIR: $\tilde{\upsilon}$ = 1143, 1311, 3263, 2932, 1614, 1067 cm^{-1}



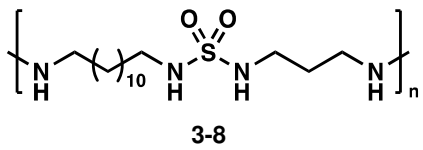
3-7

Polysulfamide 3-7 was obtained as an off-white solid through the general procedure using compound **3-3** (100 mg, 0.276 mmol) and 4,4'-diaminomethylenedianiline.

^{1}H NMR (d_6-DMSO, 500 MHz) δ = 9.97 (2 H), 7.05 (d, J = 8.5 Hz, 2 H), 7.00 (d, J = 8.5 Hz, 2 H), 3.74 (2 H) ppm.

^{13}C NMR (d_6-DMSO, 126 MHz) δ = 136.0, 135.9, 129.0, 120.8, 39.3 ppm.

FTIR: $\tilde{\upsilon}$ = 1151, 1139, 1334, 1509, 3301 cm^{-1}



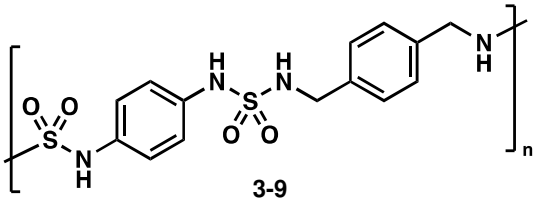
3-8

Polysulfamide 3-8 was obtained as an off-white solid by the general procedure using compound **3-4** (100 mg, .274 mmol) and 1,3-propanediamine.

^{1}H NMR (d_6-DMSO, 400 MHz) δ = 6.73 (br, 4 H, NH), 2.74-2.87 (m, 8 H), 1.63 (m, 2 H), 1.43 (m, 4 H), 1.25 (br, 16 H) ppm.

^{13}C NMR (d_6-DMSO, 126 MHz) δ = 42.1, 39.7, 39.0, 36.5, 29.0, 28.9, 28.7, 26.3 ppm.

FTIR: $\tilde{\upsilon}$ = 3281, 2920, 2850, 1441, 1308, 1143, 1065 cm^{-1}



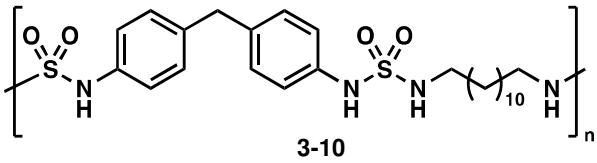
3-9

Polysulfamide 3-9 obtained as a dark orange solid through the general procedure using compound **3-2** (150 mg, 0.500 mmol, 1.0 equiv) and 1,4-phenylenediamine.

^{1}H NMR (d_6-DMSO, 500 MHz) δ = 9.56 (2 H), 7.83 (2 H), 7.17 (4 H), 7.12 (4 H), 4.00 (4 H) ppm.

^{13}C NMR (d_6-DMSO, 126 MHz) δ = 142.1, 139.3, 132.6, 125.3, 50.6 ppm.

FTIR: $\tilde{\nu}$ = 3275, 2938, 1614, 1513, 1318, 1143, 1064, 919 cm^{-1}



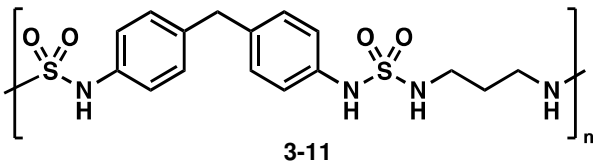
3-10

Polysulfamide 3-10 was obtained as an off-white solid through the general procedure using compound **3-3** (100 mg, 0.276 mmol) and 1,12-diaminododecane. Starting with 100 mg bis(sulfamoyl fluoride) monomer.

^{1}H NMR (d_6-DMSO, 400 MHz) δ = 7.06 (s, 8 H), 3.78 (s, 2 H), 2.78 (m, 4 H), 1.13-1.33 (m, 20 H) ppm.

^{13}C NMR (d_6-DMSO, 126 MHz) δ = 137.4, 135.9, 129.4, 118.4, 42.0, 41.8, 28.9, 28.7, 28.5, 26.1 ppm.

FTIR: $\tilde{\nu}$ = 3281, 2921, 2849, 1509, 1326, 1143, 927 cm^{-1}



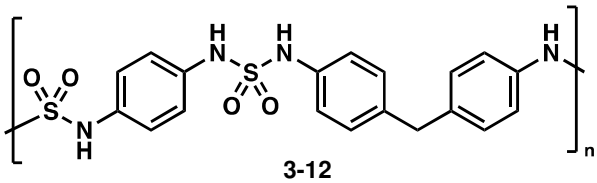
3-11

Polysulfamide 3-11 was obtained as an off-white solid through the general procedure using compound **3-3** (100 mg, 0.276 mmol) and 1,3-propanediamine.

^{1}H NMR (d_6-DMSO, 400 MHz) δ = 7.07 (q, 8 H, J = 8.5Hz), 3.08 (s, 2 H), 2.79 (t, 4 H J = 6.8 Hz), 1.54(tt, 2 H, J = 6.8 Hz) ppm.

^{13}C NMR (d_6-DMSO, 126 MHz) δ = 136.8, 135.6, 129.1, 118.7, 39.9, 36.8, 29.0, 27.3 ppm.

FTIR: $\tilde{\upsilon}$ = 3275, 1508, 1323, 1143, 933 cm^{-1}



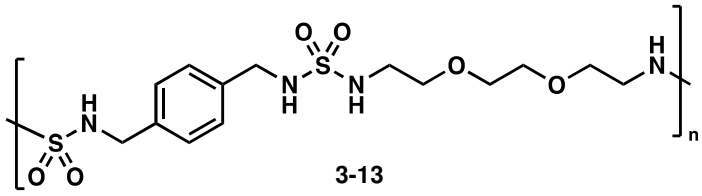
3-12

Polysulfamide 3-12 was obtained as a light purple solid through the general procedure using compound **3-1** (200 mg, 0.733 mmol), 4,4'-diaminomethylenedianiline, and pyridine as a base.

^{1}H NMR (d_6-DMSO, 500 MHz) δ = 9.92 (4 H), 7.02 (12 H), 3.75 (2 H) ppm.

^{13}C NMR (d_6-DMSO, 126 MHz) δ = 136.1, 135.9, 133.6, 129.1, 120.1, 118.9, 39.6 ppm.

FTIR: $\tilde{\upsilon}$ = 3270, 1610, 1508, 1315, 1147, 938 cm^{-1}



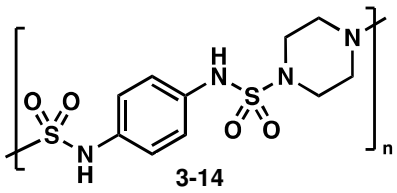
3-13

Polysulfamide 3-13 was obtained as a tan solid through the general procedure using compound **3-2** (150 mg, 0.500 mmol) and 2,2'-(ethylenedioxy)-diethylamine.

^{1}H NMR (d_6-DMSO, 500 MHz) δ = 7.29 (4 H), 6.92 (2 H), 3.99 (4 H), 3.51 (4 H), 3.46 (4 H), 3.31 (2 H), 2.98 (4 H) ppm.

^{13}C NMR (d_6-DMSO, 126 MHz) δ = 137.1, 127.5, 69.5, 69.1, 45.5, 41.8 ppm.

FTIR: $\tilde{\upsilon}$ = 3276, 2865, 1614, 1430, 1312, 1142, 1067 cm^{-1}



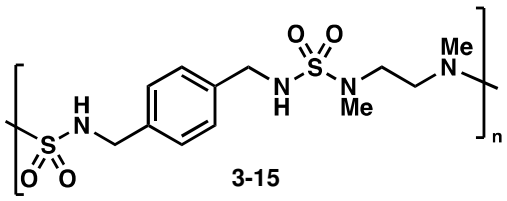
3-14

Polysulfamide 3-14 was obtained as a pink solid through general procedure using compound **3-1** (200 mg, 0.733 mmol), piperazine, and pyridine as a base.

^{1}H NMR (d_6-DMSO, 500 MHz) δ = 9.89 (2 H), 7.11 (4 H), 3.09 (8 H) ppm.

^{13}C NMR (d_6-DMSO, 126 MHz) δ = 134.0, 121.2, 45.2 ppm.

FTIR: $\tilde{\upsilon}$ = 3237, 2926, 2866, 1510, 1324, 1147, 1119, 943 cm^{-1}



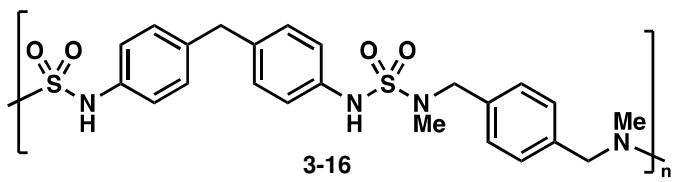
3-15

Polysulfamide 3-15 was obtained as a white solid through the general procedure using compound **3-2** (150 mg, 0.500 mmol) and *N,N'*-dimethylethylenediamine.

^{1}H NMR (d_6-DMSO, 500 MHz) δ = 7.67 (2 H), 7.30 (4 H), 4.06 (4 H), 3.18 (4 H), 2.70 (6 H) ppm.

^{13}C NMR (d_6-DMSO, 126 MHz) δ = 137.2, 127.5, 47.7, 45.8, 34.8 ppm.

FTIR: $\tilde{\upsilon}$ = 3261, 2938, 2863, 1612, 1426, 1308, 1145, 1056, 967 cm^{-1}



3-16

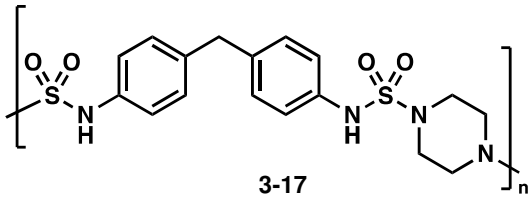
Polysulfamide 3-16 was obtained as an off-white solid through the general procedure using compound **3-3** (100 mg, 0.276 mmol) and *N,N'*-dimethyl-*p*-xylylenediamine. The

diamine was prepared following the previous reported procedure (*Dalton Trans.*, **2011**, *40*, 12235).

^{1}H NMR (d_6-DMSO, 400 MHz) δ = 9.90 (2 H), 7.13 (8 H), 7.06 (4 H), 4.16 (4 H), 3.84 (2 H), 2.52 (6 H) ppm.

^{13}C NMR (d_6-DMSO, 126 MHz) δ = 136.8, 135.6, 129.1, 118.9, 118.7, 52.9, 39.4, 28.9 ppm.

FTIR: $\tilde{\upsilon}$ = 3471, 3016, 2948, 1739, 1508, 1449, 1366, 1216, 1150, 909 cm^{-1}



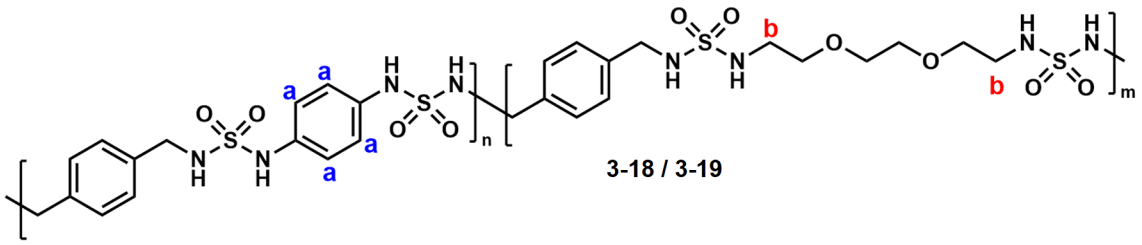
3-17

Polysulfamide 3-17 was obtained as an off-white solid through the general procedure using compound **3-3** (100 mg, 0.276 mmol) and piperazine.

^{1}H NMR (d_6-DMSO, 400 MHz) δ = 9.87 (br, 2 H), 7.07 (s, 8 H), 3.80 (s, 2 H), 3.05 (s, 8 H) ppm.

^{13}C NMR (d_6-DMSO, 126 MHz) δ = 136.5, 136.0, 129.2, 120.1, 41.8, 40.0, 39.3 ppm.

FTIR: $\tilde{\upsilon}$ = 3454, 3018, 2966, 1738, 1509, 1448, 1367, 1217, 1149, 912 cm^{-1}



3-18 / 3-19

Polysulfamide 3-18 was obtained as an orange solid through the general procedure using compound **3-2** (50 mg, 167 μmol, 3 equiv), 1,4-phenylenediamine (12 mg, 0.112 mmol, 2 equiv), and 2,2'-(ethylenedioxy)-diethylamine (8 mg, 0.056 mmol, 1 equiv)

^{1}H NMR (*d*$_6$-DMSO, 500 MHz) δ = 9.54, 7.83, 7.29, 7.13, 4.01, 3.52, 3.46, 2.98

^{13}C NMR (*d*$_6$-DMSO, 126 MHz) δ = 137.2, 134.1, 127.4, 120.6, 69.6, 69.1, 45.5, 41.8

Polysulfamide 3-19 was obtained as an orange solid through the general procedure using compound **3-2** (50 mg, 167 μmol, 3 equiv), 1,4-phenylenediamine (6 mg, 0.056 mmol, 1 equiv), and 2,2'-(ethylenedioxy)-diethylamine (16 mg, 0.112 mmol, 2 equiv)

^{1}H NMR (*d*$_6$-DMSO, 500 MHz) δ = 9.54, 7.83, 7.29, 7.13, 6.92, 4.00, 3.52, 3.46, 2.98

^{13}C NMR (*d*$_6$-DMSO, 126 MHz) δ = 137.2, 134.1, 128.2, 120.6, 69.6, 69.1, 45.5, 41.9

Based on the integration of the peaks located at 7.13 and 2.98 ppm, corresponding to the protons marked at positions "a" and "b" respectively, it was found that for **3-18** n:m ≈ 1:4, and for **3-19** n:m ≈ 1:1. The observed discrepancies between the initial ratios of monomer and the ratios of incorporated repeating units are likely due to the higher nucleophilicity of aliphatic amines compared to that of aryl amines.

3.4.3 Hydrolysis Study of Polysulfamides

To a vial containing polymer **3-5** (15 mg, 88 μmol, based on monomer unit $C_6H_6N_2O_2S$), 2 mL (excess in all cases) of the respective aqueous base or acid solution was added. The mixture was stirred at the indicated temperature for 40 h. If the aqueous solution was

acidic, the solution was placed in an ice bath and solid sodium hydroxide was added to the mixture until a pH of 14 was reached. The aqueous mixture was extracted with EtOAc (3 x 1 mL). The organic fractions were combined, dried over $MgSO_4$, and concentrated *in vacuo*. Yields were determined based on the mass of product obtained.

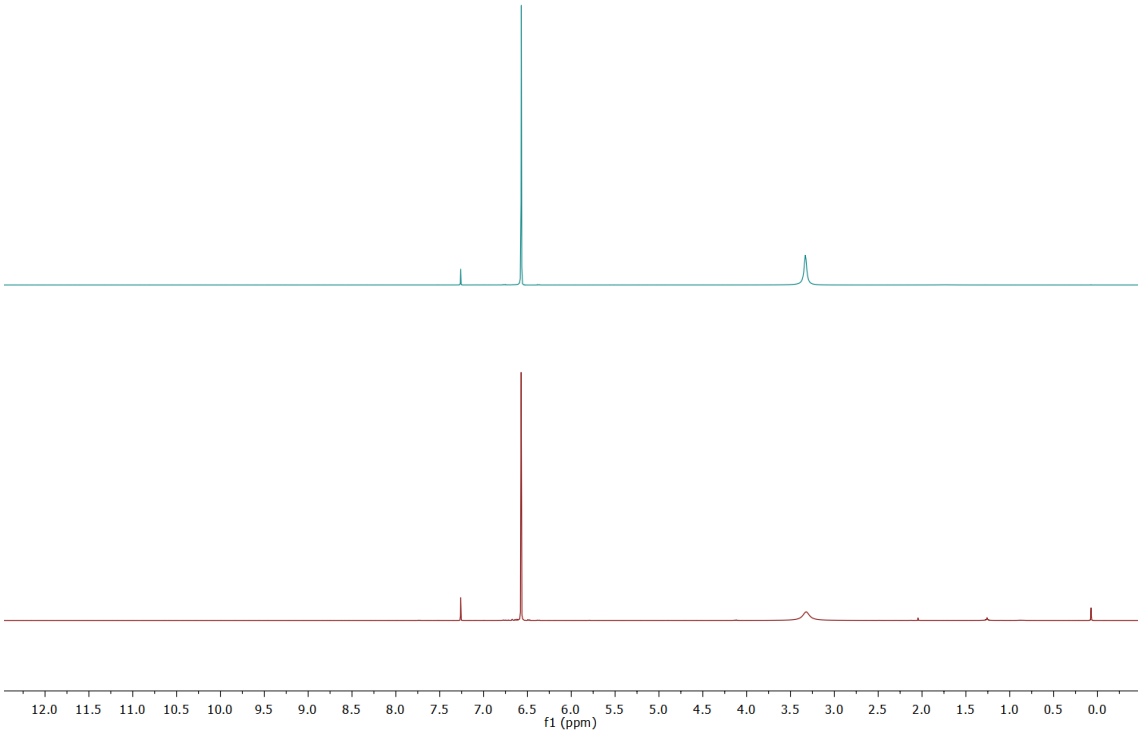
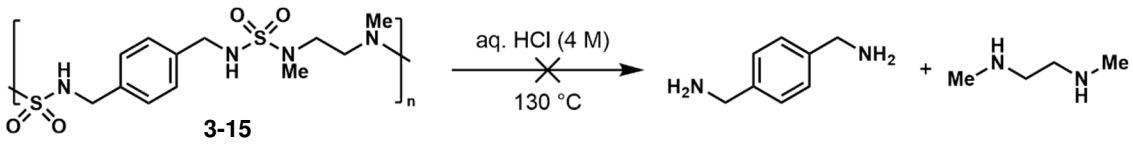


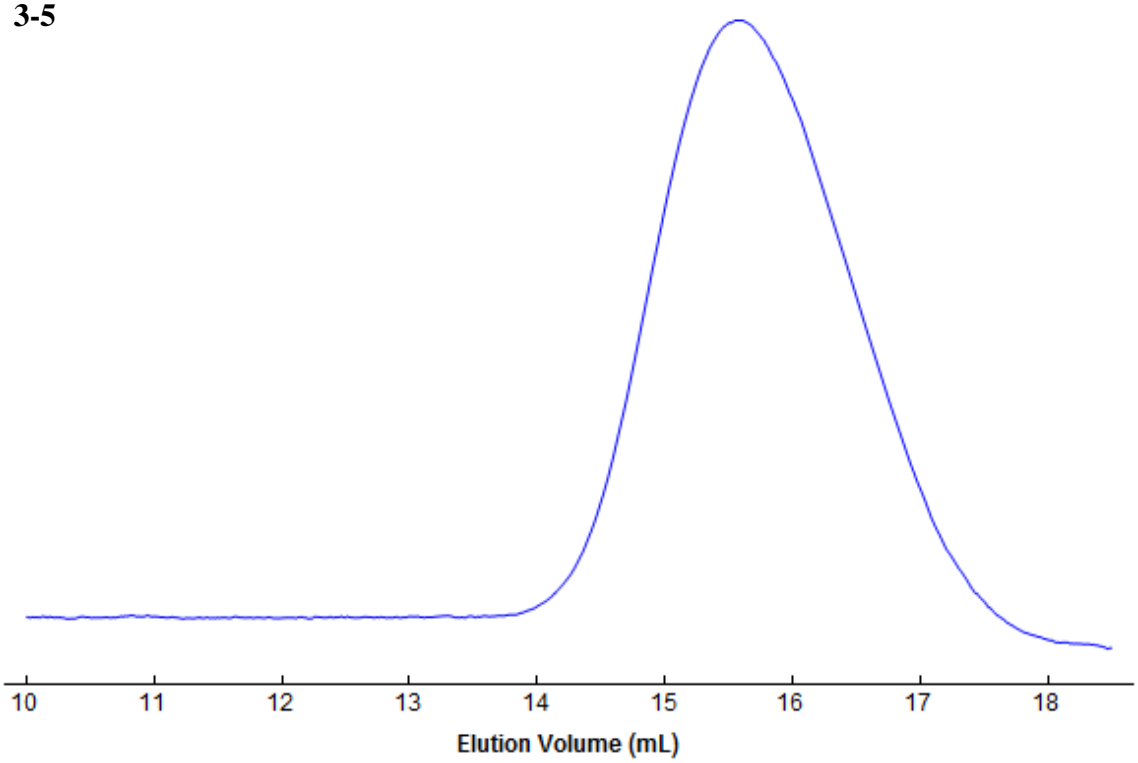
Figure 3-5. Top: ^{1}H NMR of purchased 1,4-phenylenediamine ($CDCl_3$, 400 MHz), Bottom: ^{1}H NMR of solid obtained after treatment of polymer **3-5** with aq. HCl (4 M) at 130 °C ($CDCl_3$, 400 MHz). Copied with permission from the Royal Society of Chemistry (*Ibid.*)



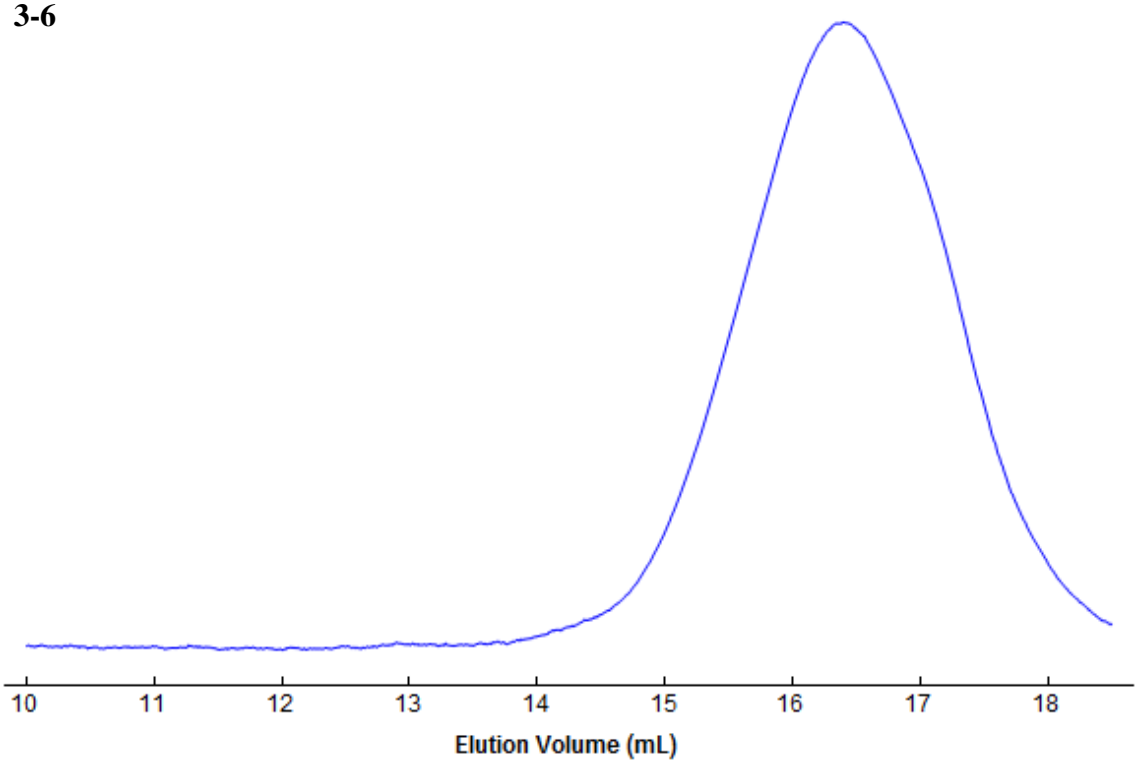
When polymer **3-15** was mixed with HCl (4 M) at 130 °C following the above procedure, the mixture remained a suspension of the polymer after 40 h. The solution was made alkaline and extracted with EtOAc, but no detectable amount of *p*-xylylenediamine or *N,N'*-dimethylethylenediamine was isolated

3.4.4 SEC Traces of Polysulfamides

3-5



3-6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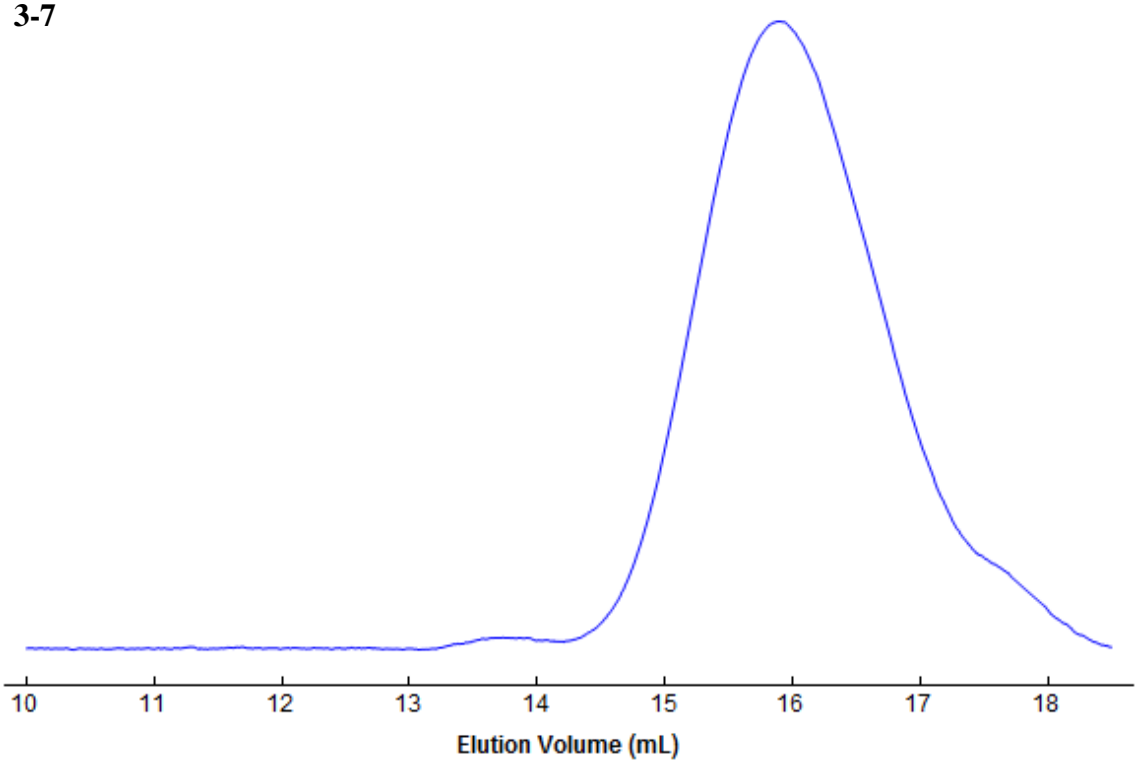
Elution Volume (mL)

3-7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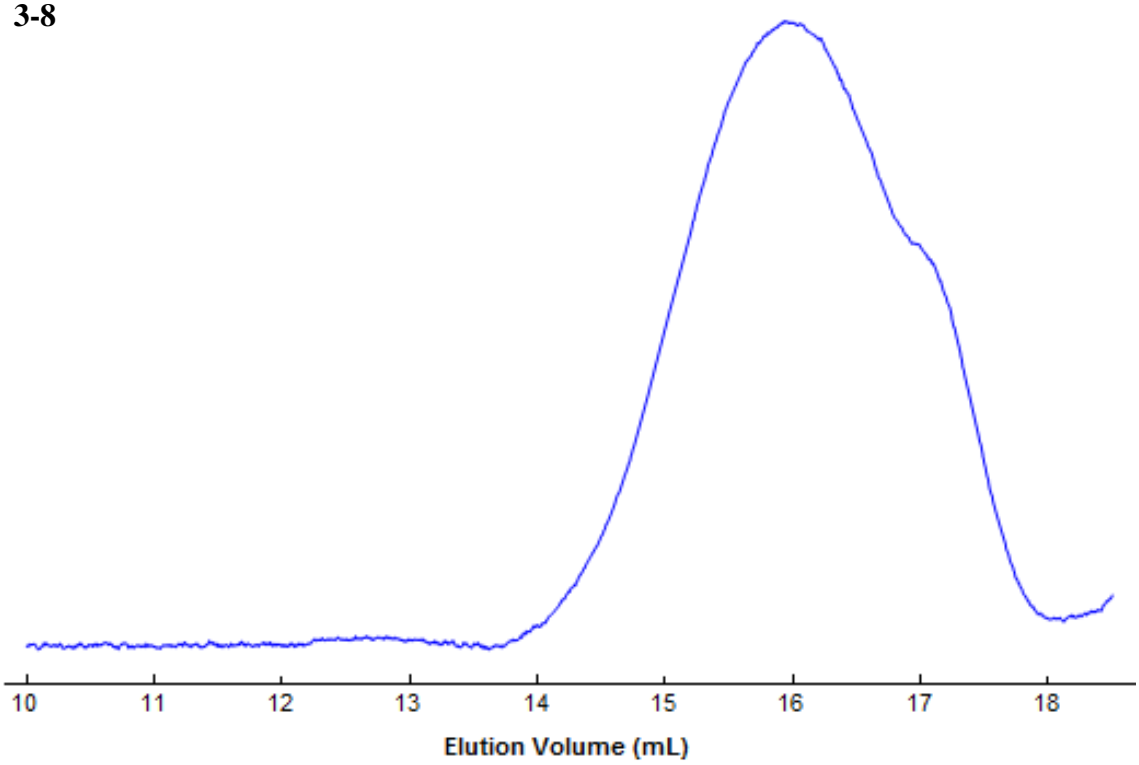
Elution Volume (mL)

3-8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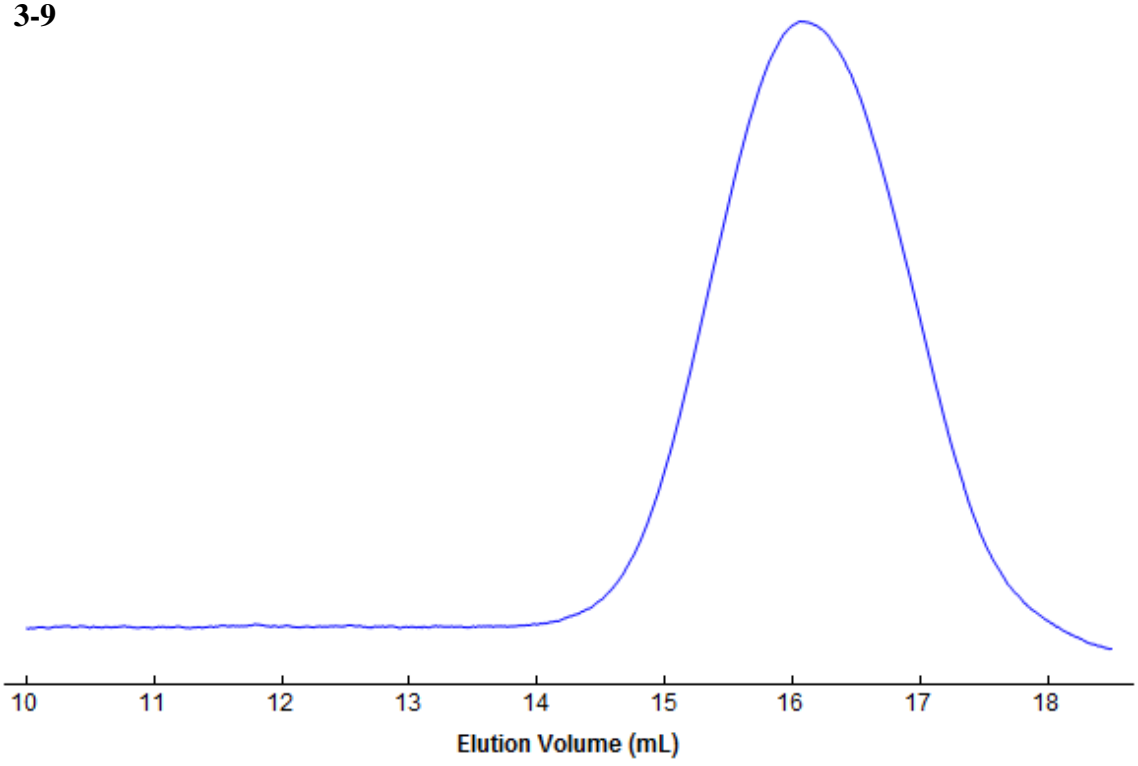
Elution Volume (mL)

3-9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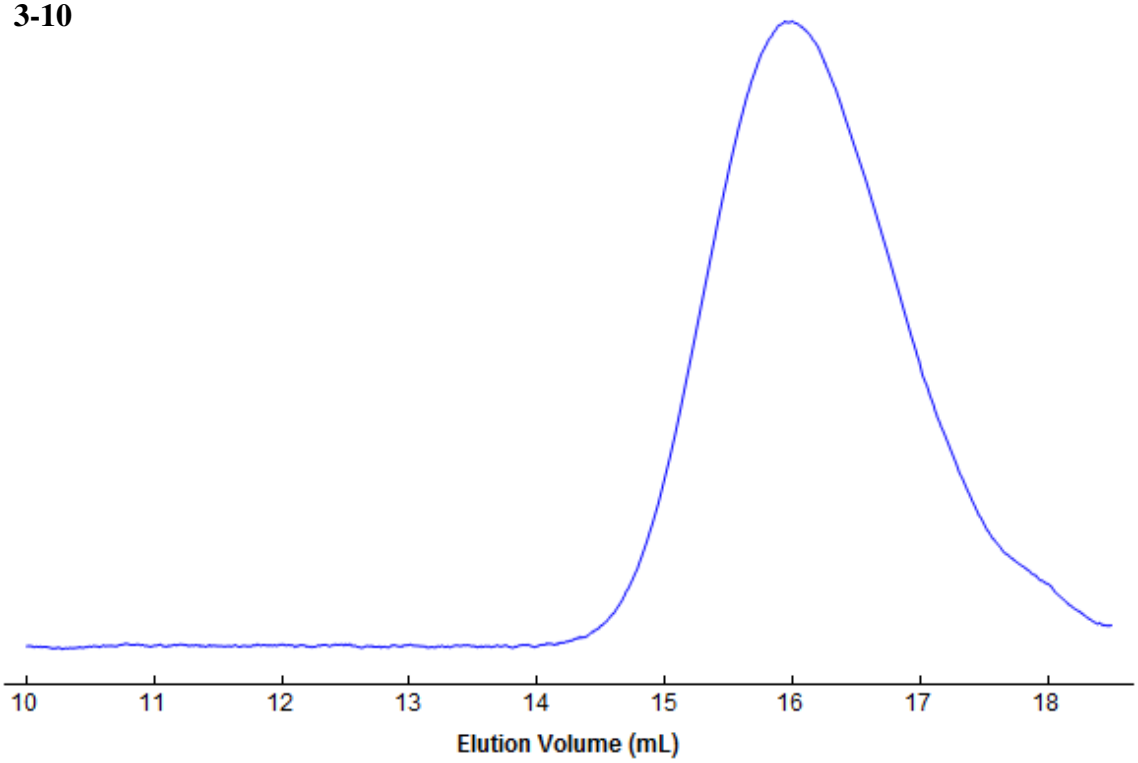
Elution Volume (mL)

3-10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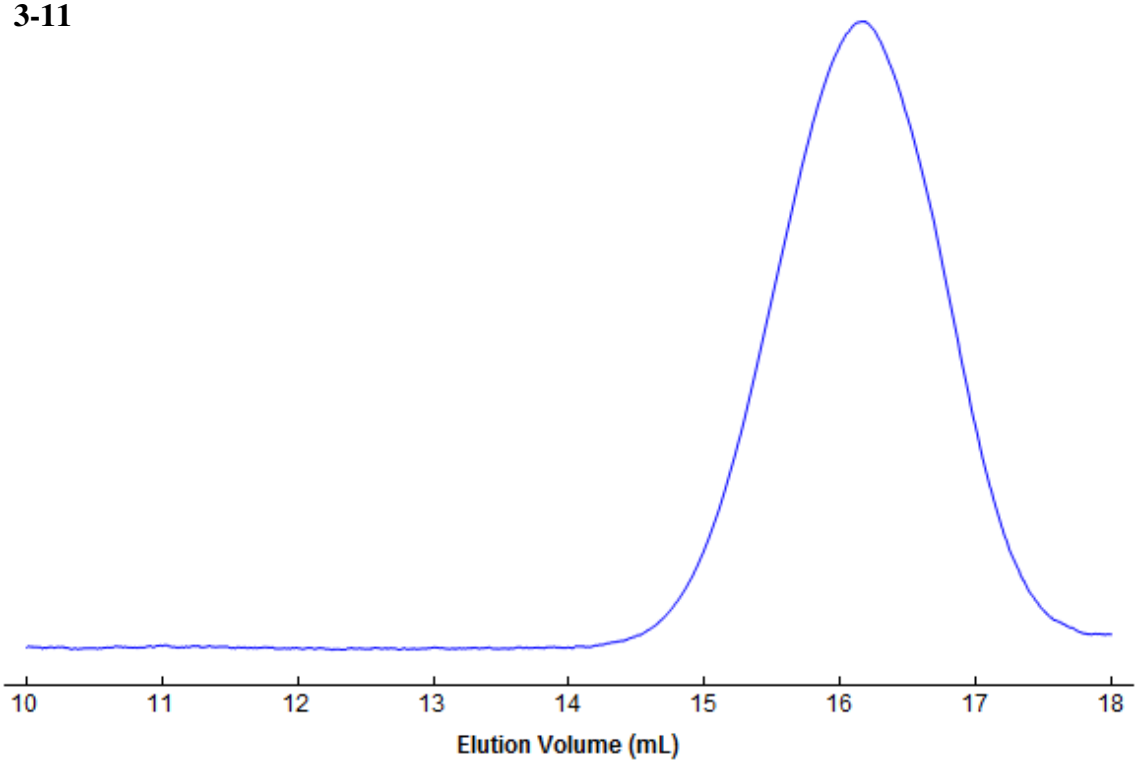
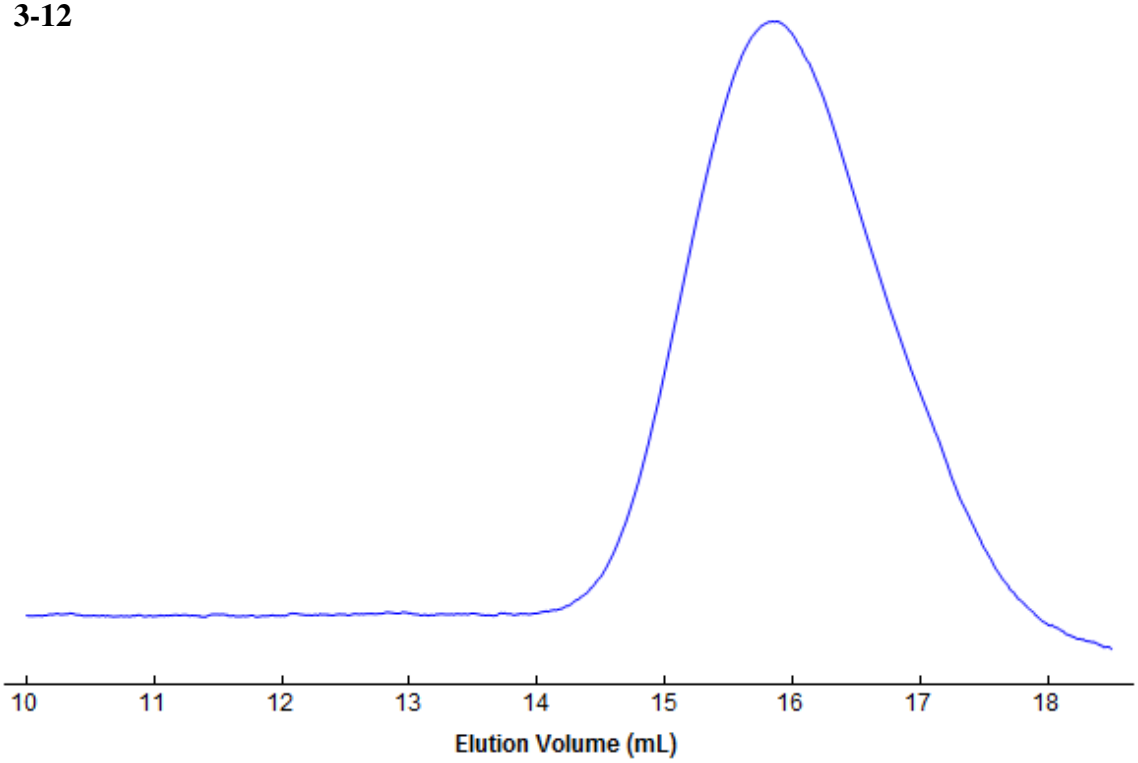
Elution Volume (mL)

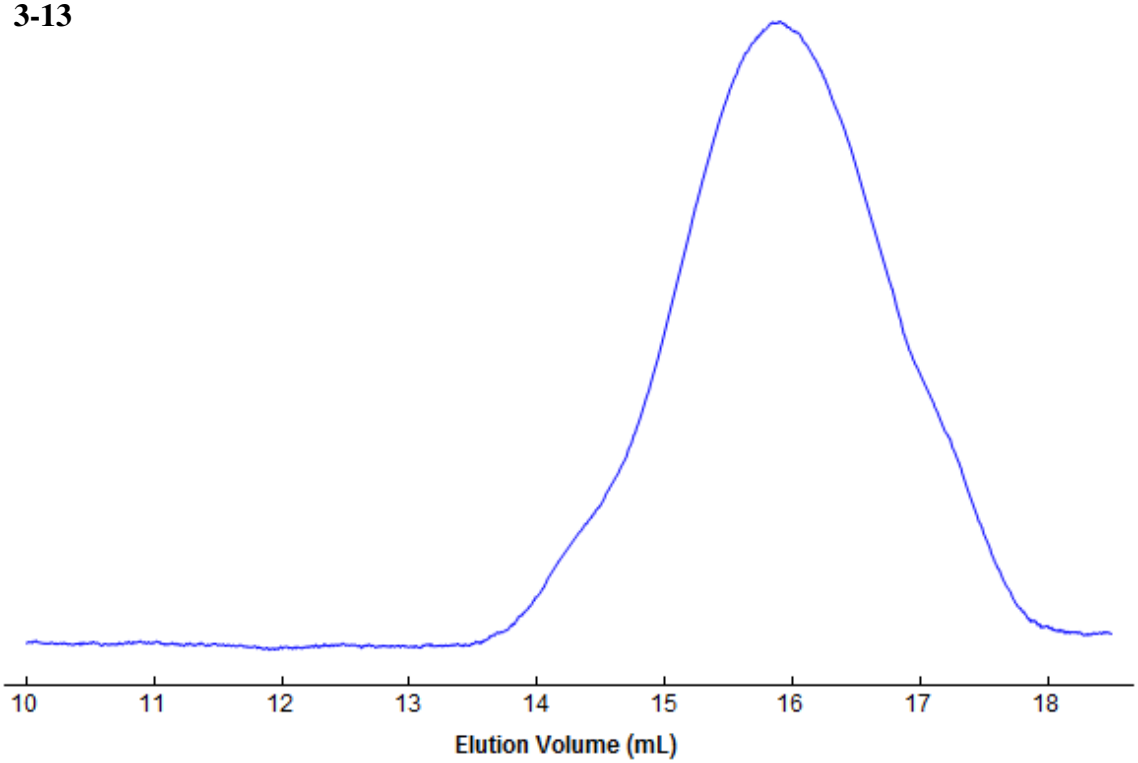
3-11


10
11
12
13
14
15
16
17
18
Elution Volume (mL)

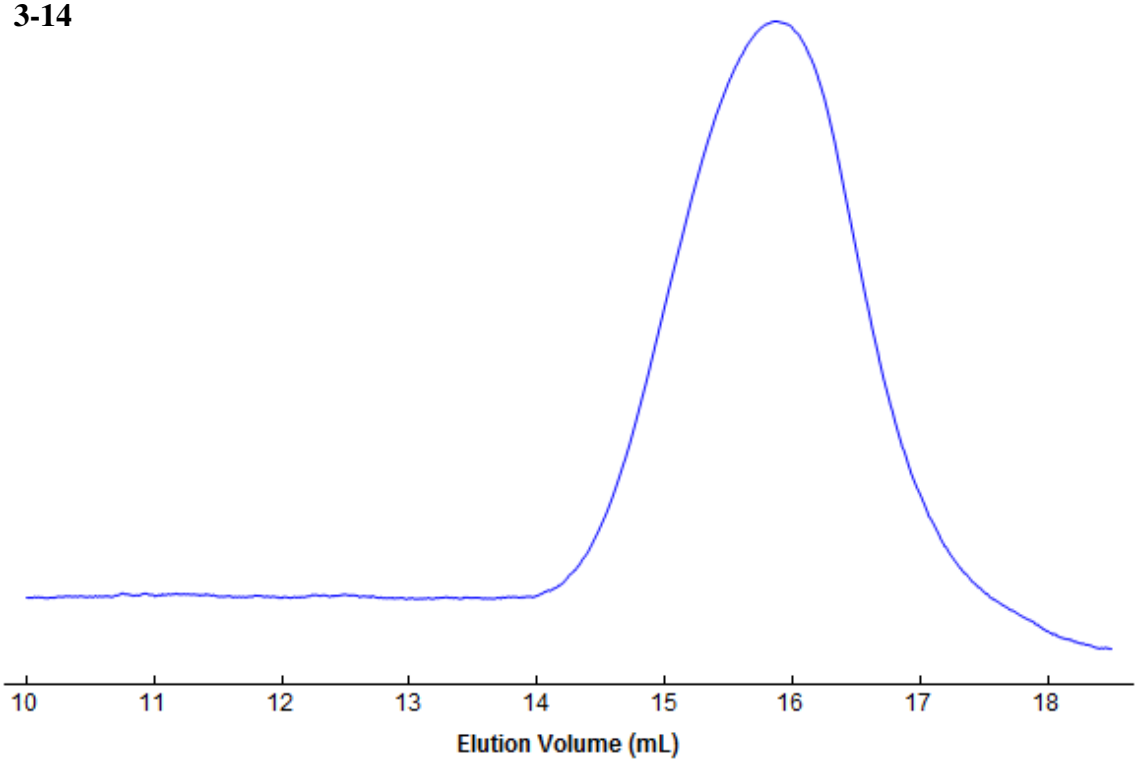
3-12


10
11
12
13
14
15
16
17
18
Elution Volume (mL)

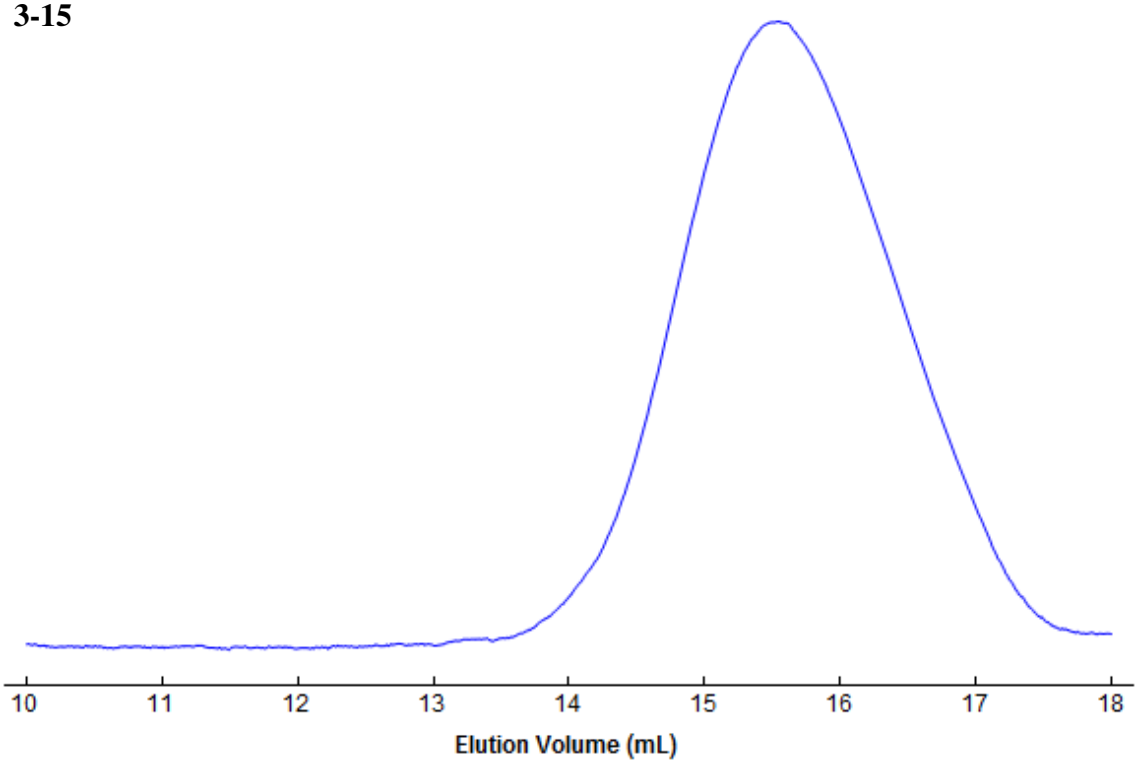
3-13


10
11
12
13
14
15
16
17
18
Elution Volume (mL)

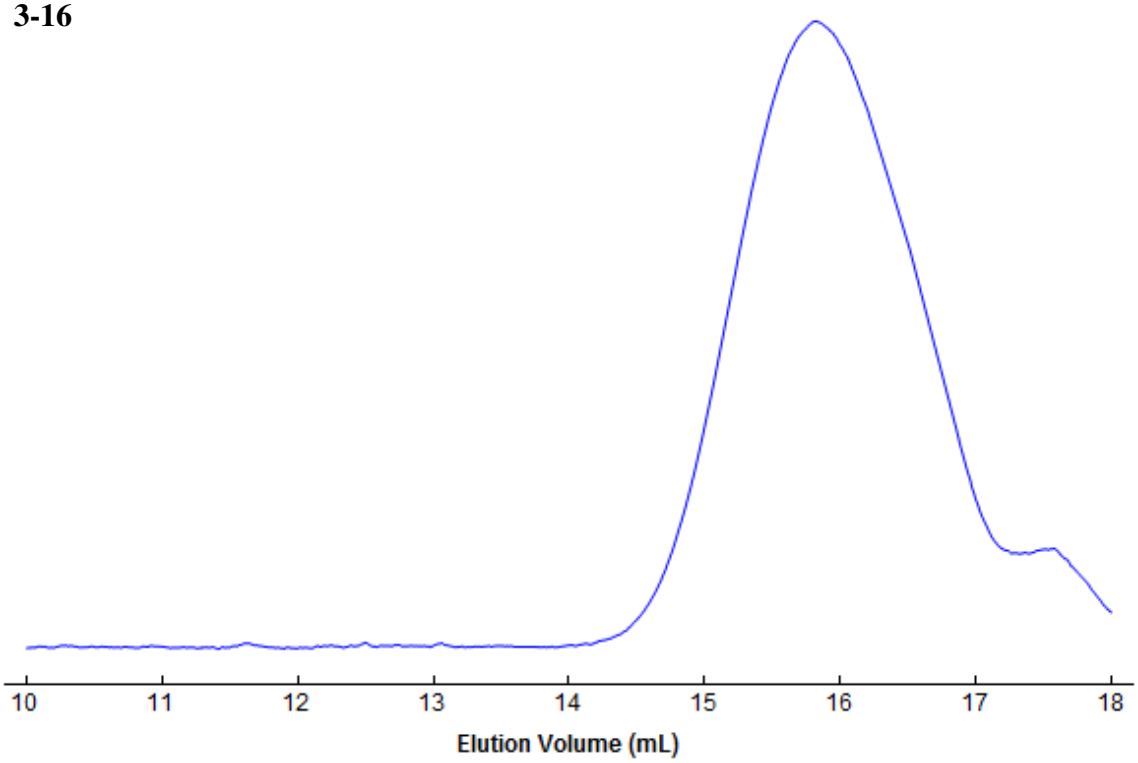
3-14


10
11
12
13
14
15
16
17
18
Elution Volume (mL)

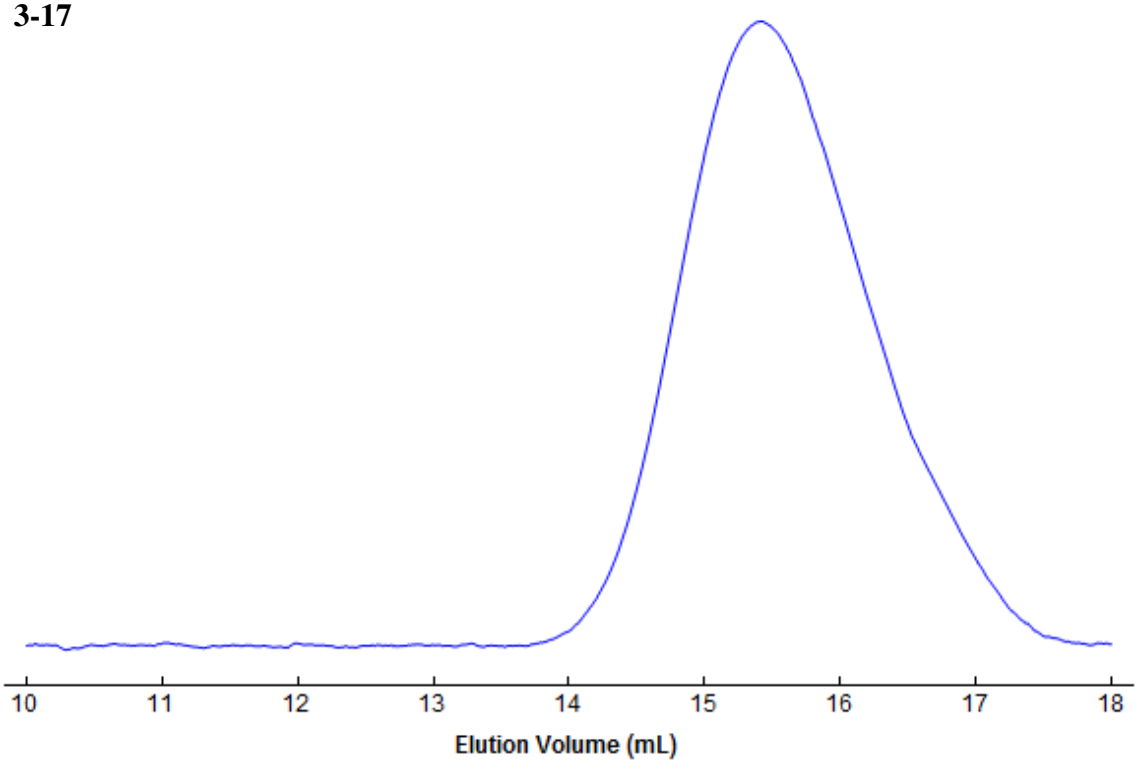
3-15


10
11
12
13
14
15
16
17
18
Elution Volume (mL)

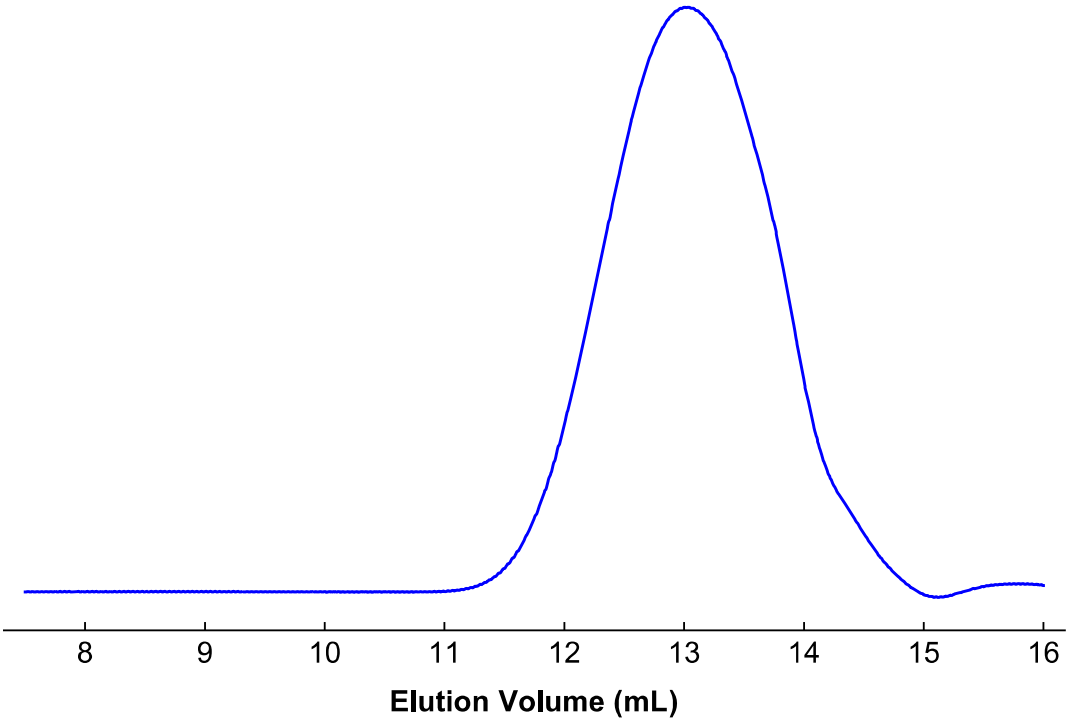
3-16


10
11
12
13
14
15
16
17
18
Elution Volume (mL)

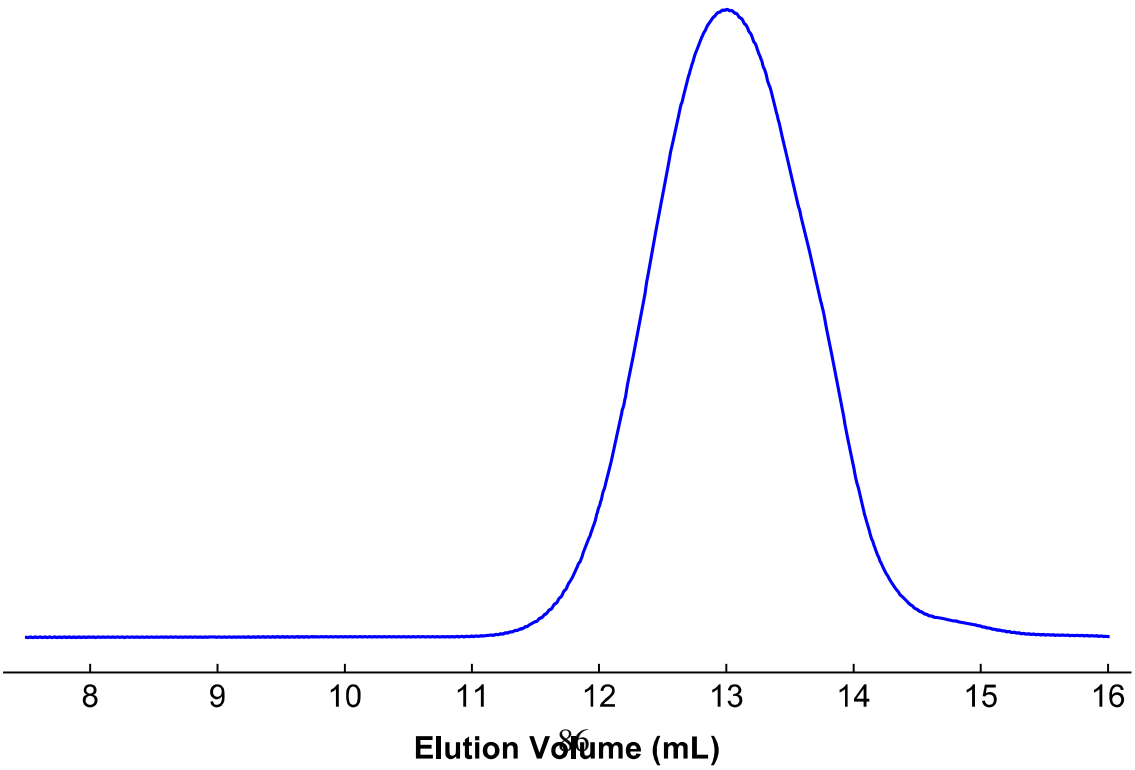
3-17


10
11
12
13
14
15
16
17
18
Elution Volume (mL)

3-18


8
9
10
11
12
13
14
15
16
Elution Volume (mL)

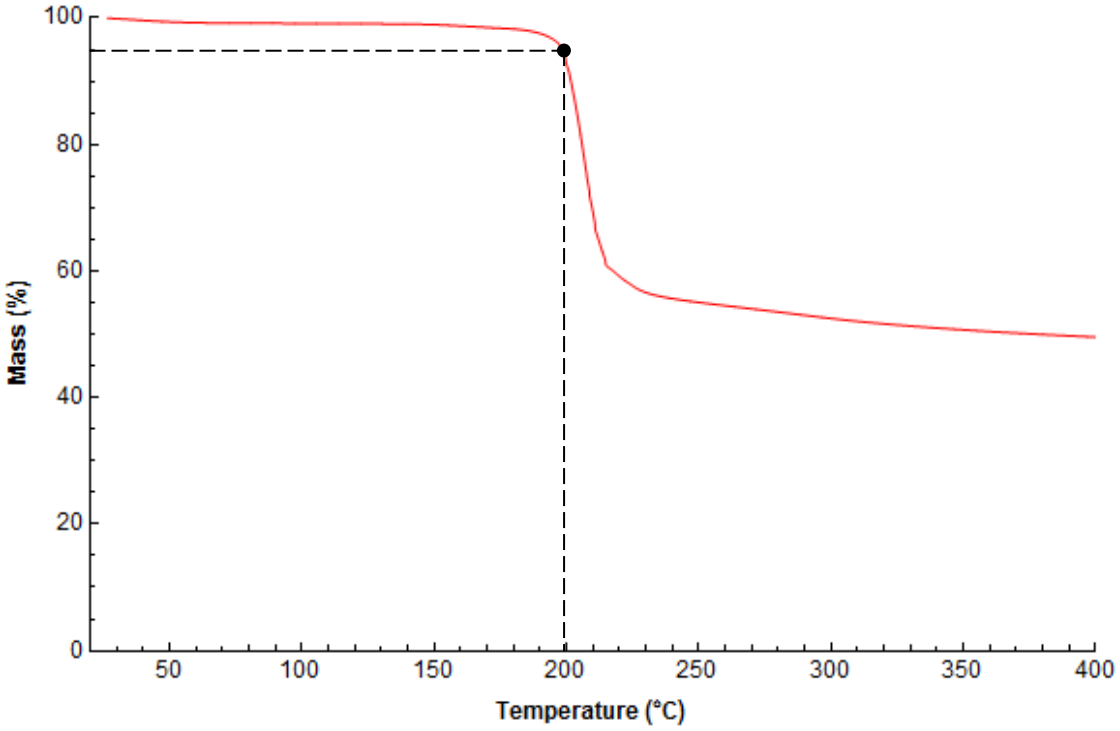
3-19


8
9
10
11
12
13
14
15
16
Elution Volume (mL)

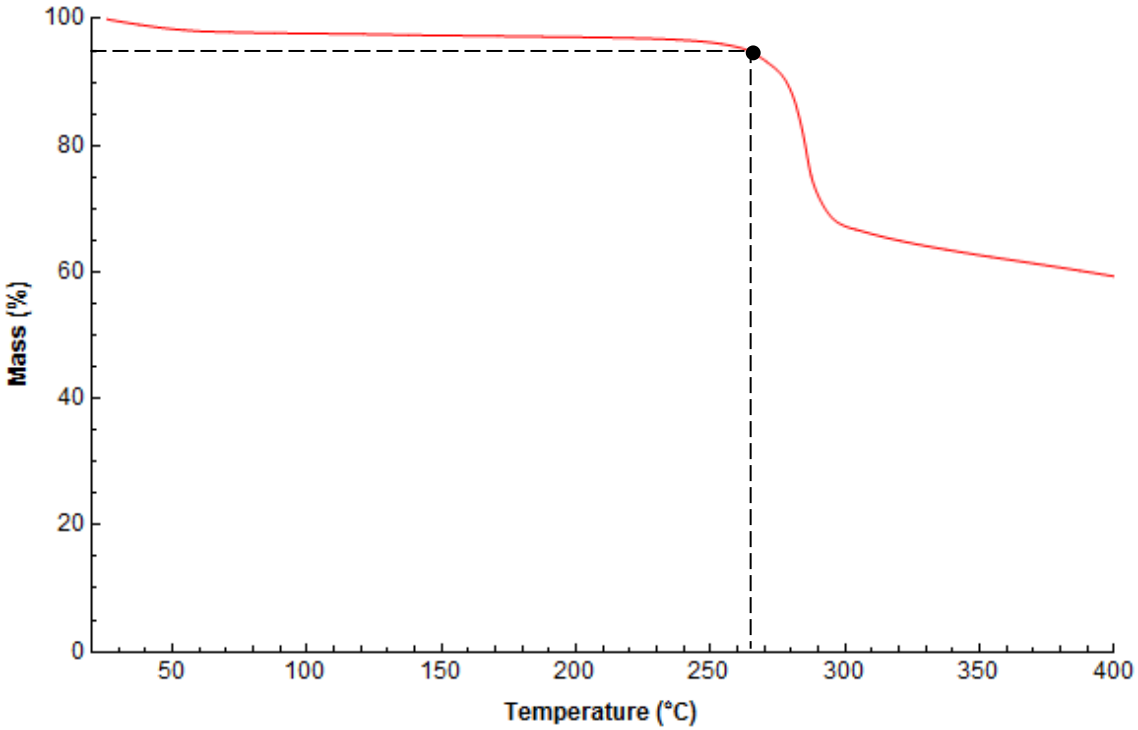
3.4.5 TGA Plots of Polysulfamides

(For all polymers, T_d was determined by finding the point where percent of initial mass reached 95%, rounding to the nearest degree Celsius)

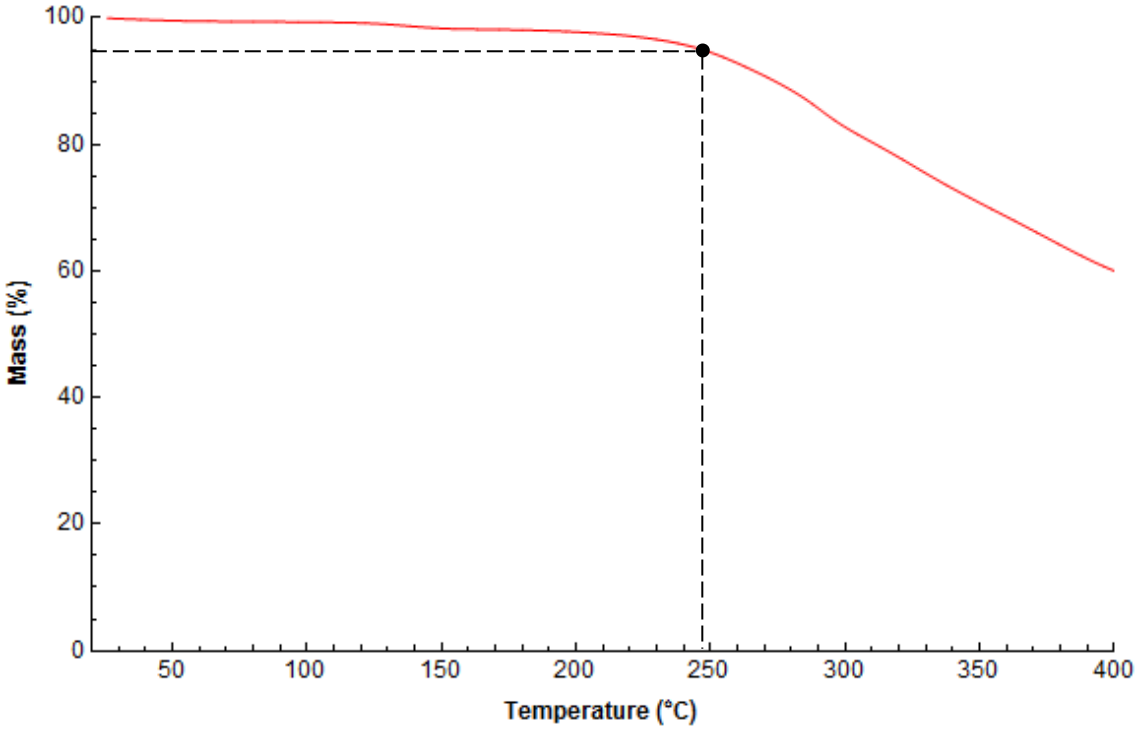
Polymer **3-5**



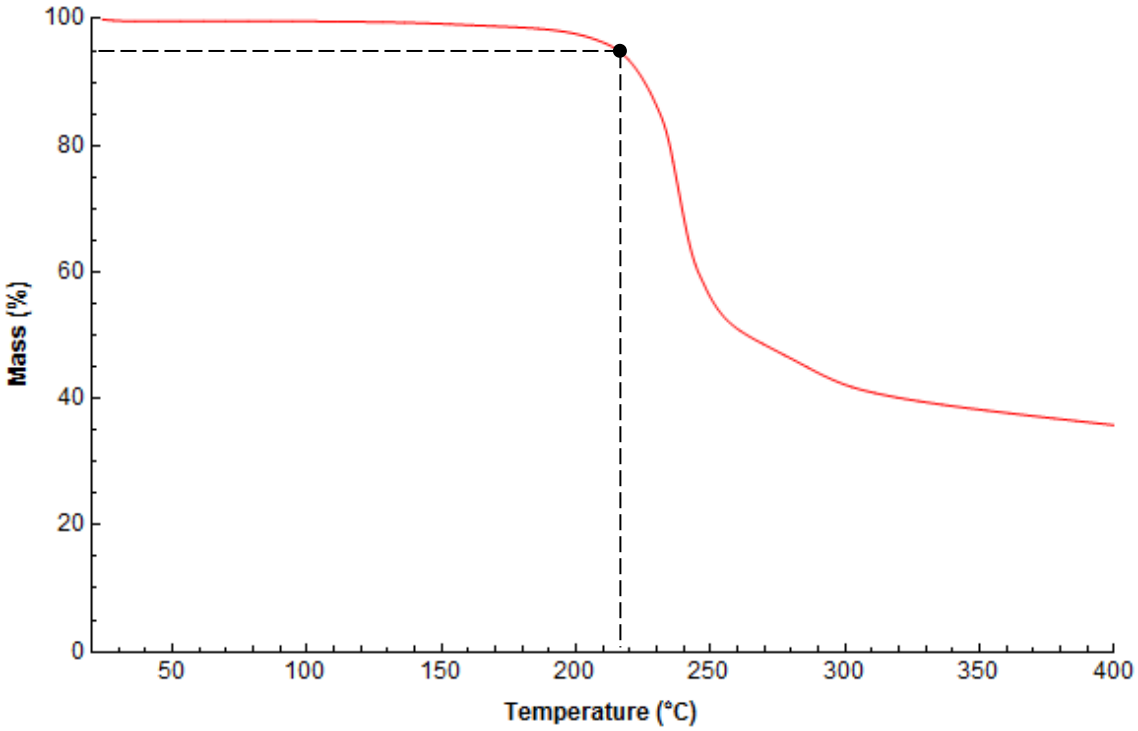
Polymer **3-6**



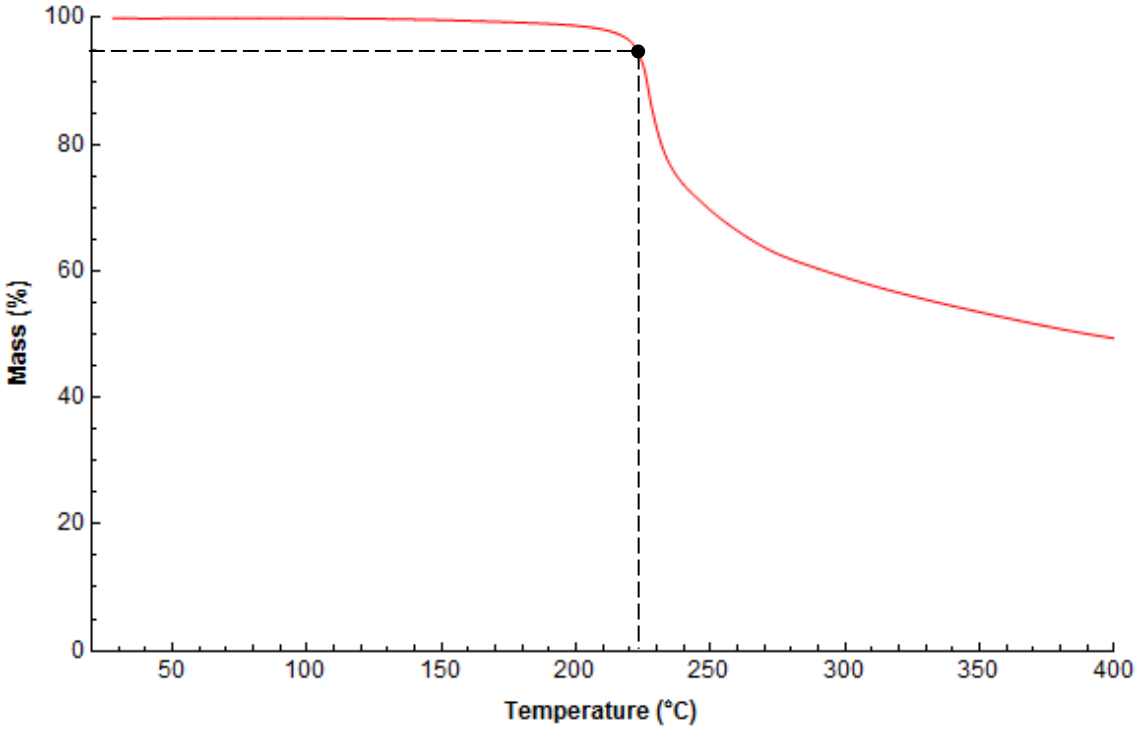
Polymer **3-7**



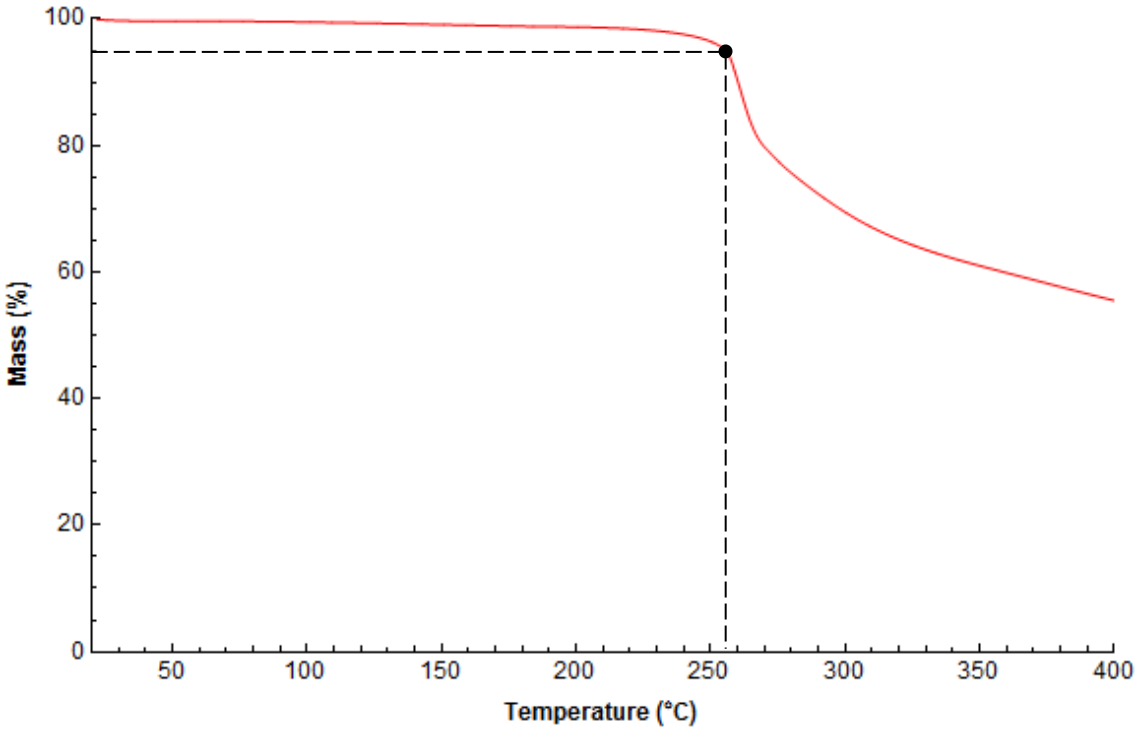
Polymer **3-8**



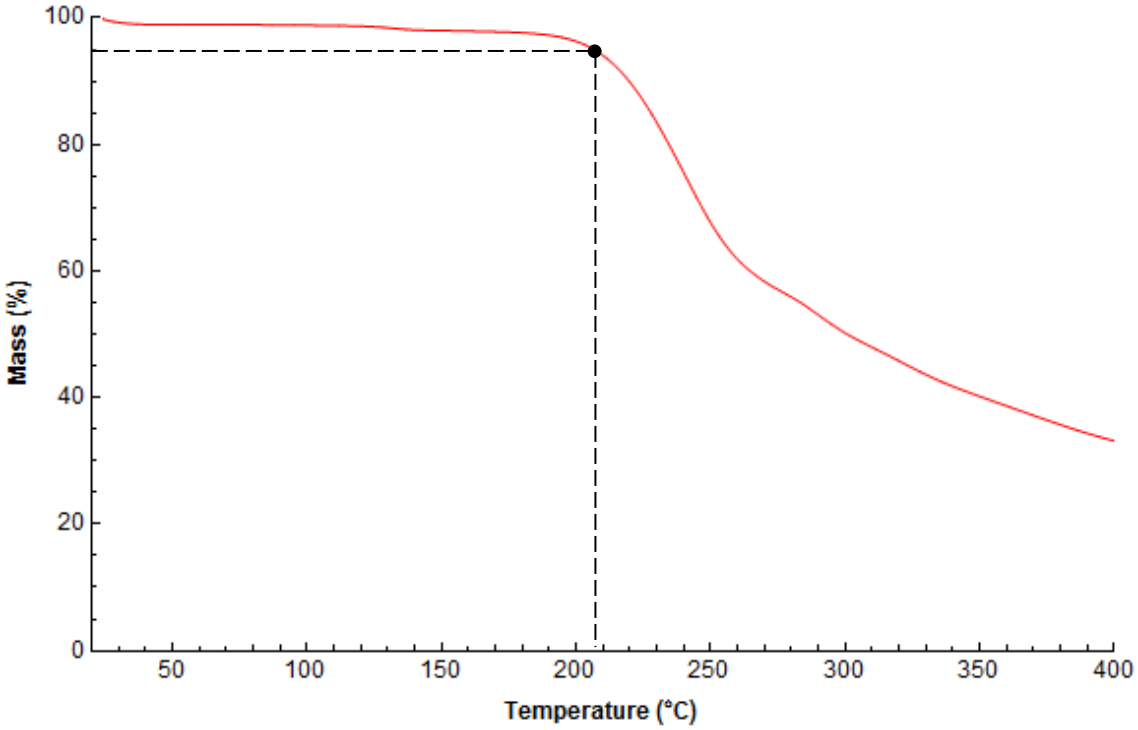
Polymer **3-9**



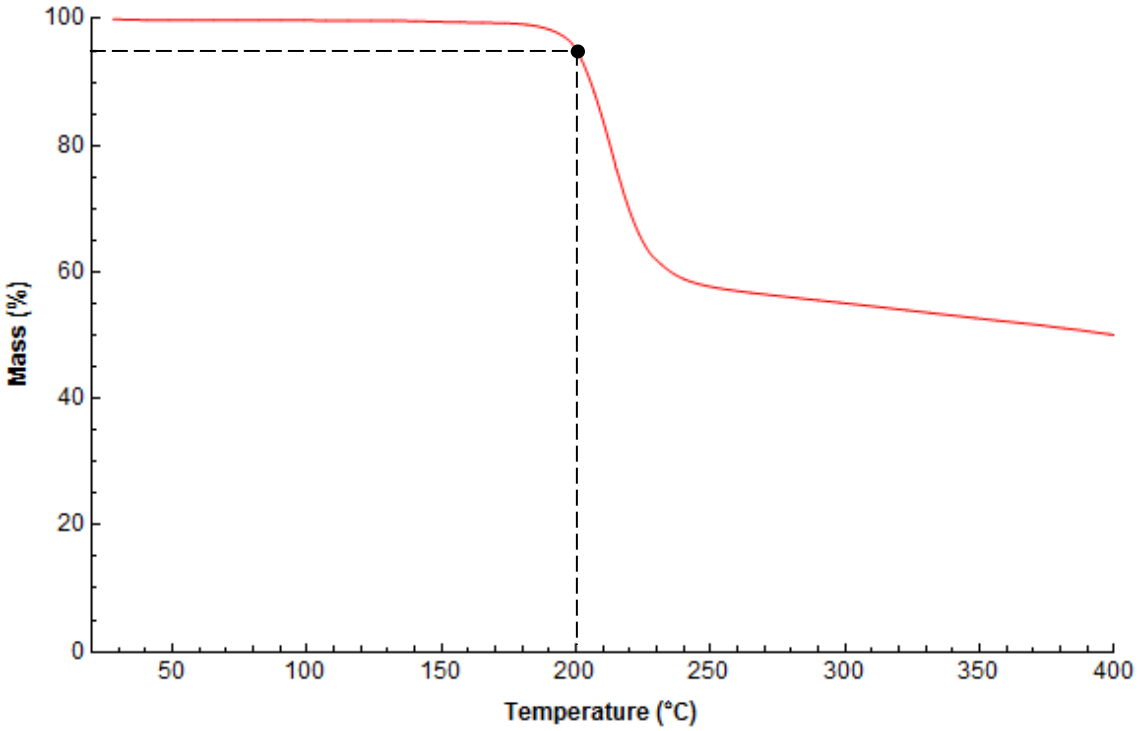
Polymer **3-10**



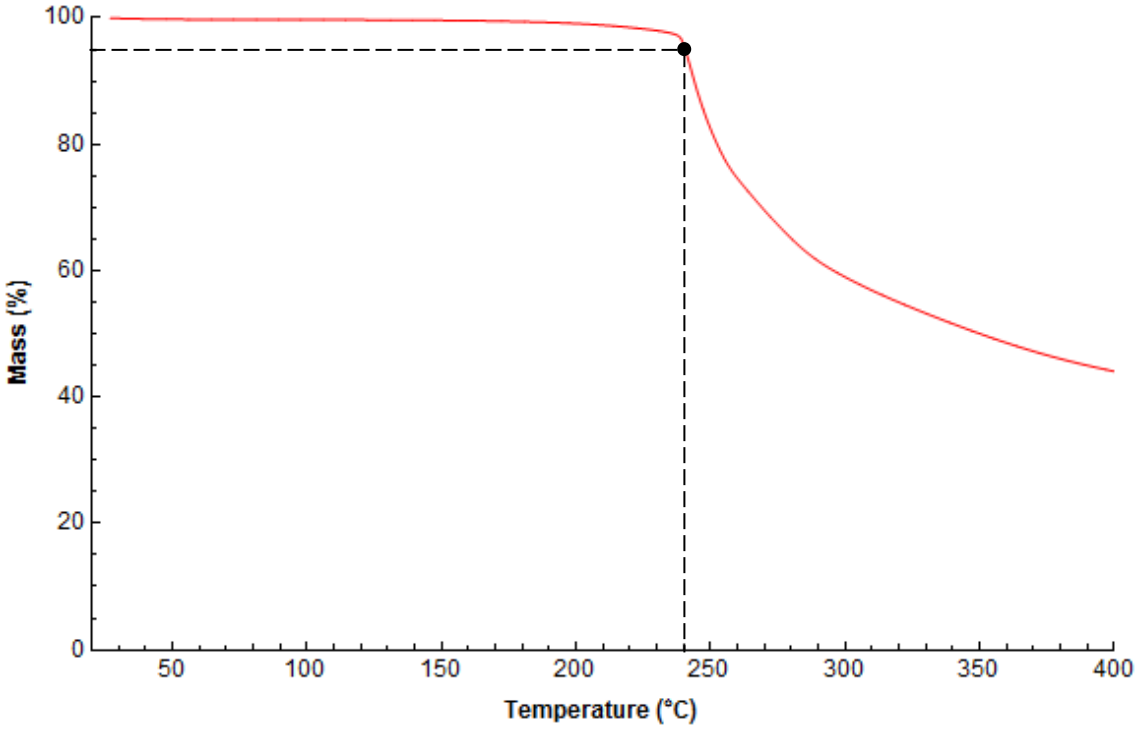
Polymer **3-11**



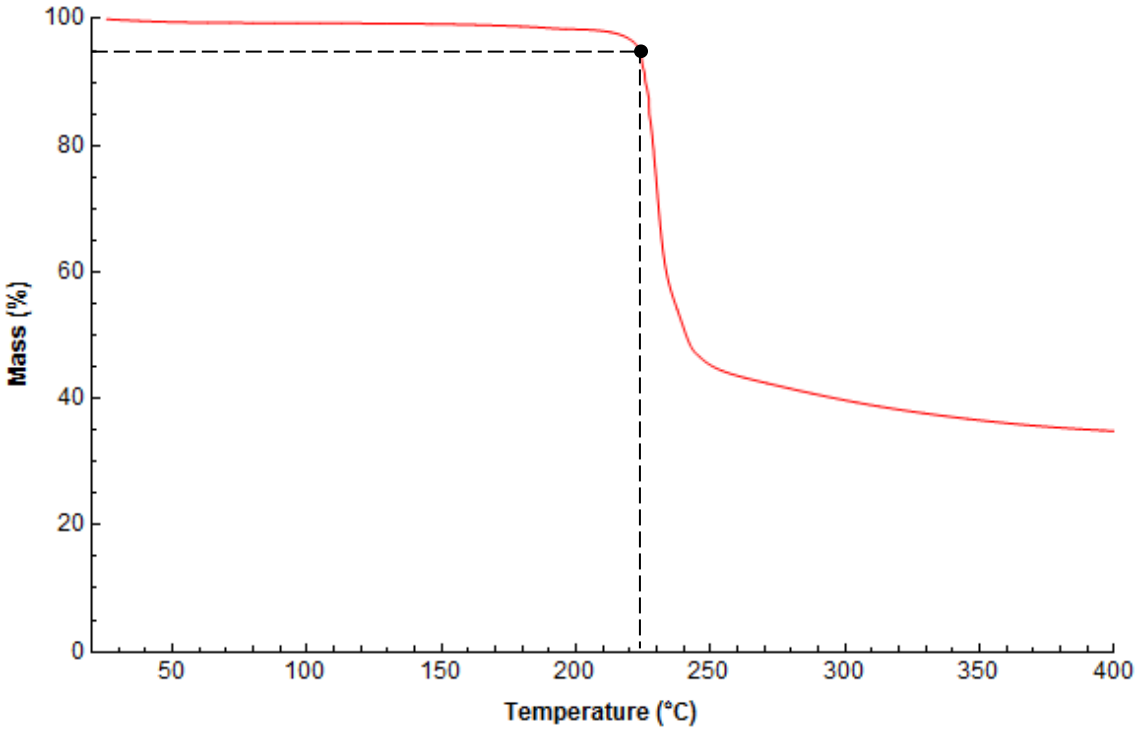
Polymer **3-12**



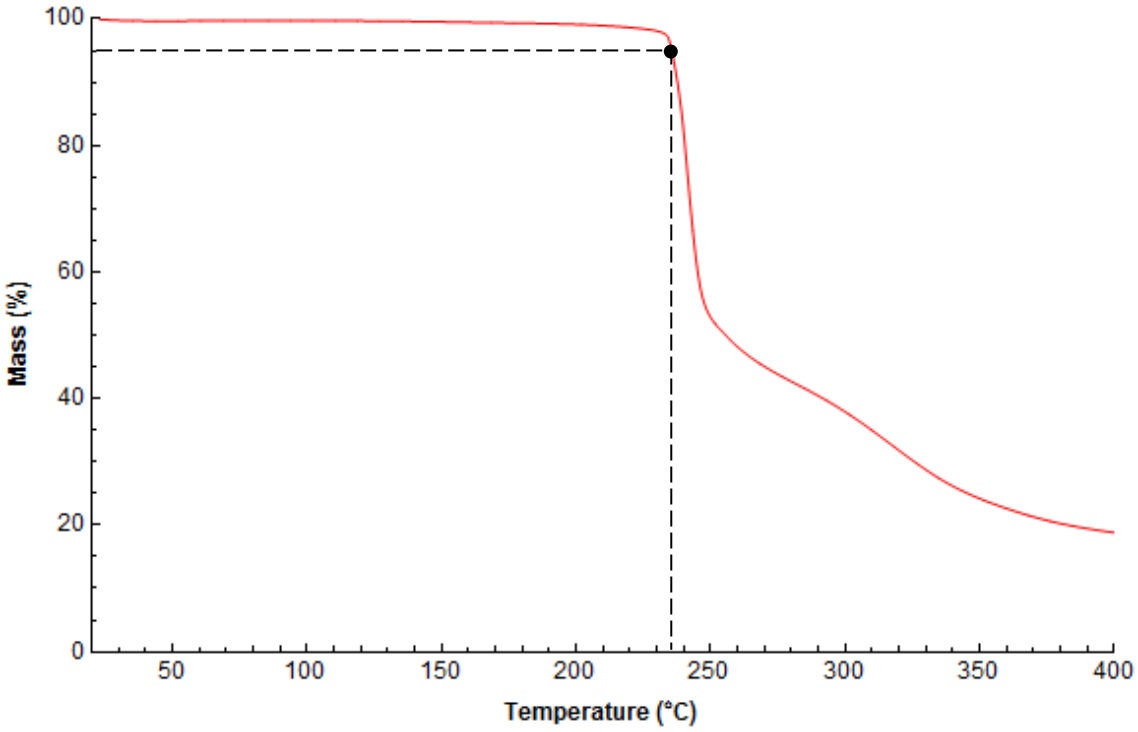
Polymer **3-13**



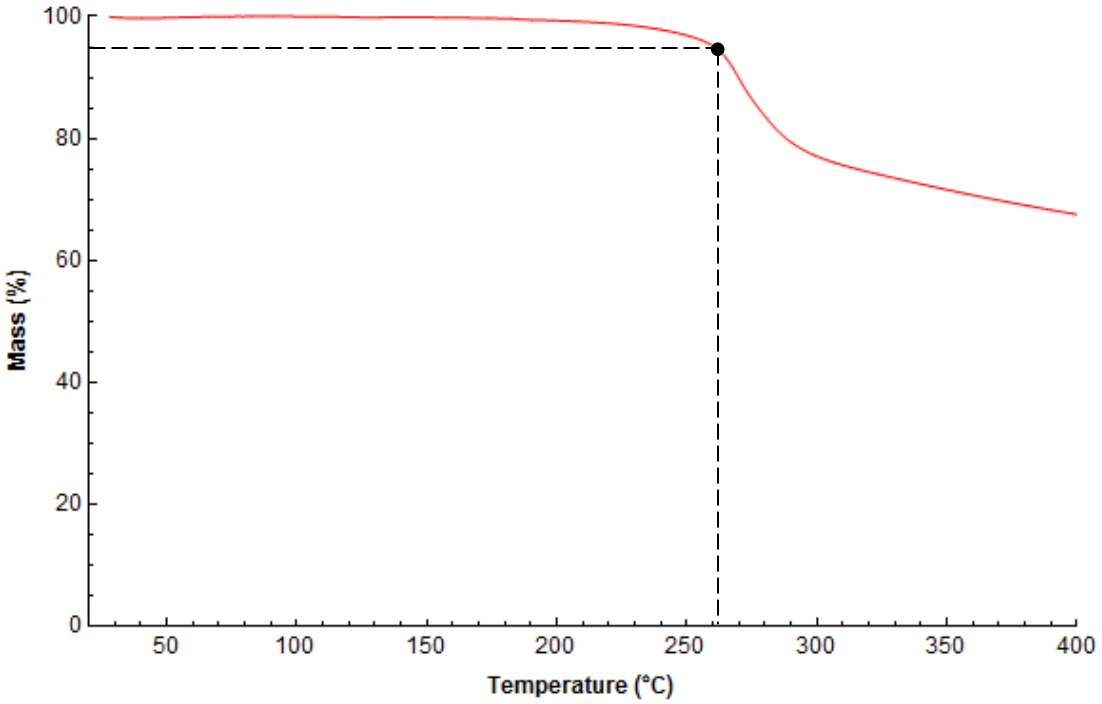
Polymer **3-14**



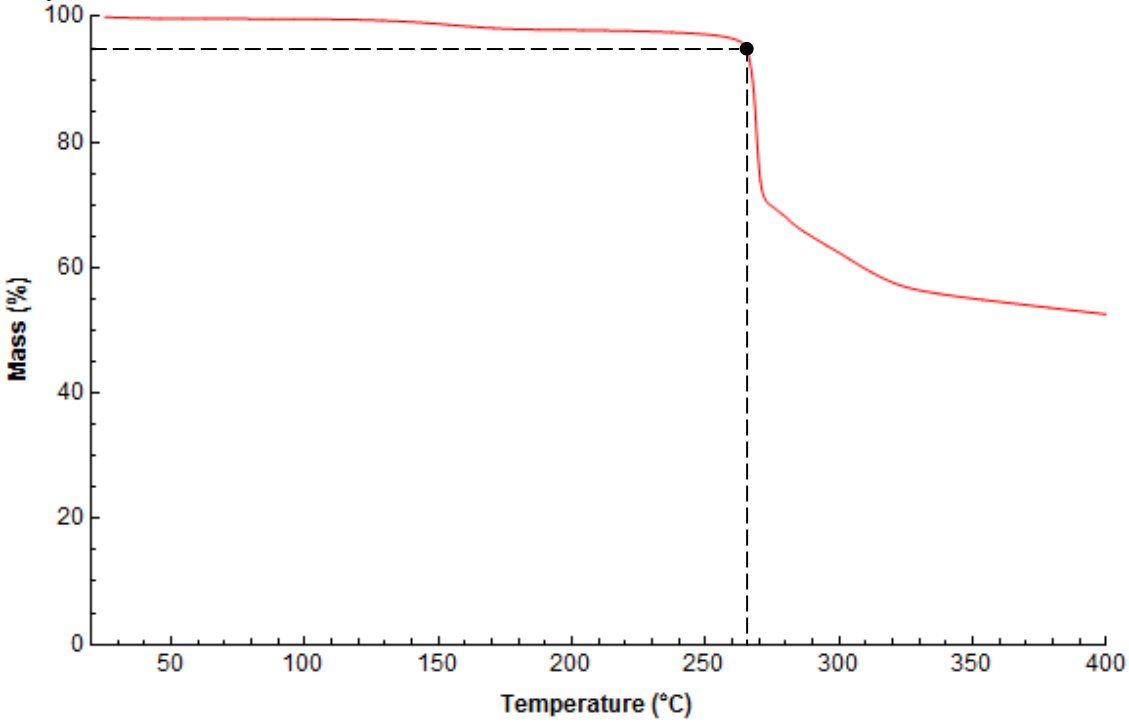
Polymer **3-15**



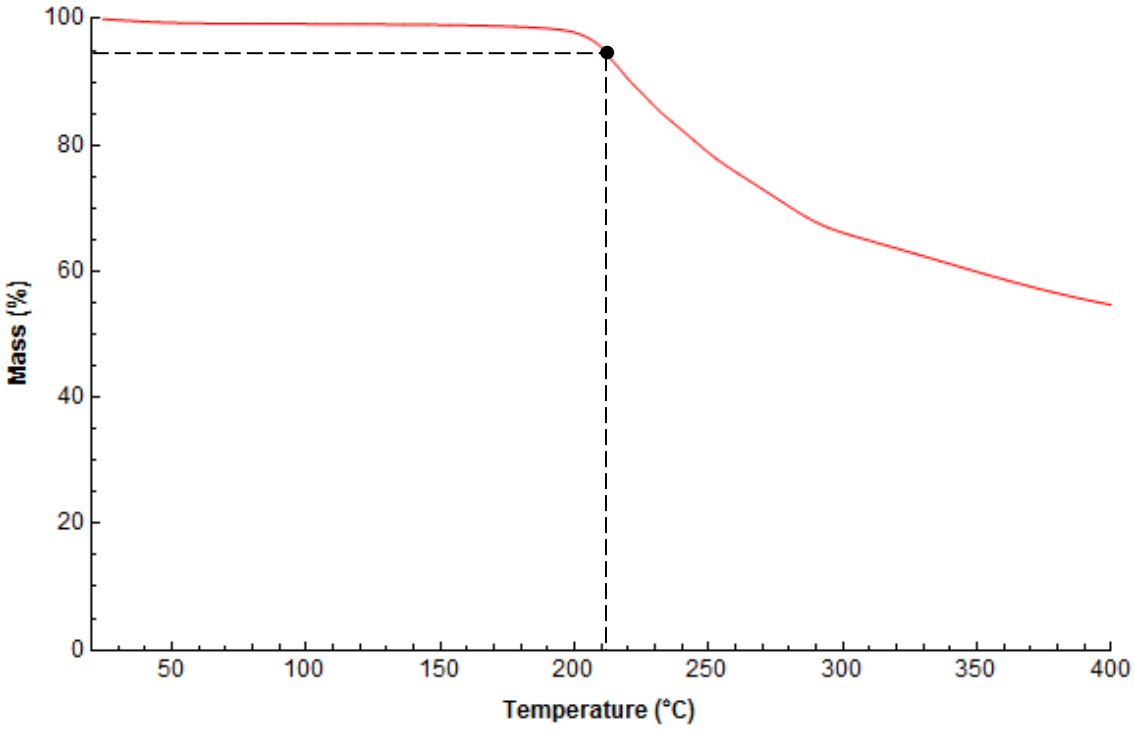
Polymer **3-16**



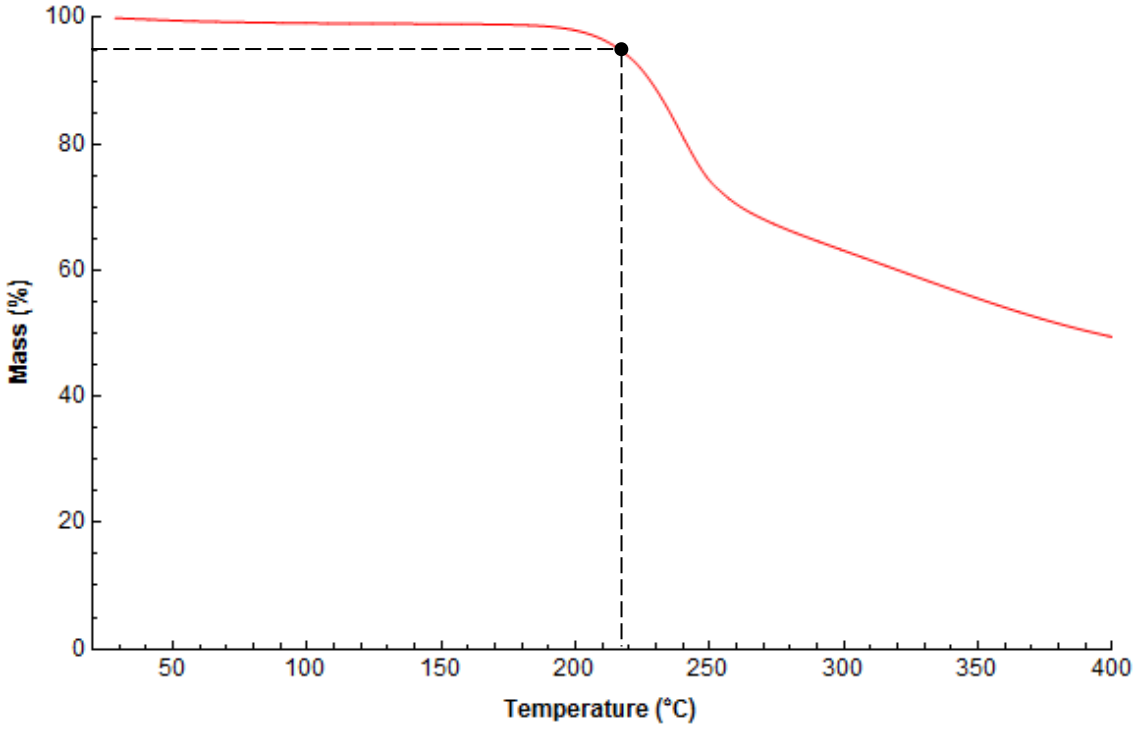
Polymer **3-17**



Polymer **3-18**

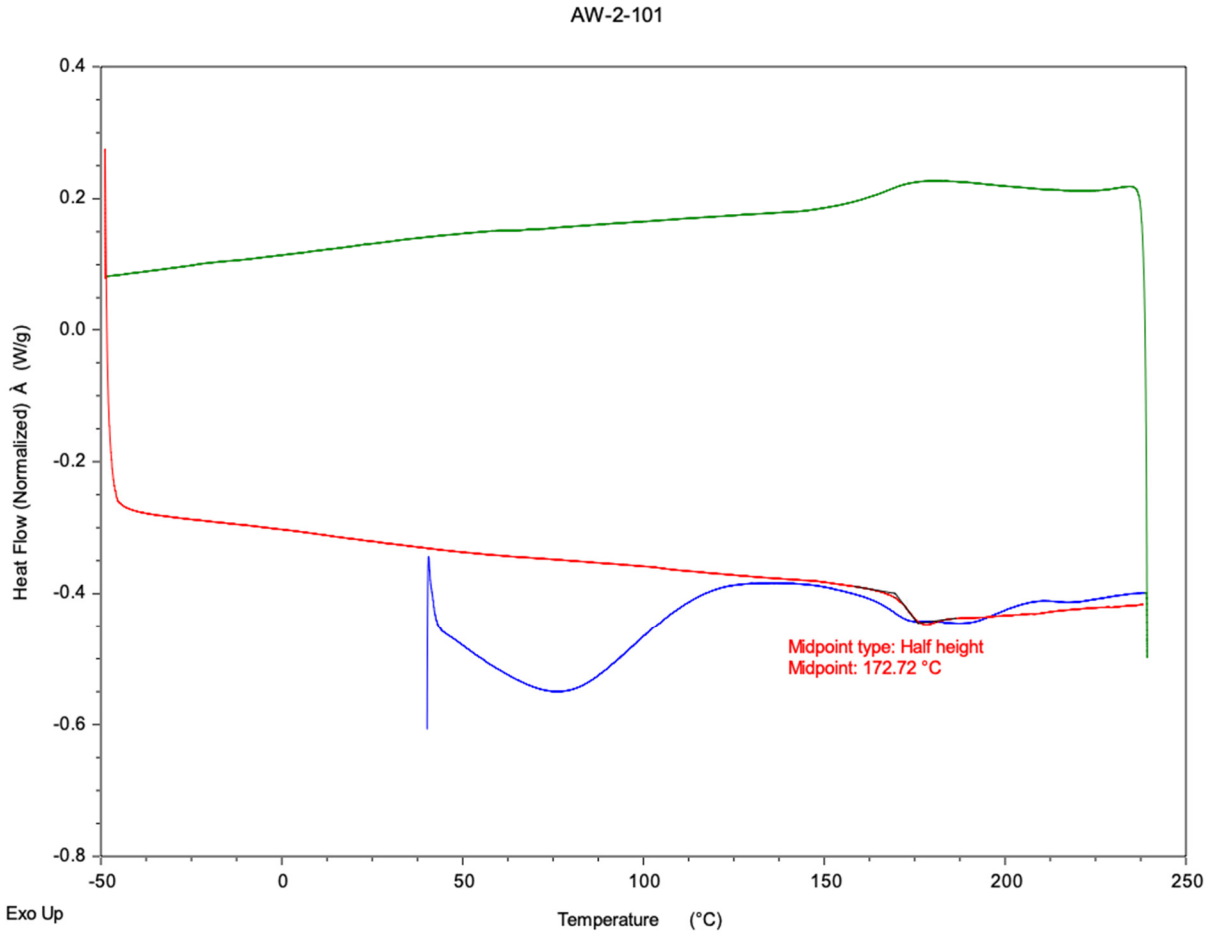


Polymer **3-19**



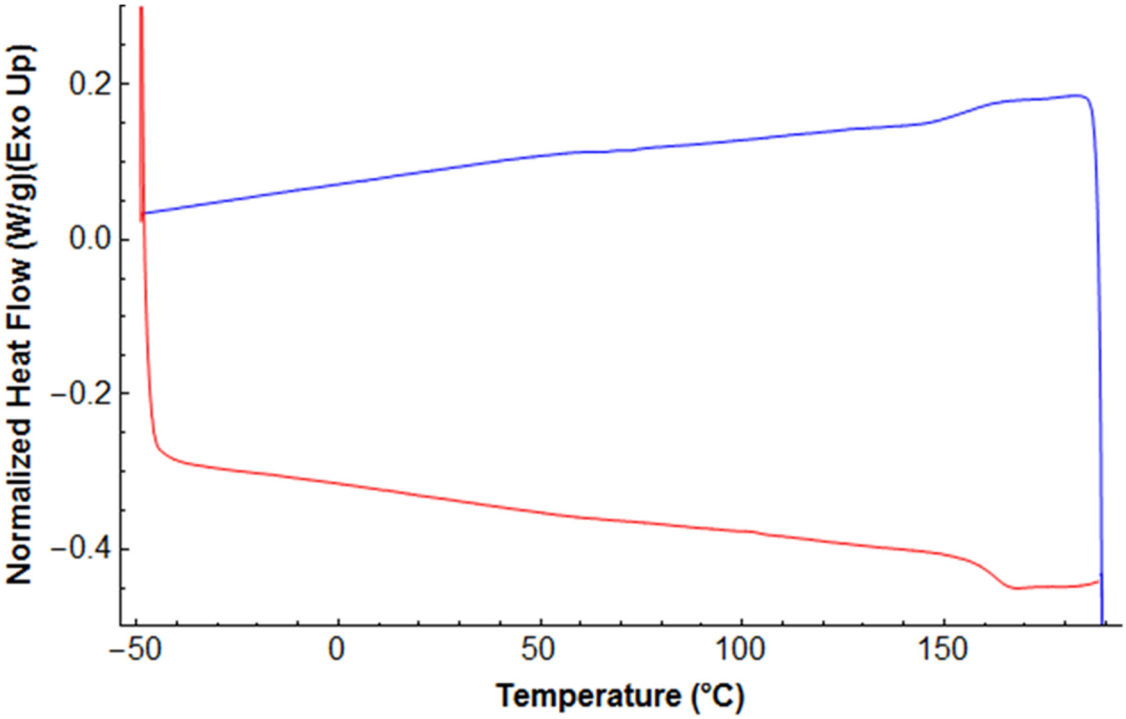
3.4.6 DSC Plots of Polysulfamides

Example of in-software calculation of T_g for polymer **3-17** (Performed using TRIOS Software, Developed by TA Instruments) (Blue: First Heating Cycle, Green: First Cooling Cycle, Red: Second Heating Cycle)

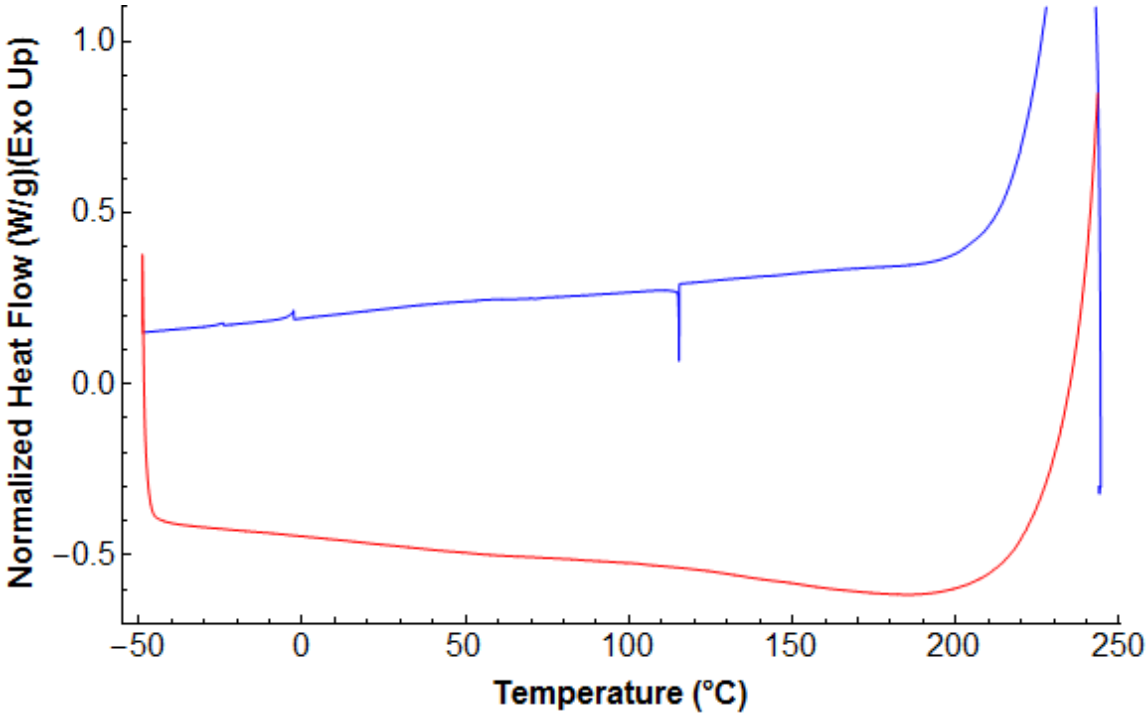


(For all plots shown below, Blue: First Cooling Cycle, Red: Second Heating Cycle)

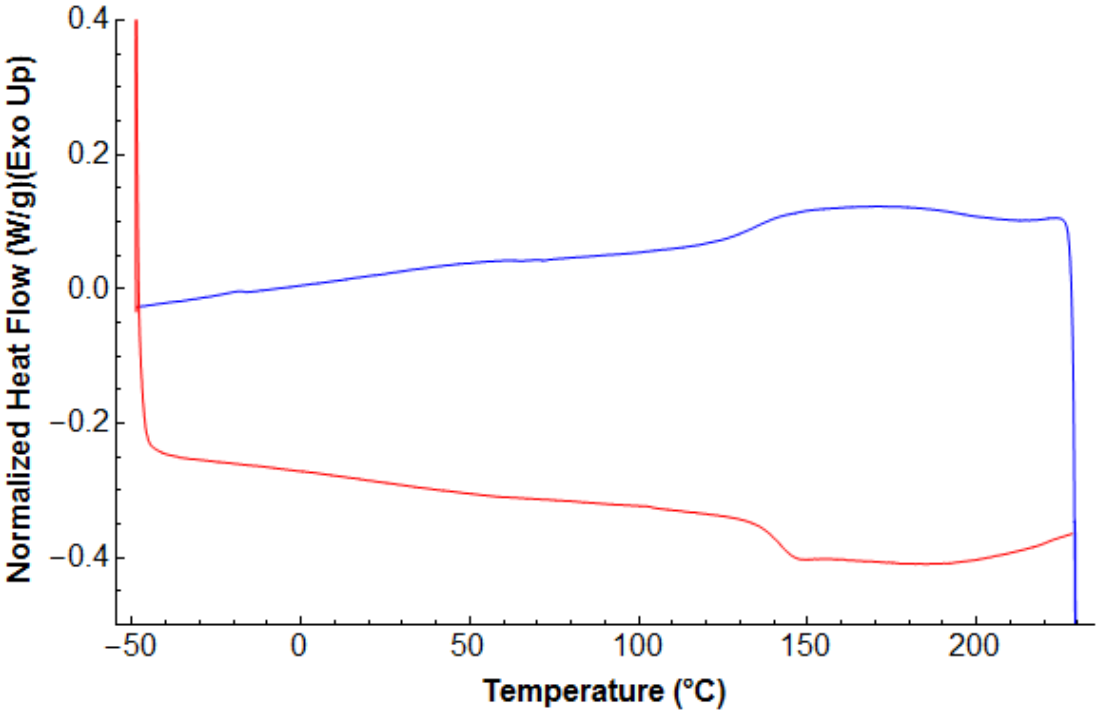
Polymer **3-5**



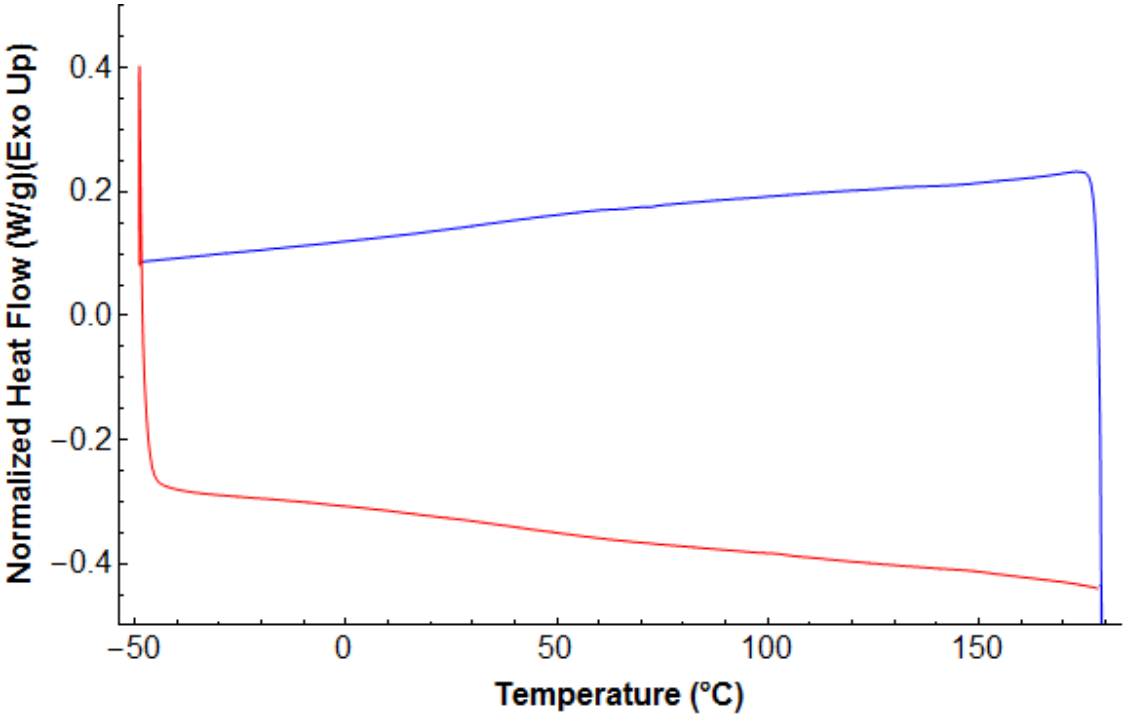
Polymer **3-6**



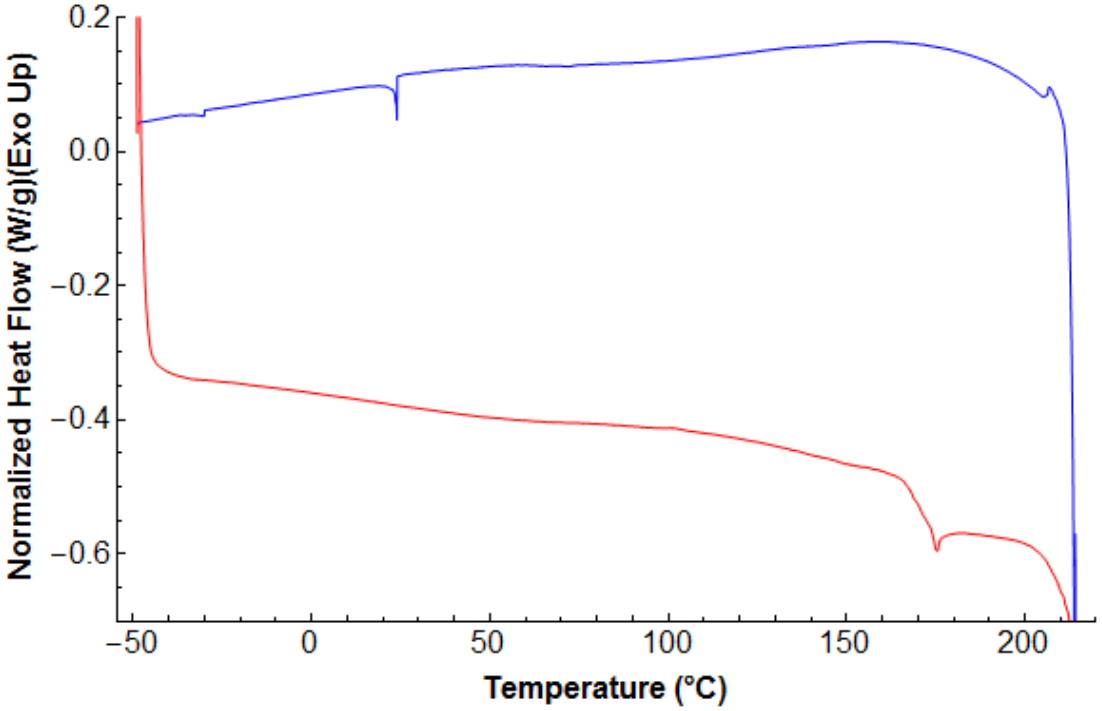
Polymer **3-7**



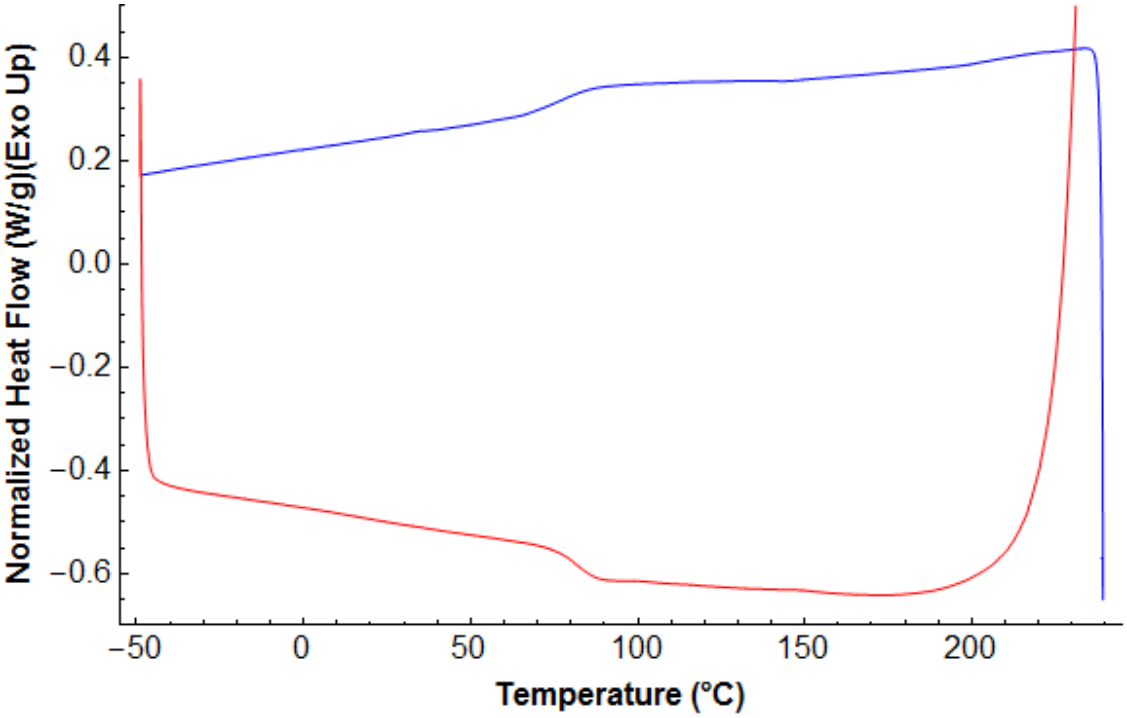
Polymer **3-8**



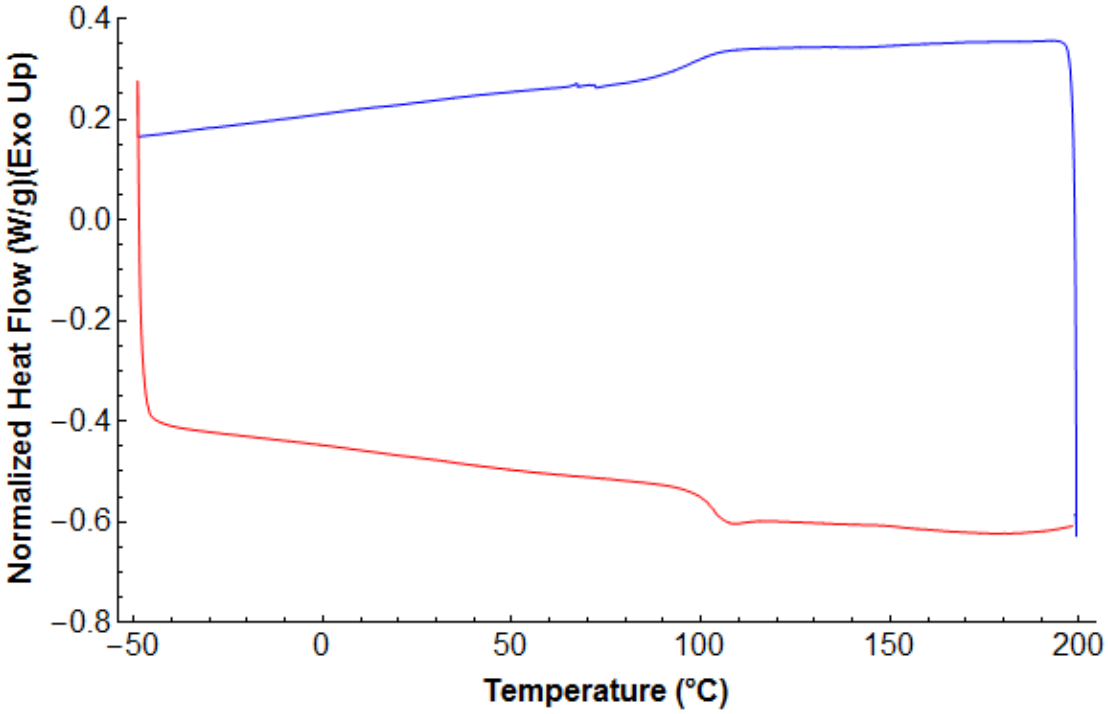
Polymer **3-9**



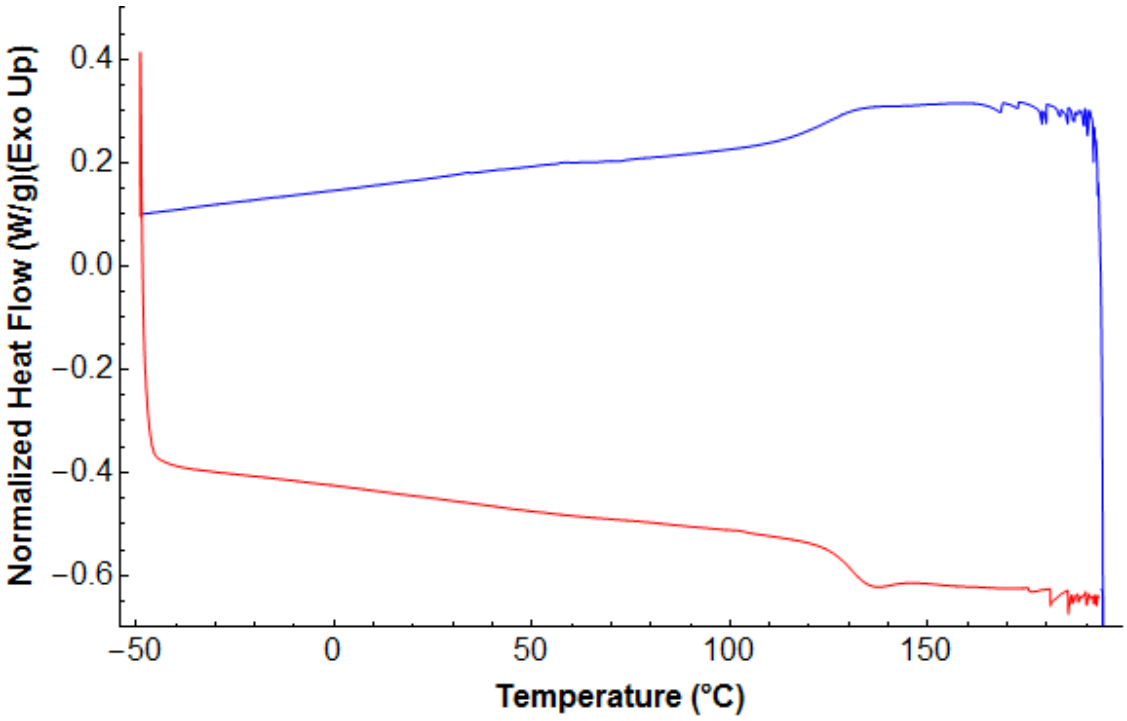
Polymer **3-10**



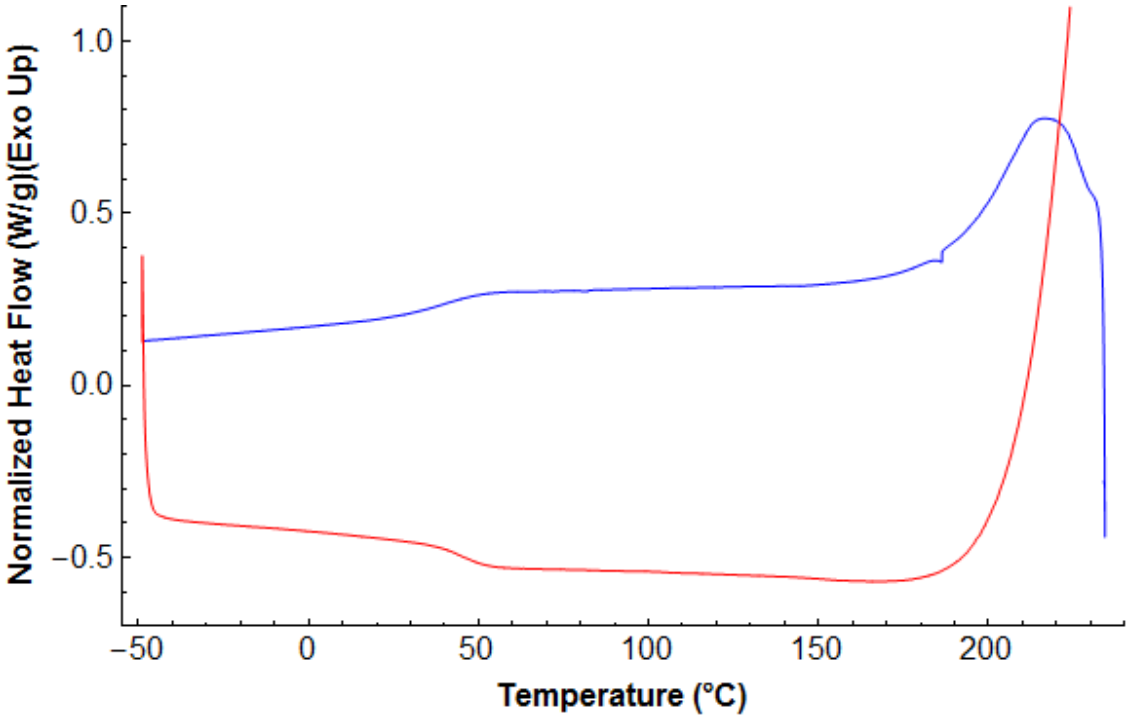
Polymer **3-11**



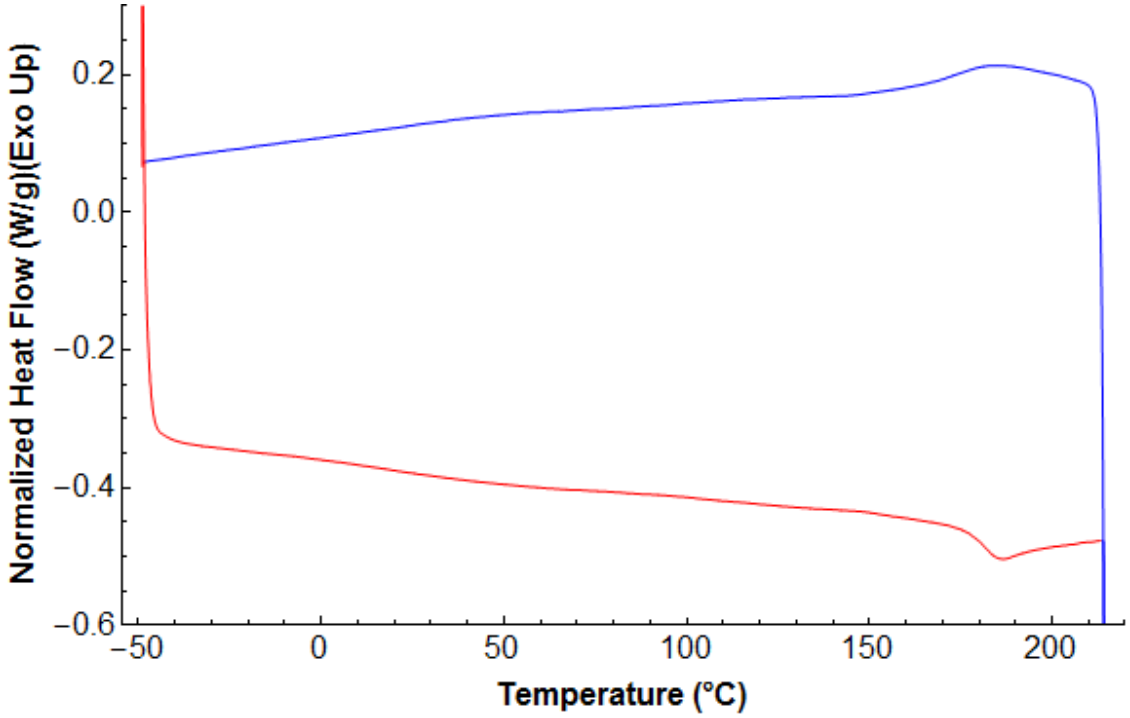
Polymer **3-12**



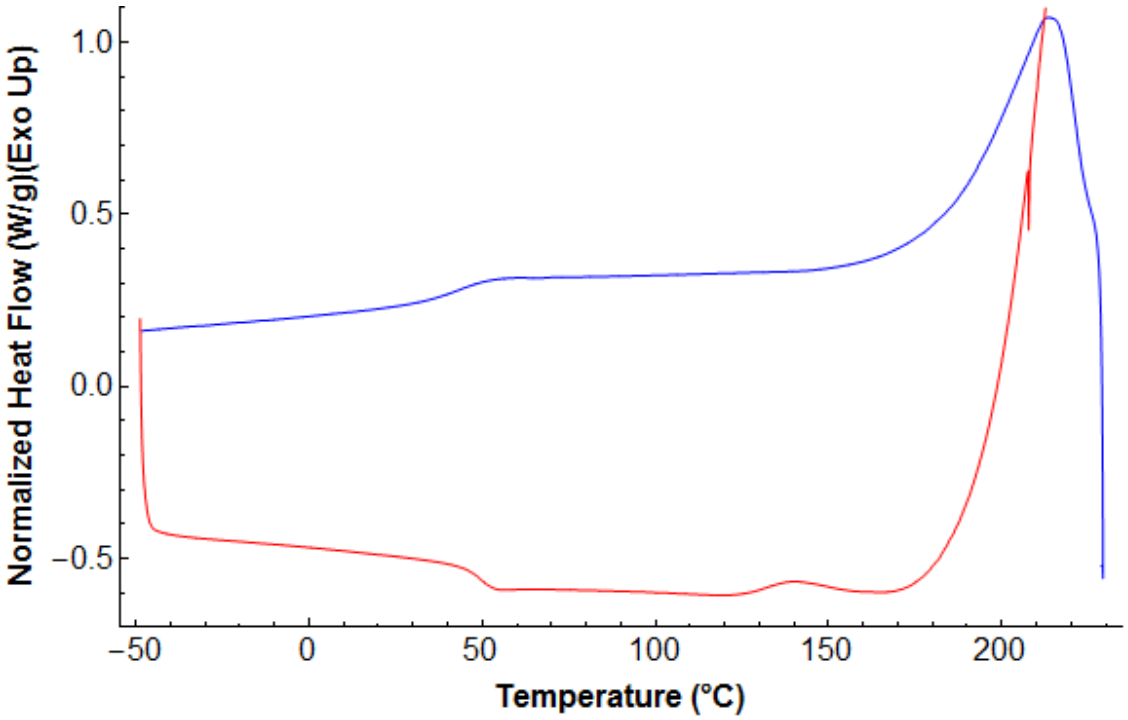
Polymer **3-13**



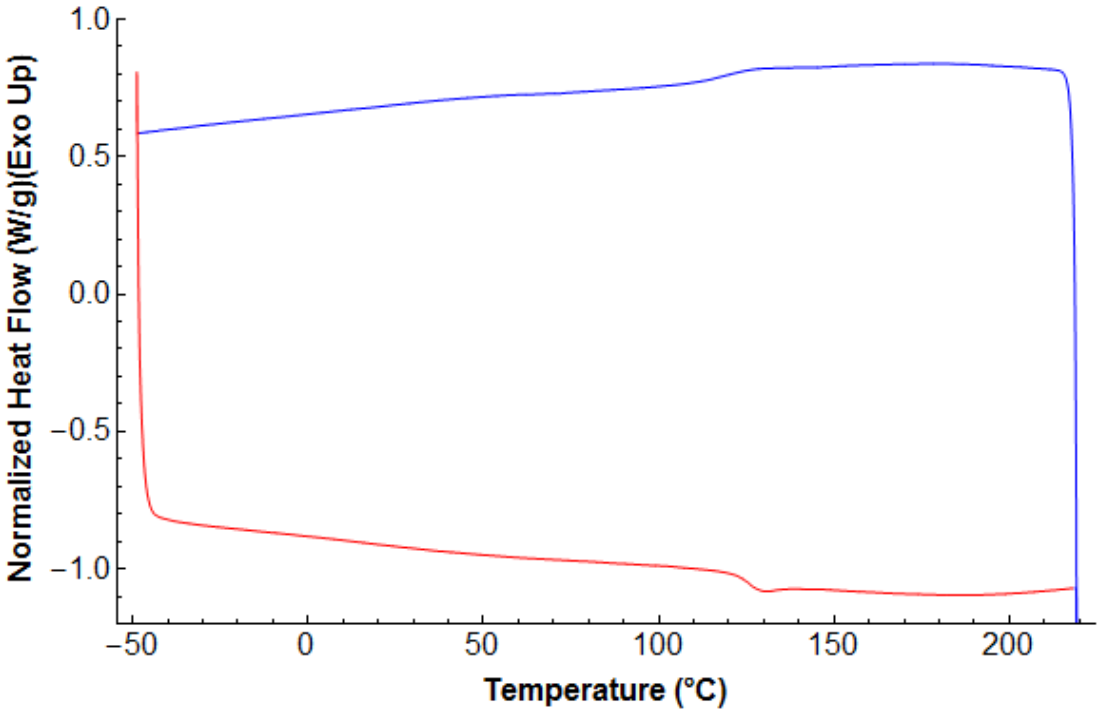
Polymer **3-14**



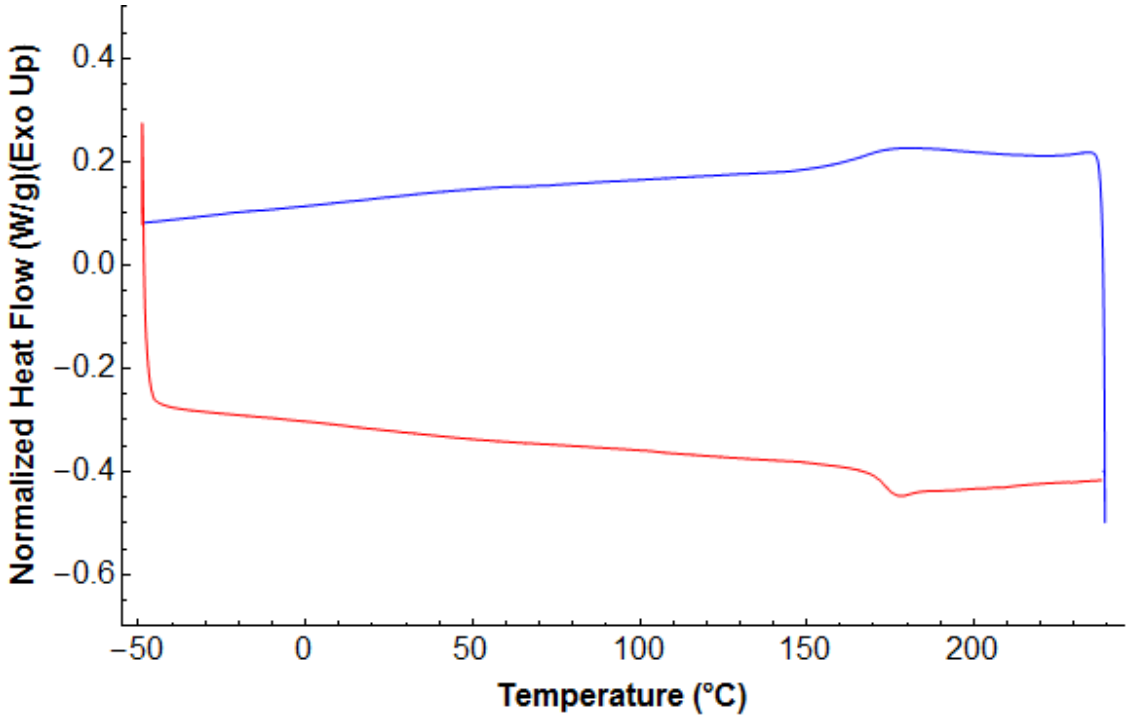
Polymer **3-15**



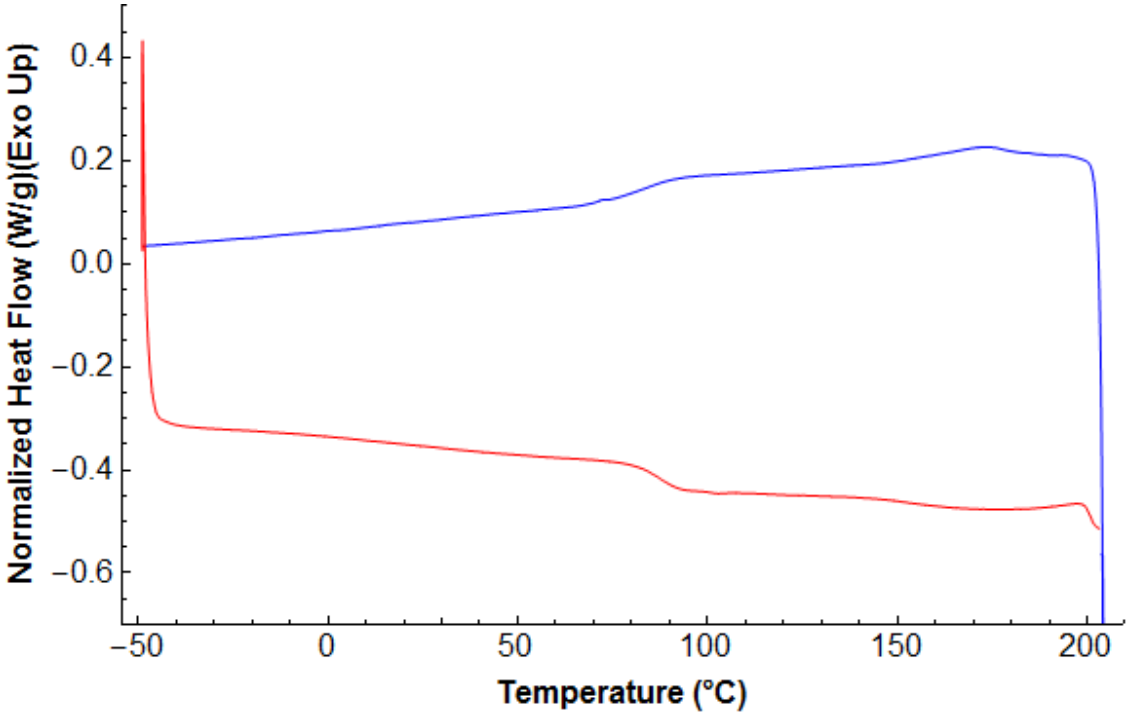
Polymer **3-16**



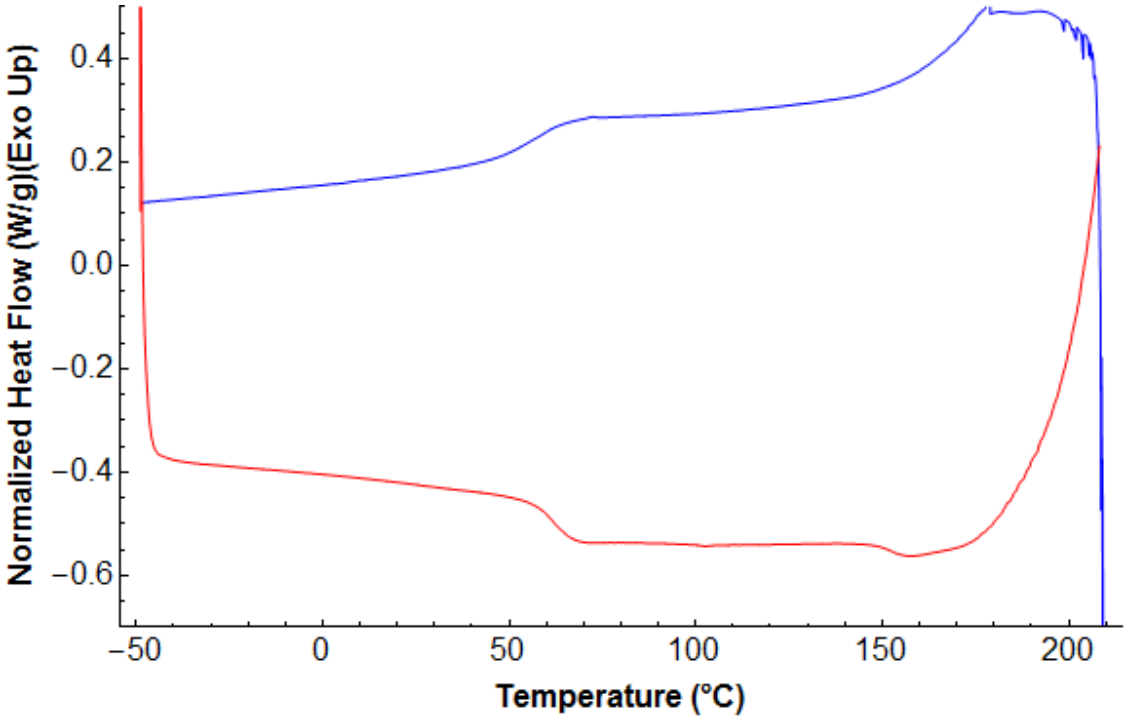
Polymer **3-17**



Polymer **3-18**

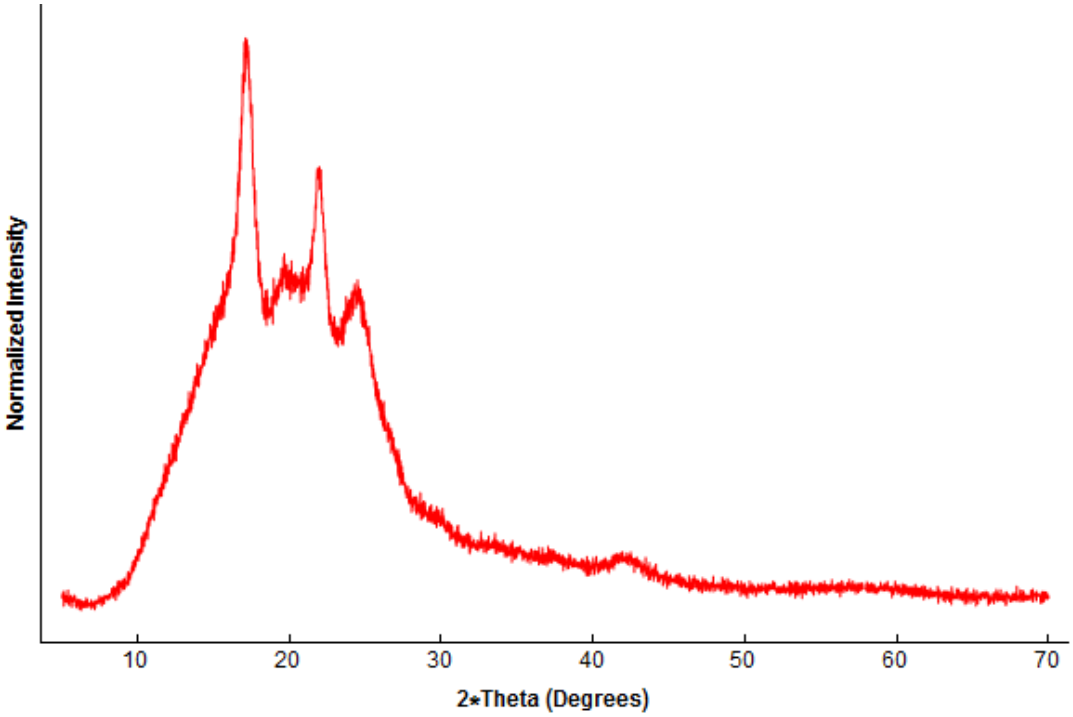


Polymer **3-19**

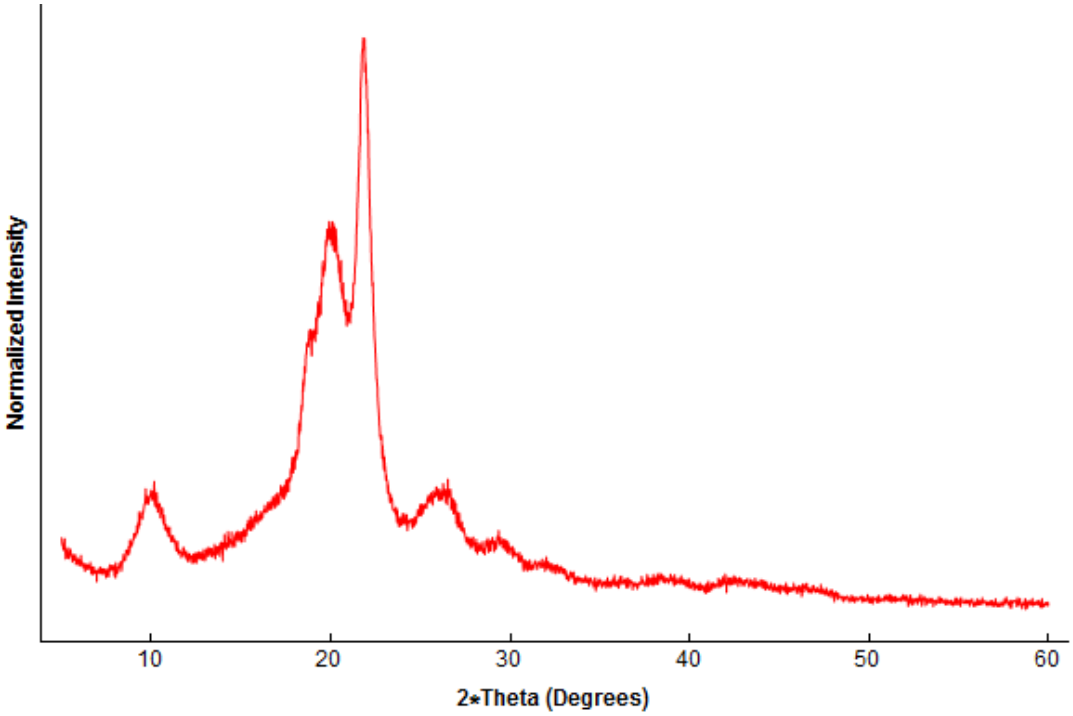

Normalized Heat Flow (W/g)(Exo Up)
0.4
0.2
0.0
−0.2
−0.4
−0.6
−50
0
50
100
150
200
Temperature (°C)

3.4.7 X-ray Diffraction Spectra of Polysulfamides

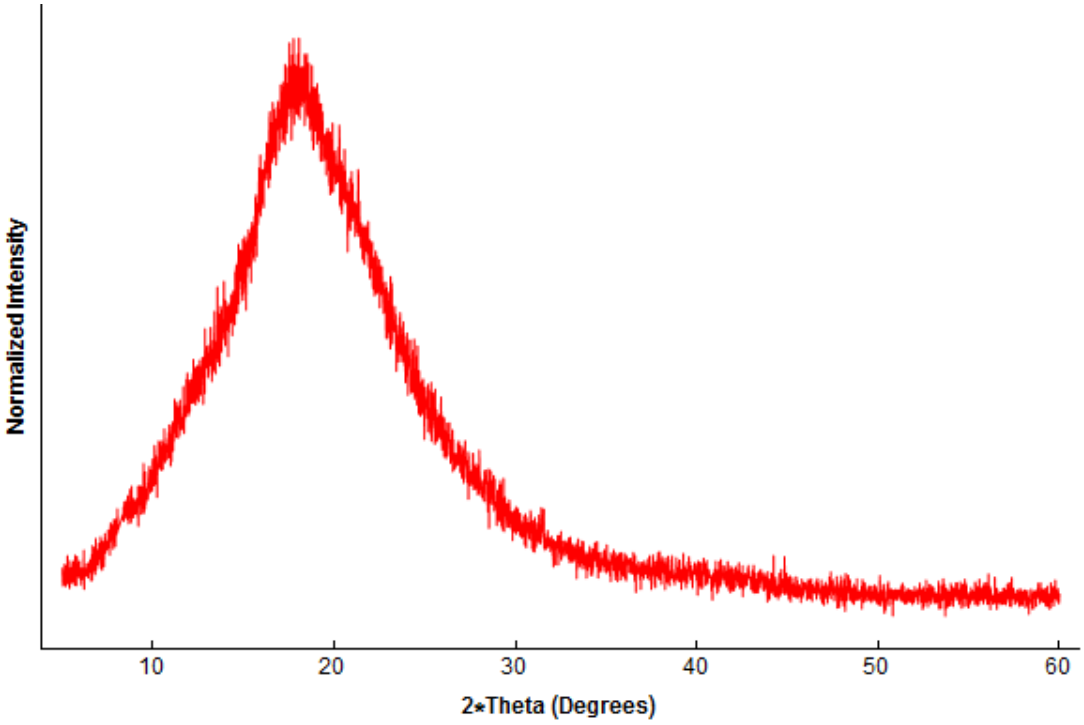
Polysulfamide **3-5**



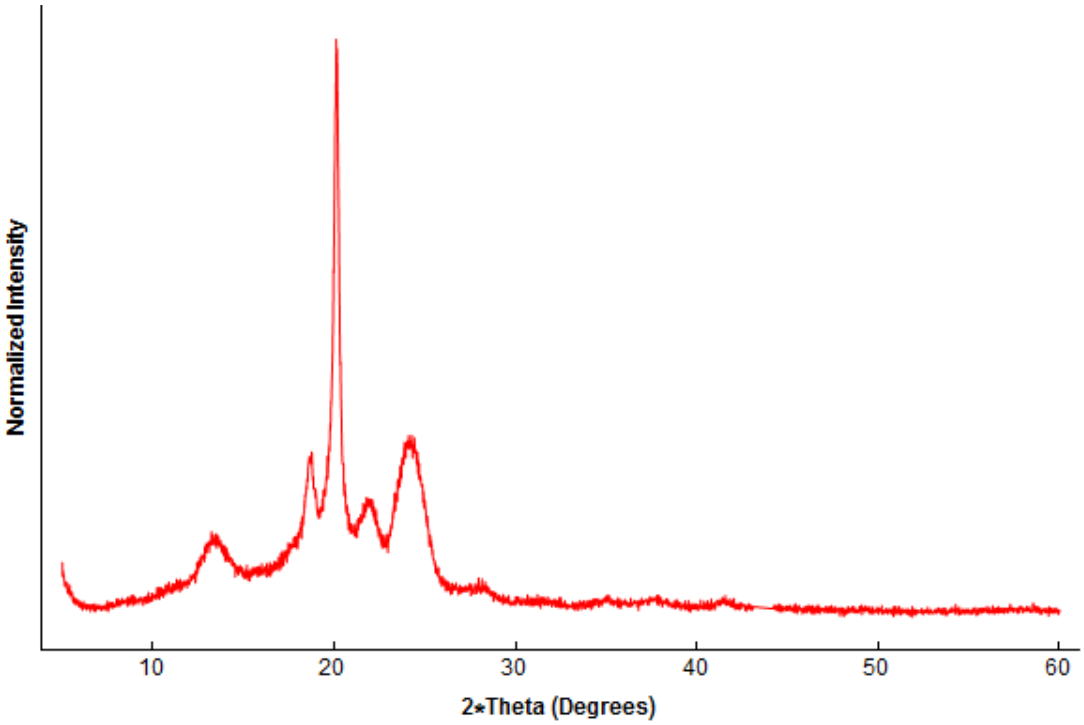
Polysulfamide **3-6**



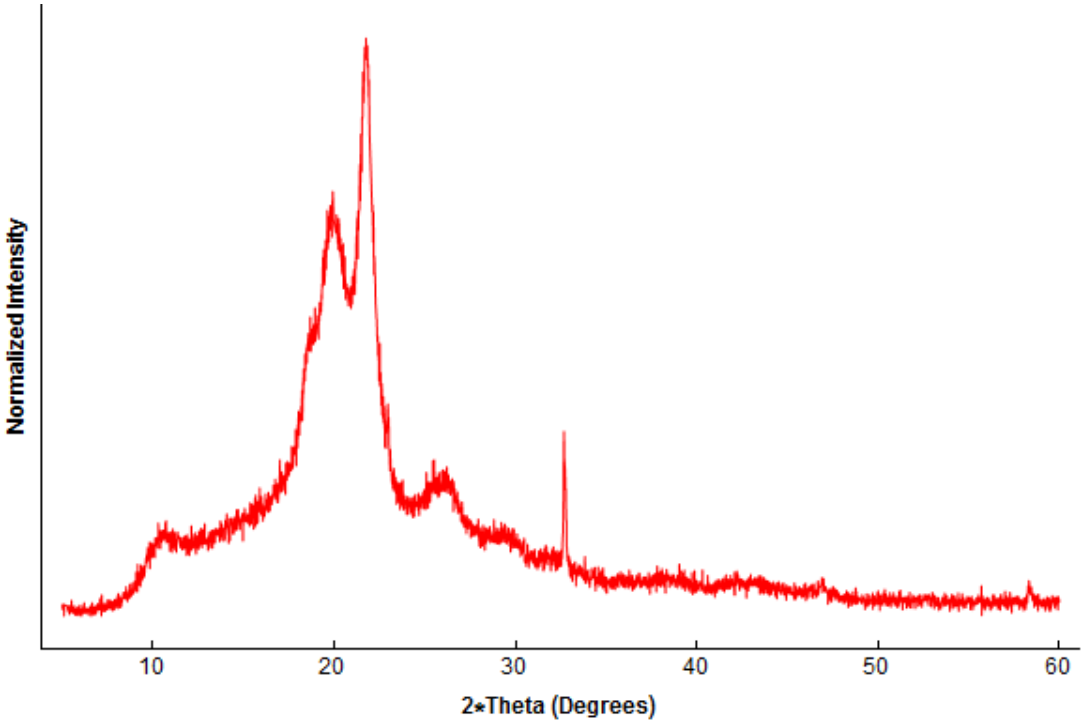
Polysulfamide **3-7**



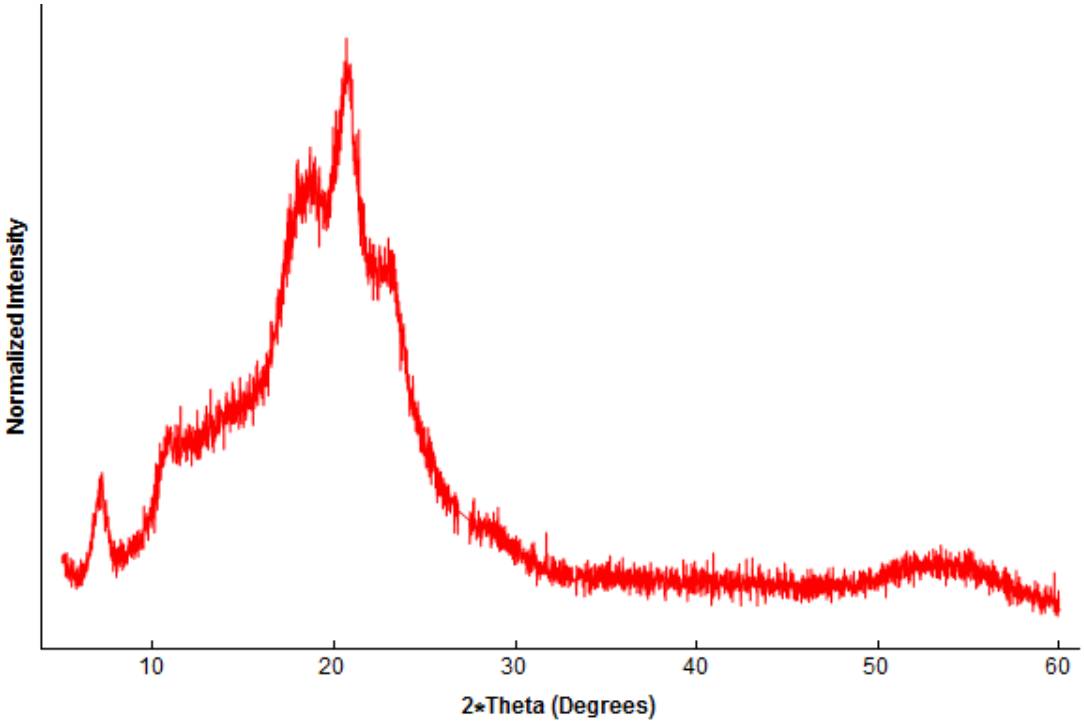
Polysulfamide **3-8**



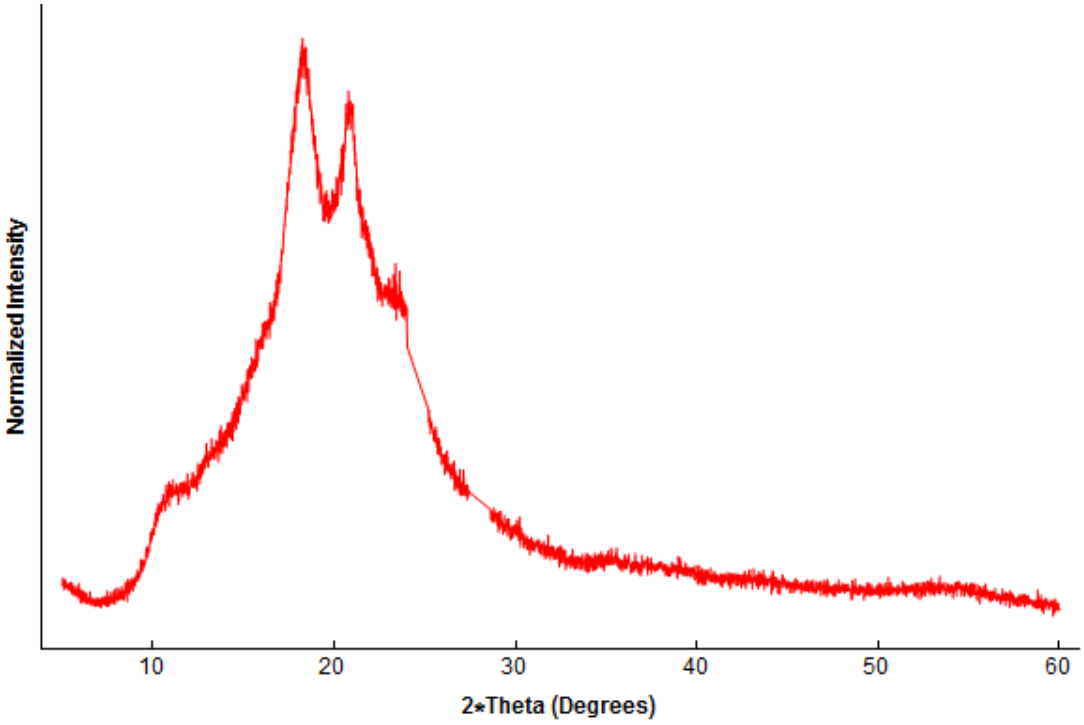
Polysulfamide **3-9**



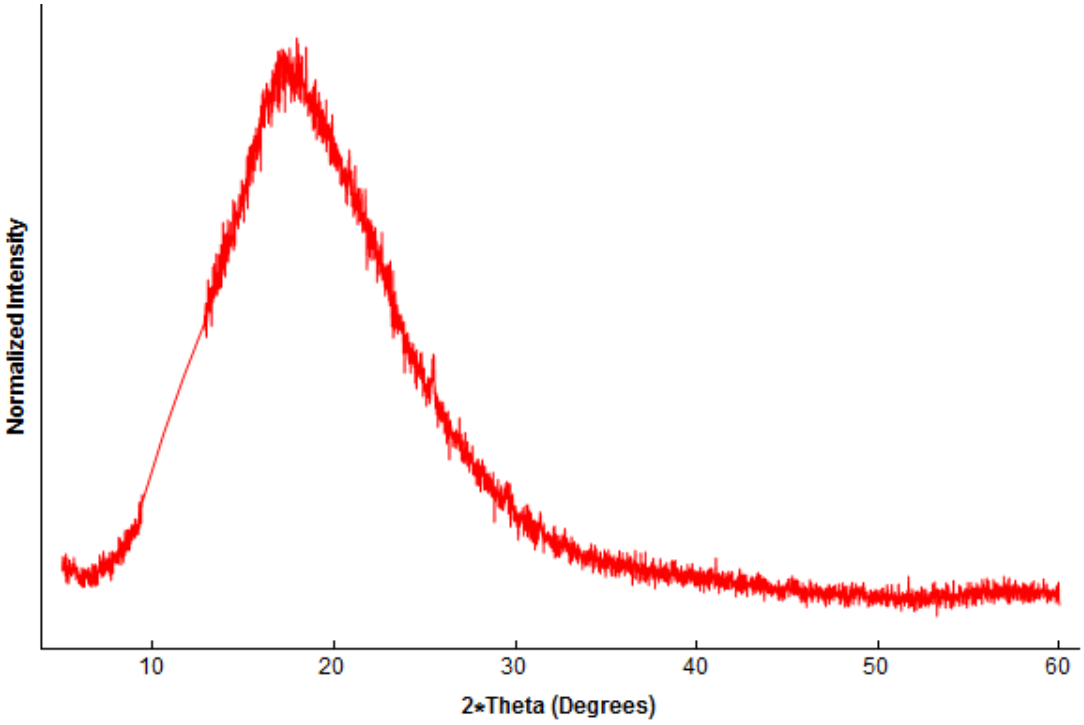
Polysulfamide **3-10**



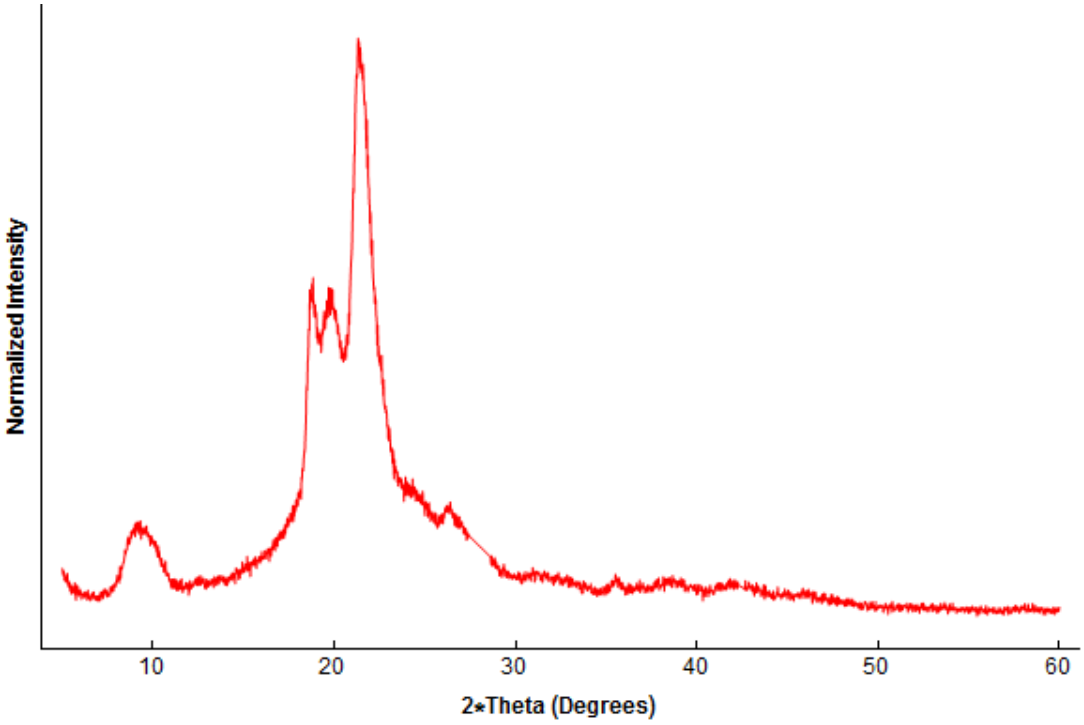
Polysulfamide **3-11**



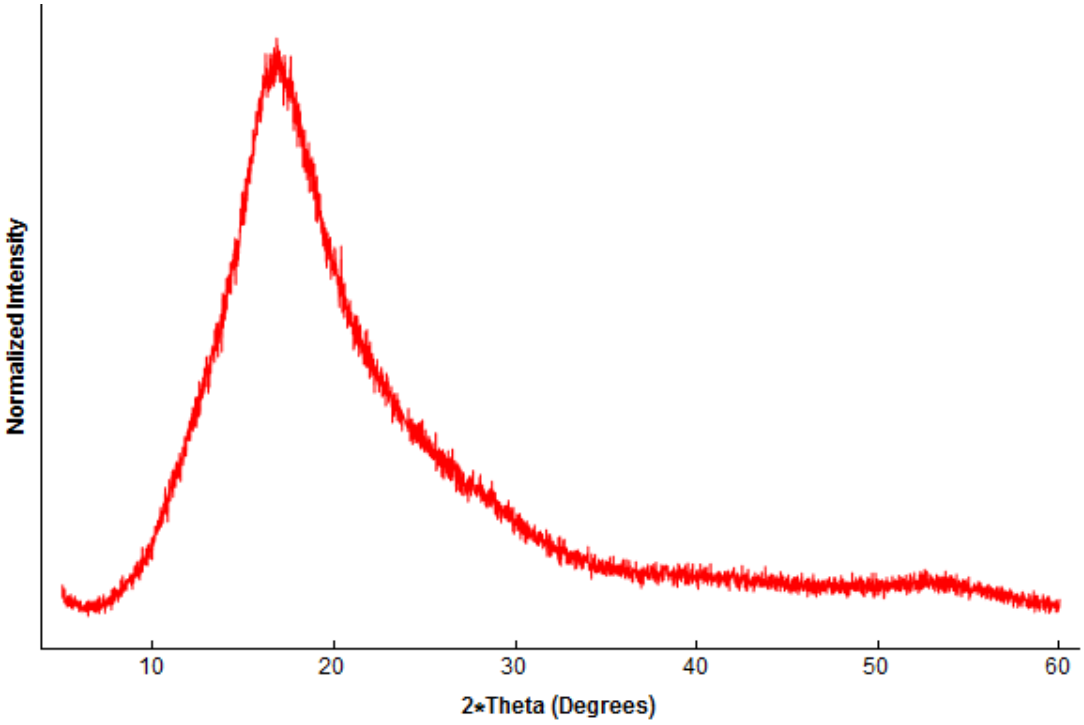
Polysulfamide **3-12**



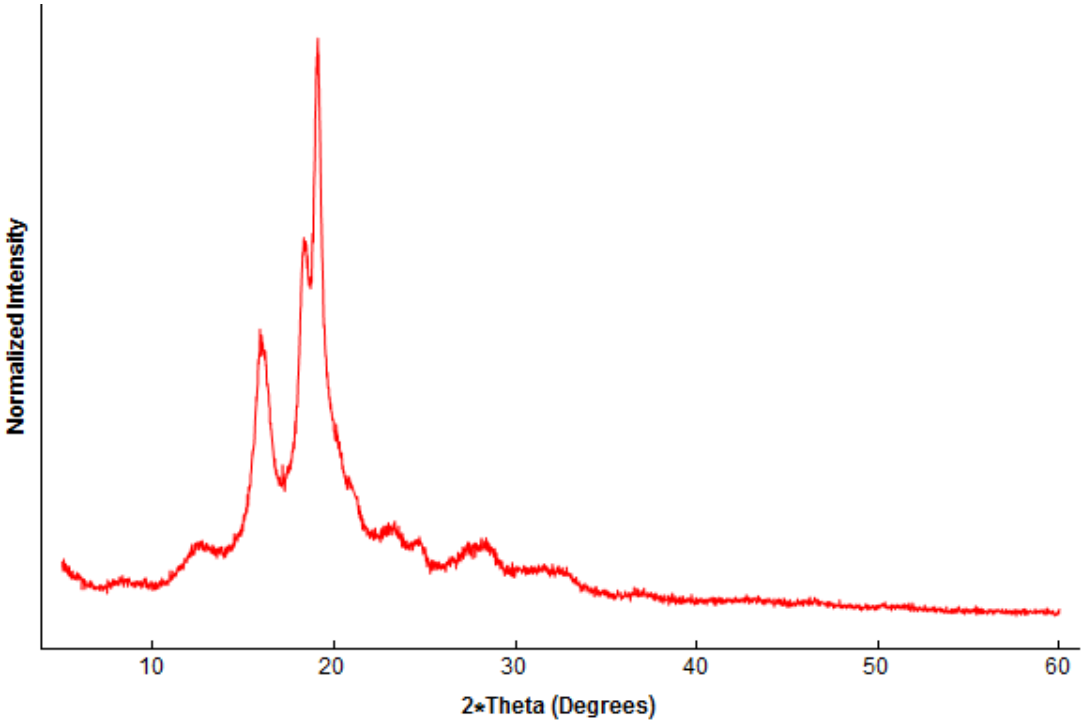
Polysulfamide **3-13**



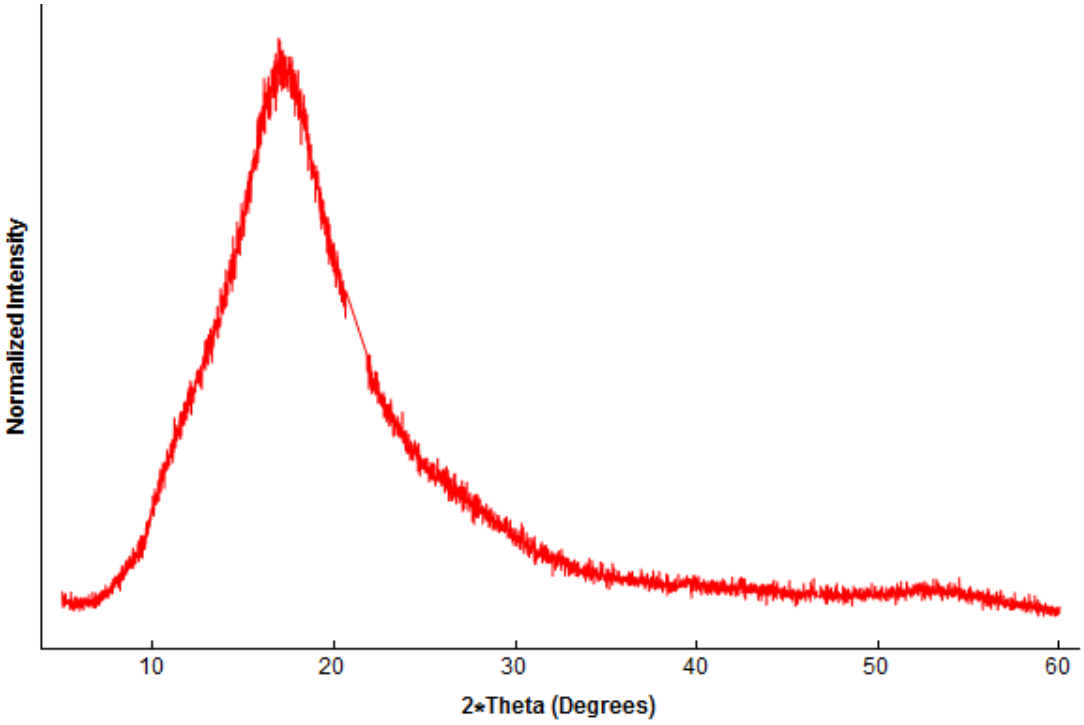
Polysulfamide **3-14**



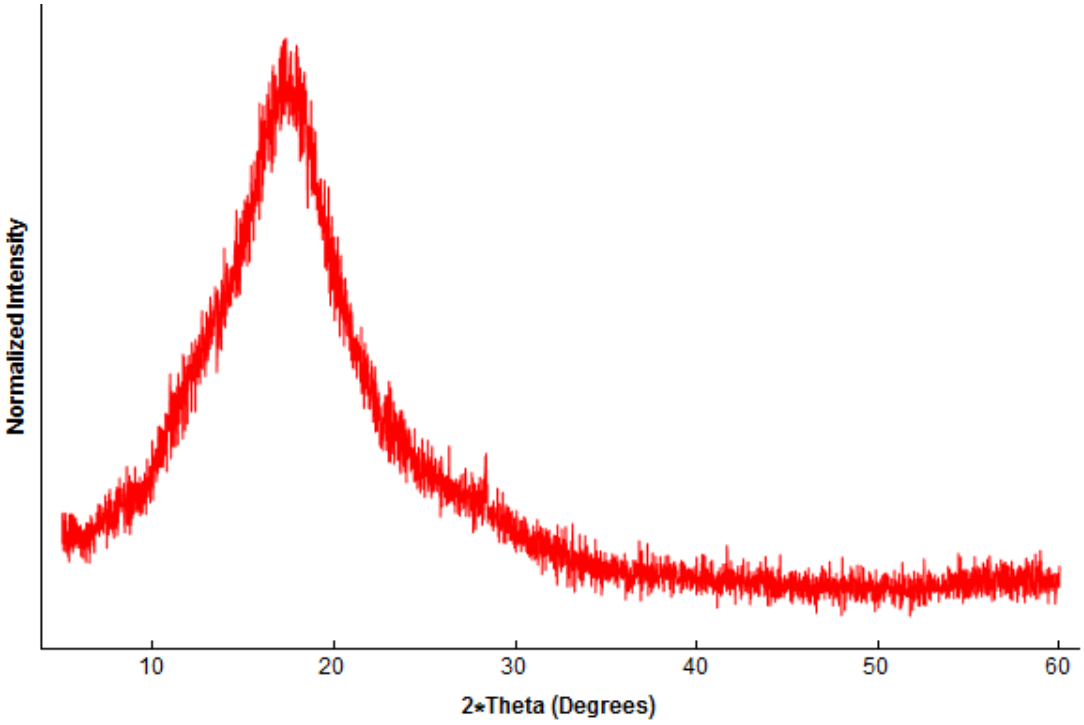
Polysulfamide **3-15**



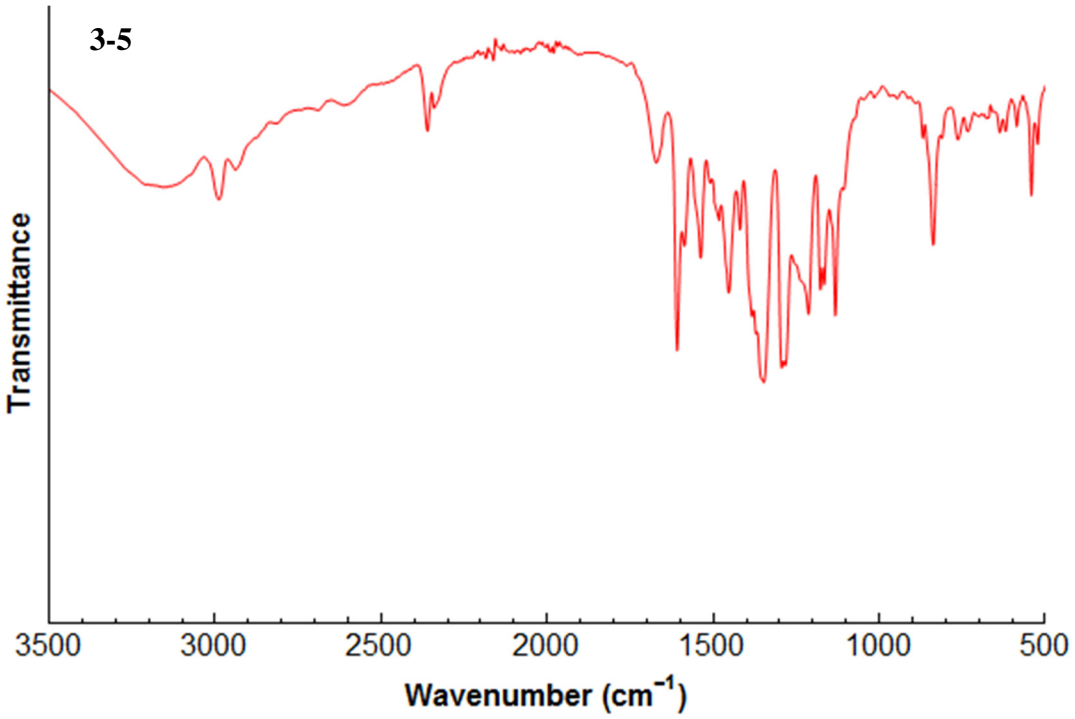
Polysulfamide **3-16**

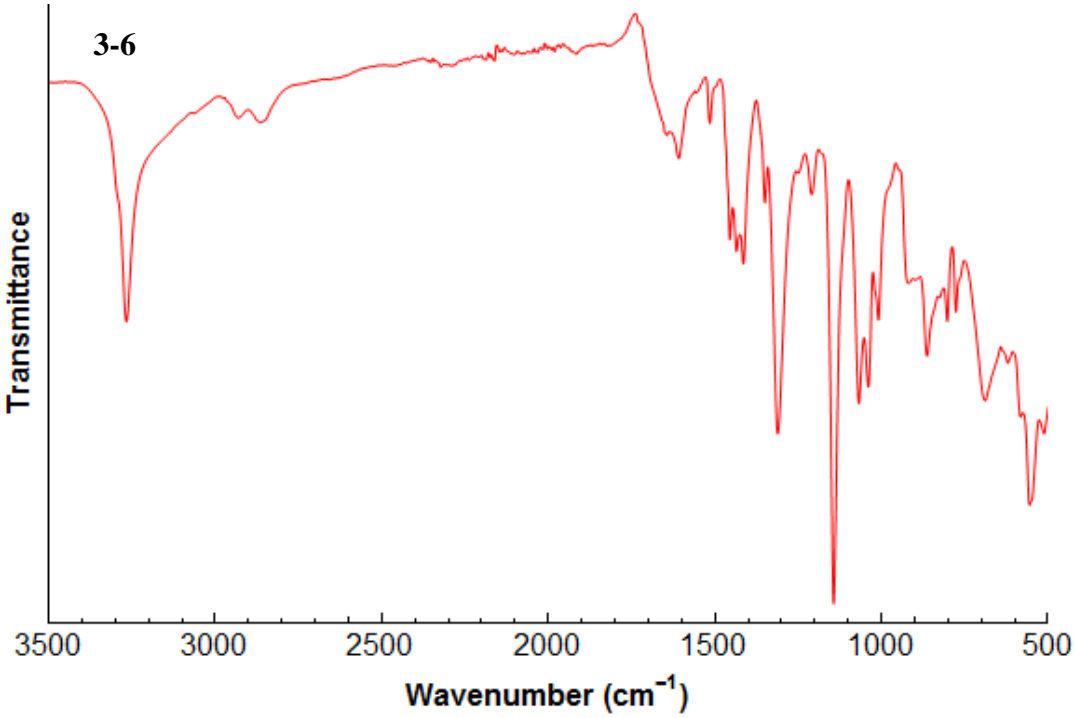


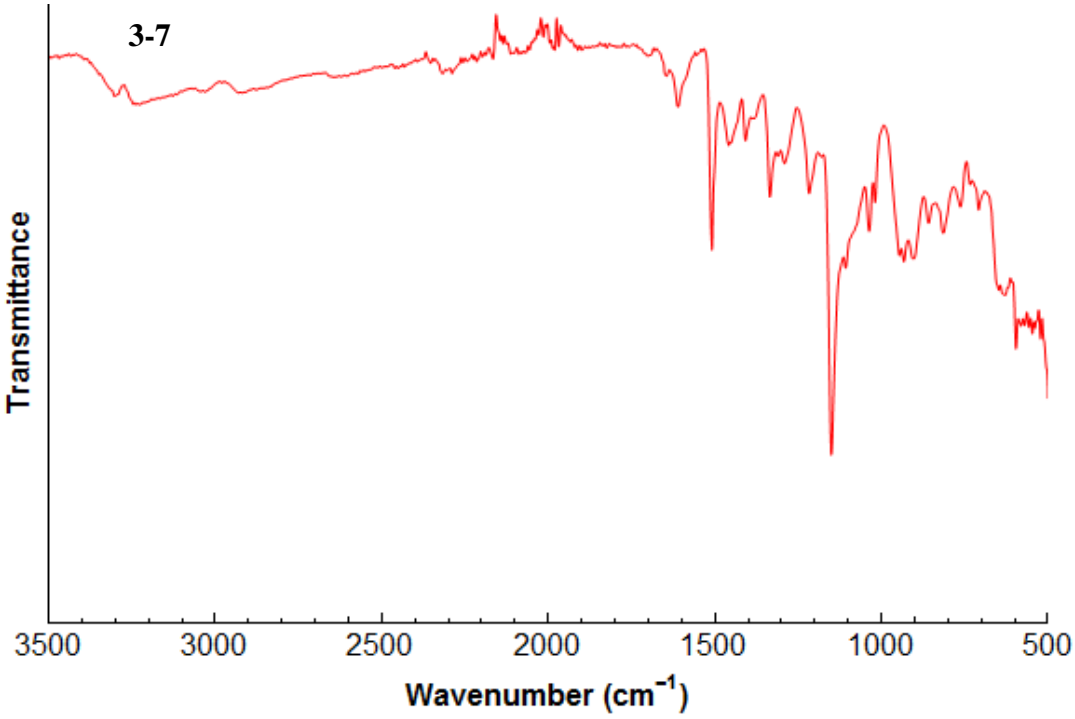
Polysulfamide **3-17**

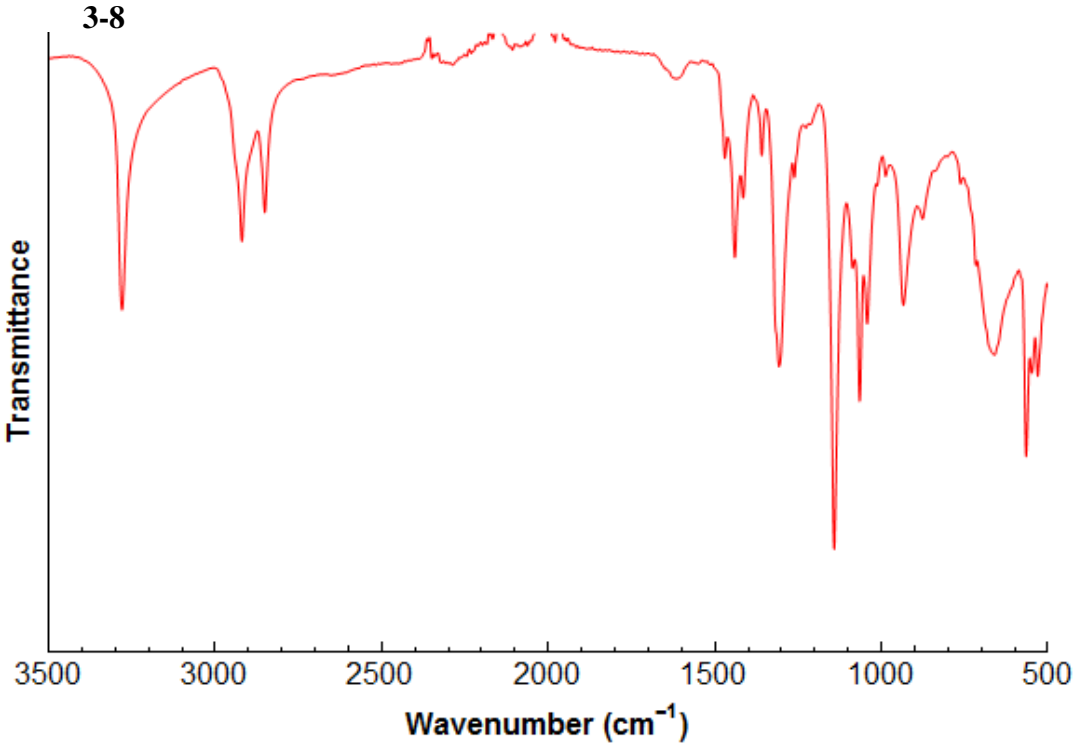


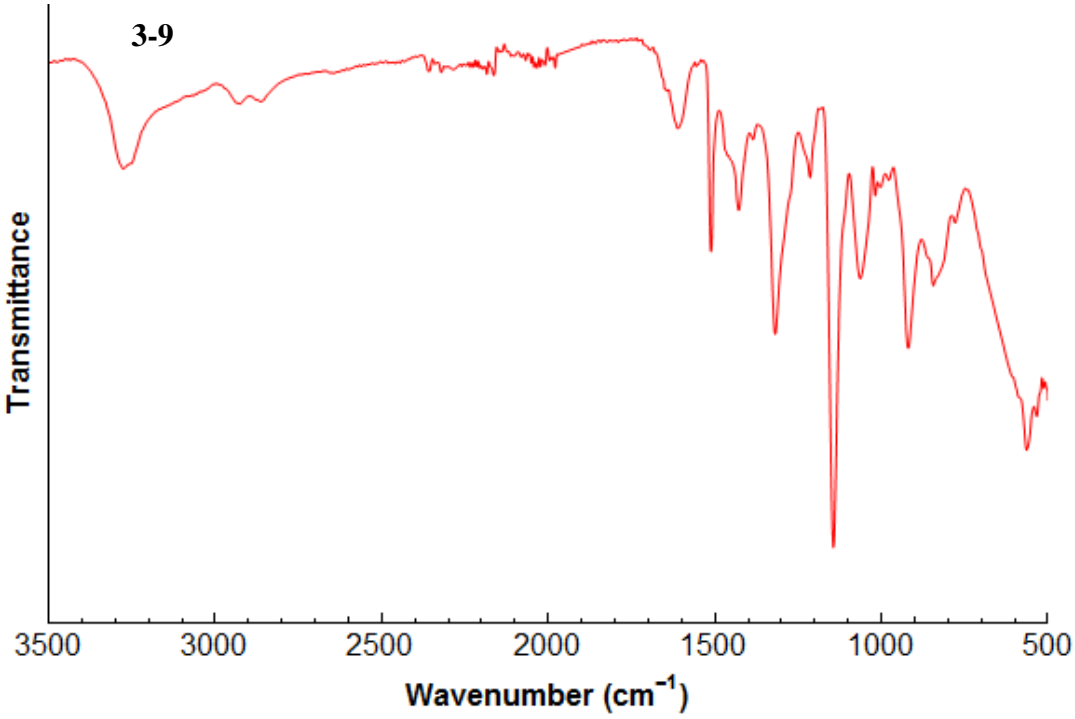
3.4.8 Infrared Spectra of Sulfamides and Polysulfamides

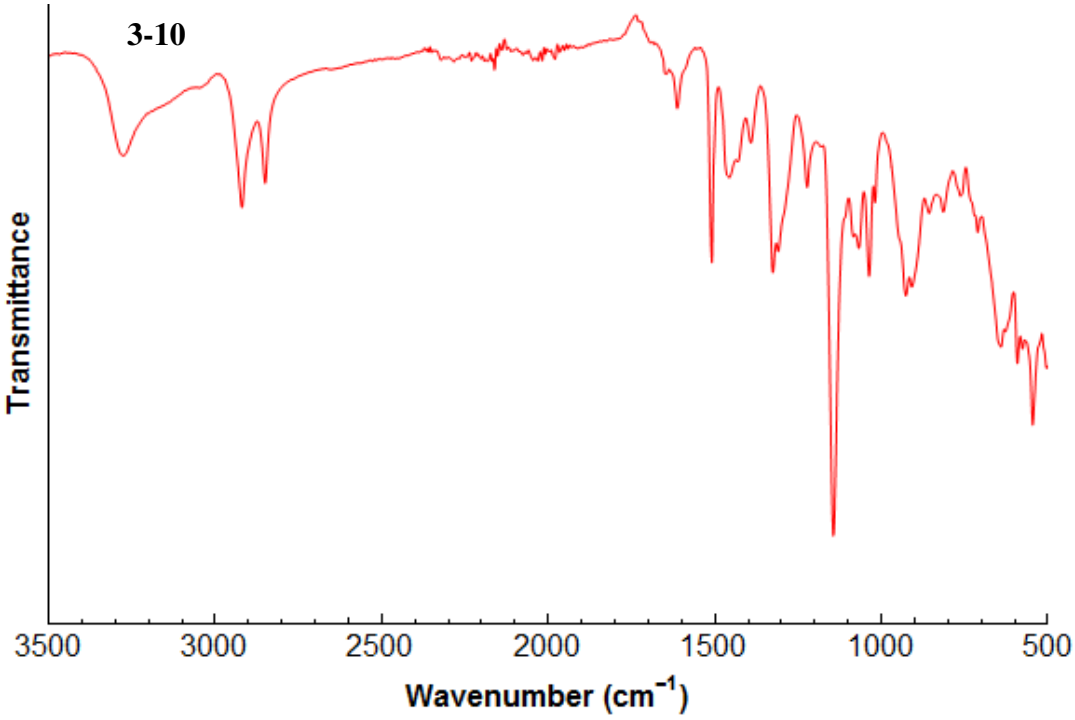


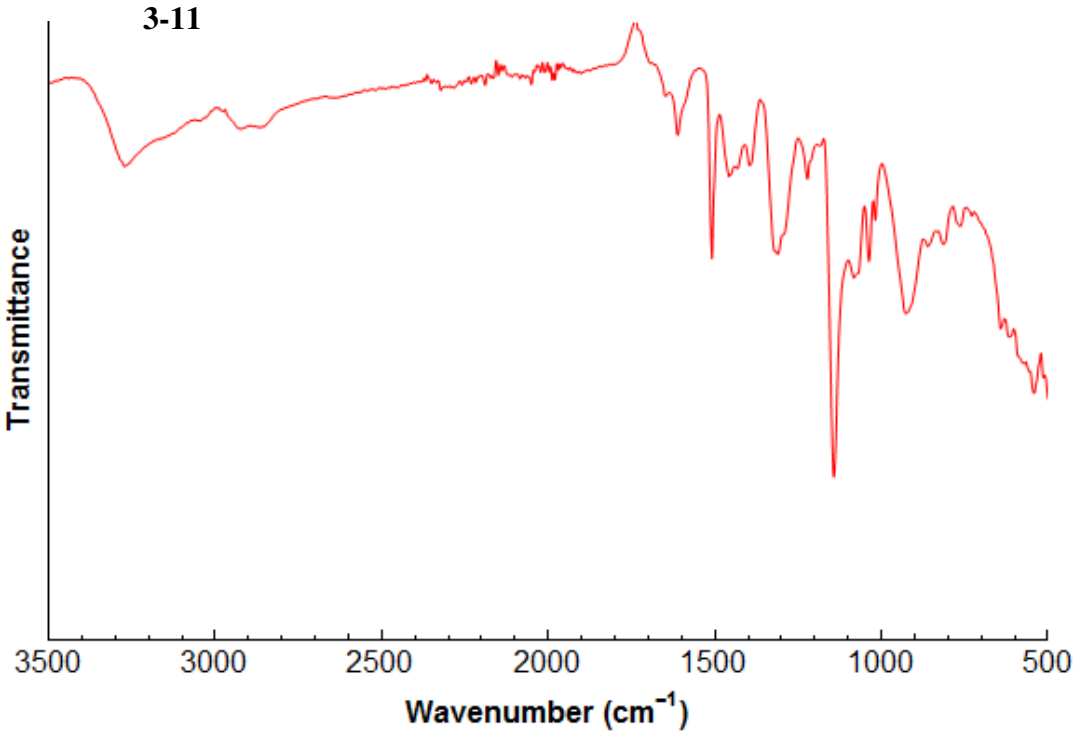


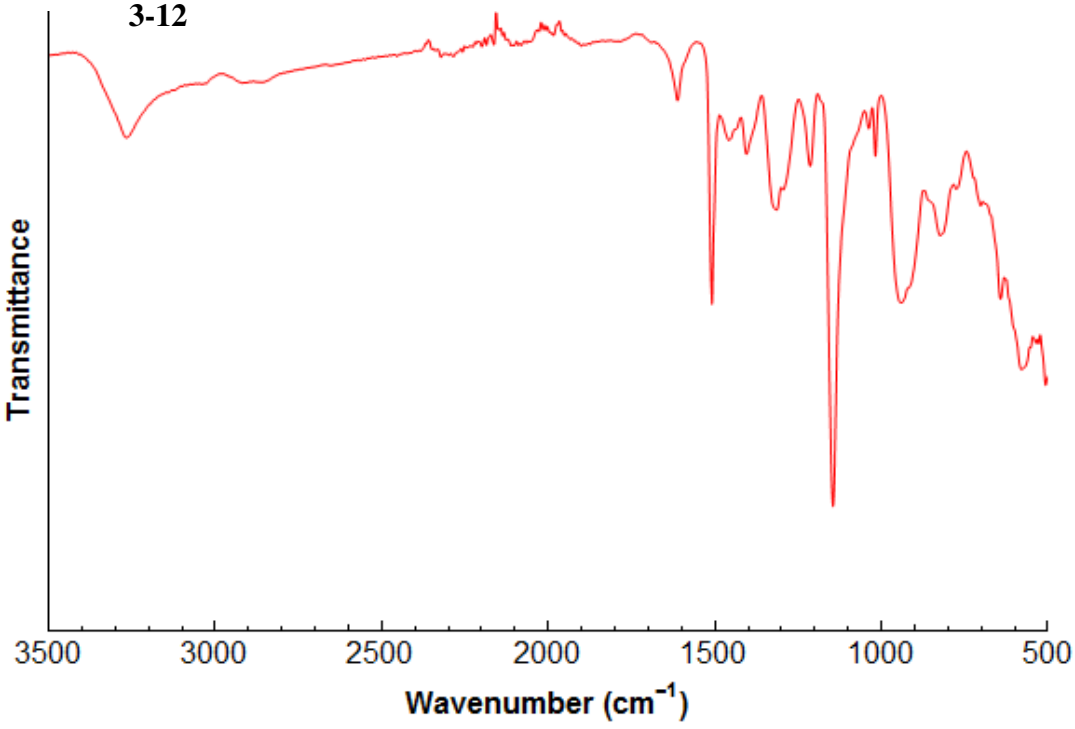

3-7
Transmittance
3500
3000
2500
2000
1500
1000
500
Wavenumber (cm^{-1})

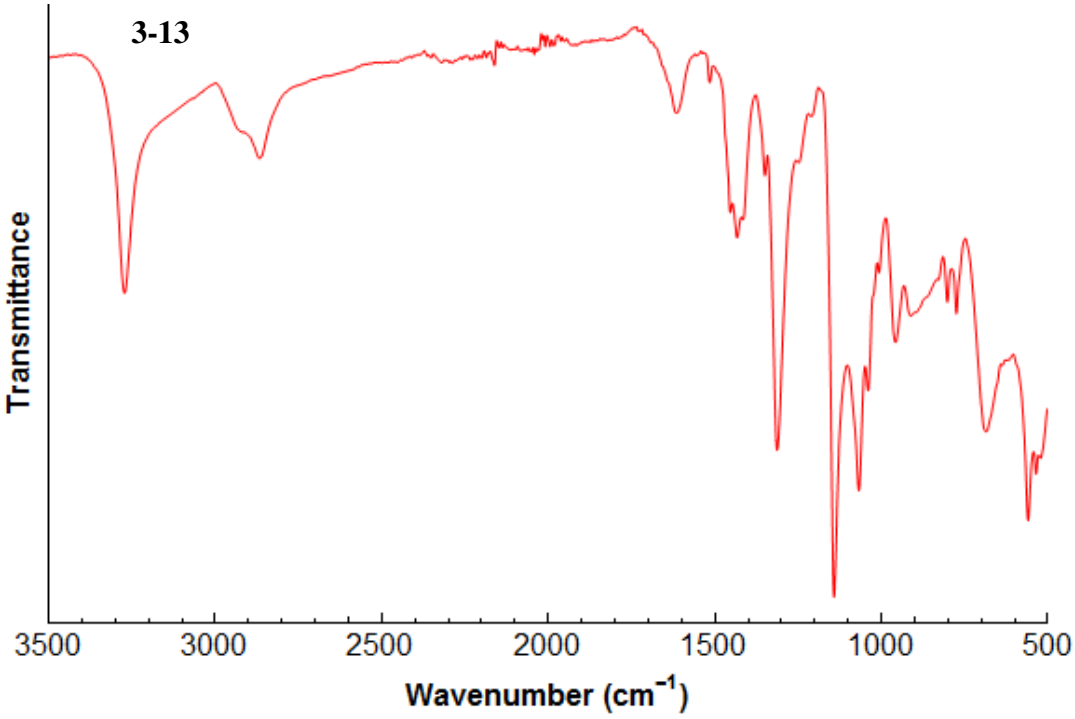

3-8
Transmittance
3500
3000
2500
2000
1500
1000
500
Wavenumber (cm^{-1})

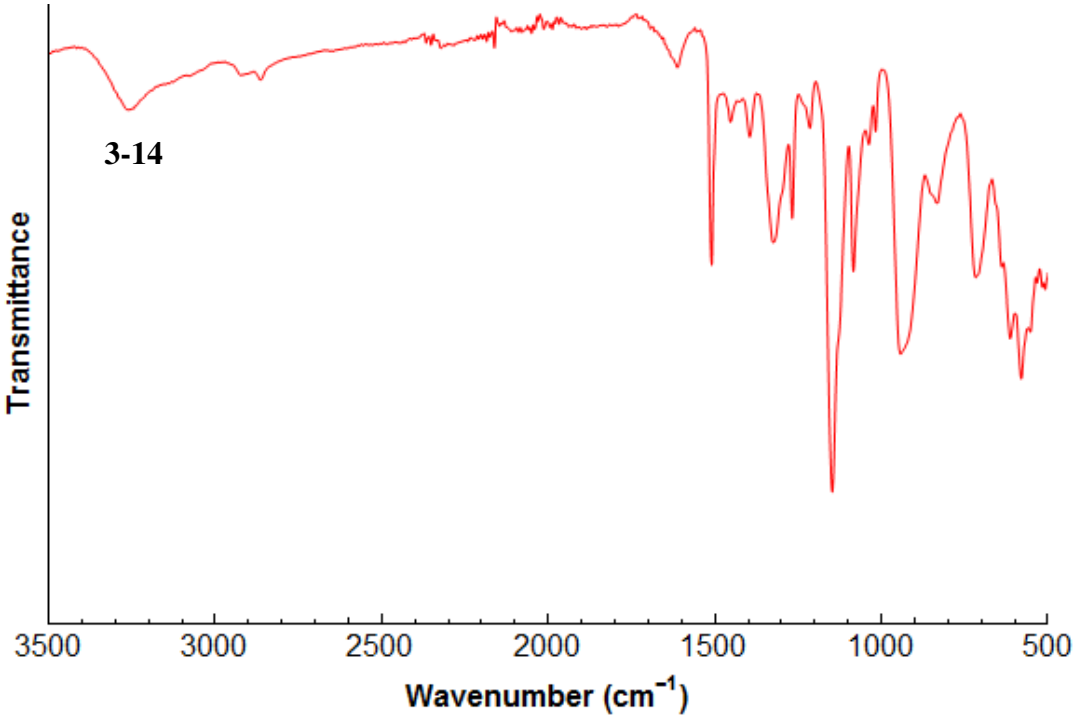

3-9
Transmittance
3500
3000
2500
2000
1500
1000
500
Wavenumber (cm^{-1})

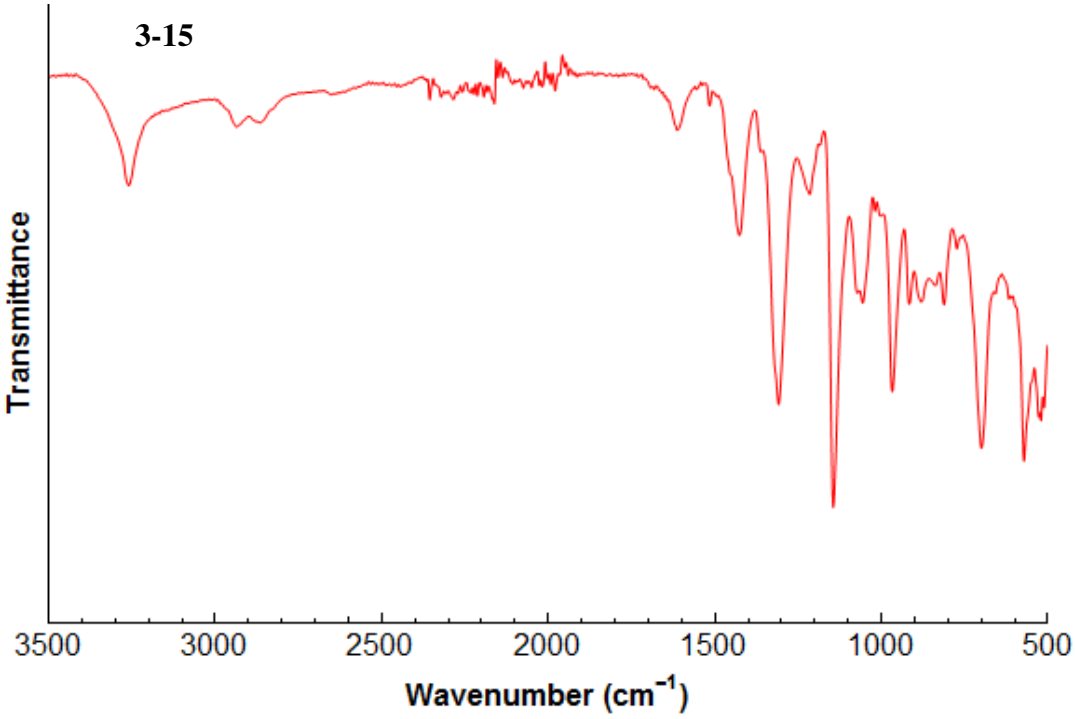

3-10
Transmittance
3500
3000
2500
2000
1500
1000
500
Wavenumber (cm^{-1})

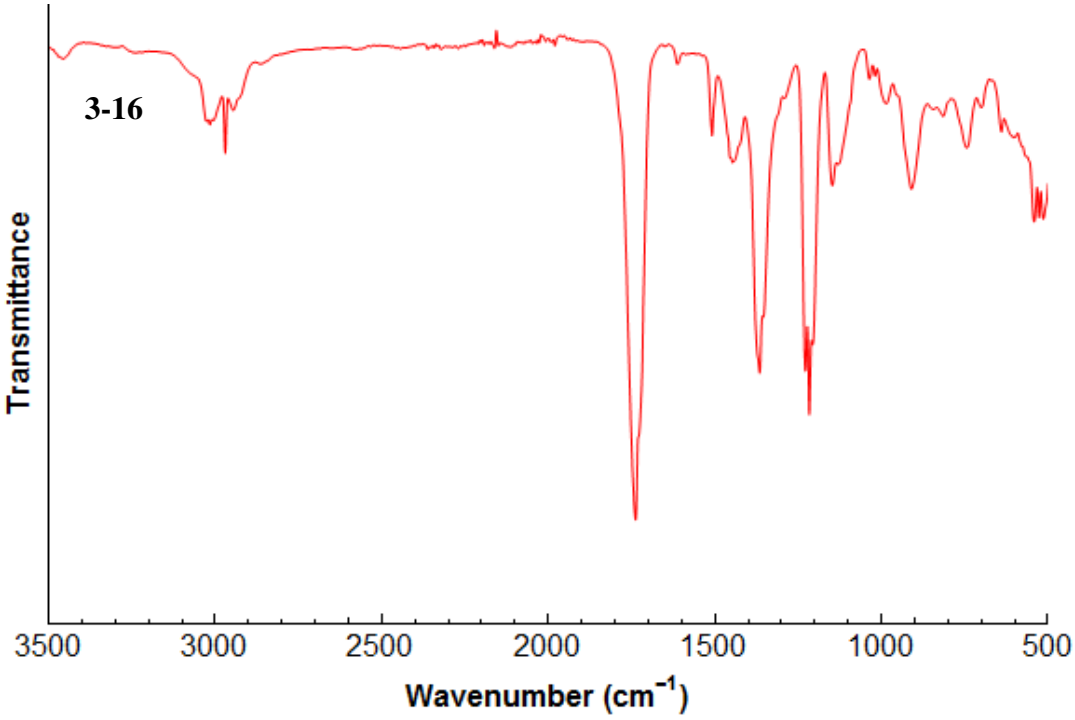

3-11
Transmittance
3500
3000
2500
2000
1500
1000
500
Wavenumber (cm^{-1})

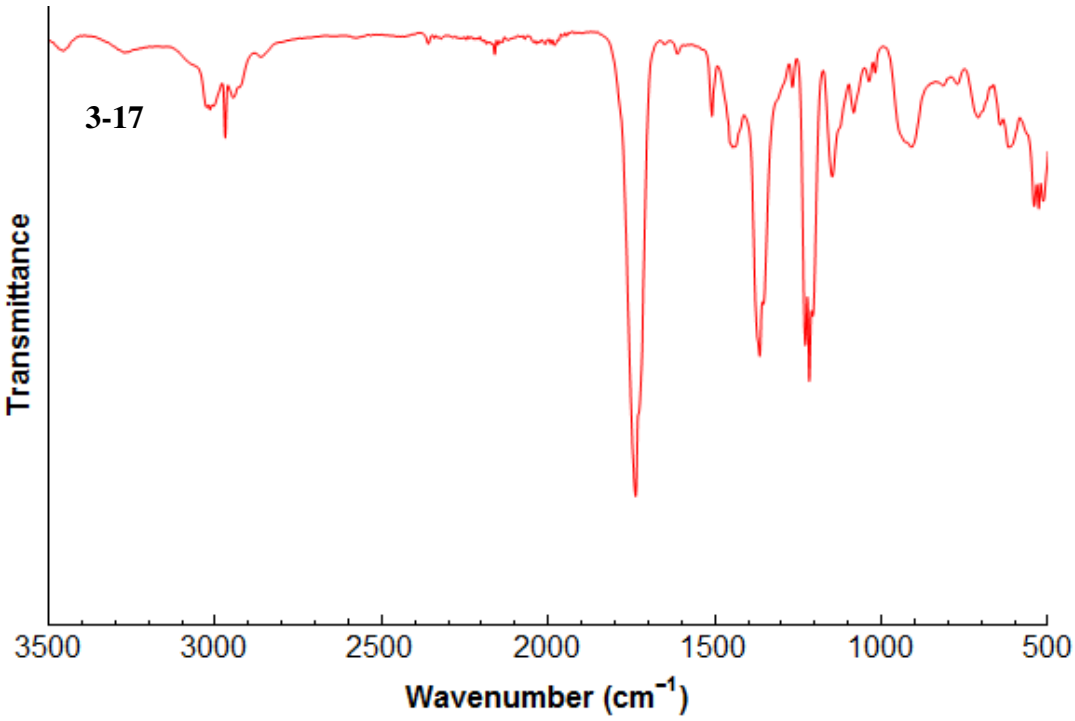

3-12
Transmittance
3500
3000
2500
2000
1500
1000
500
Wavenumber (cm^{-1})


3-13
Transmittance
3500
3000
2500
2000
1500
1000
500
Wavenumber (cm^{-1})


3-14
Transmittance
3500
3000
2500
2000
1500
1000
500
Wavenumber (cm^{-1})

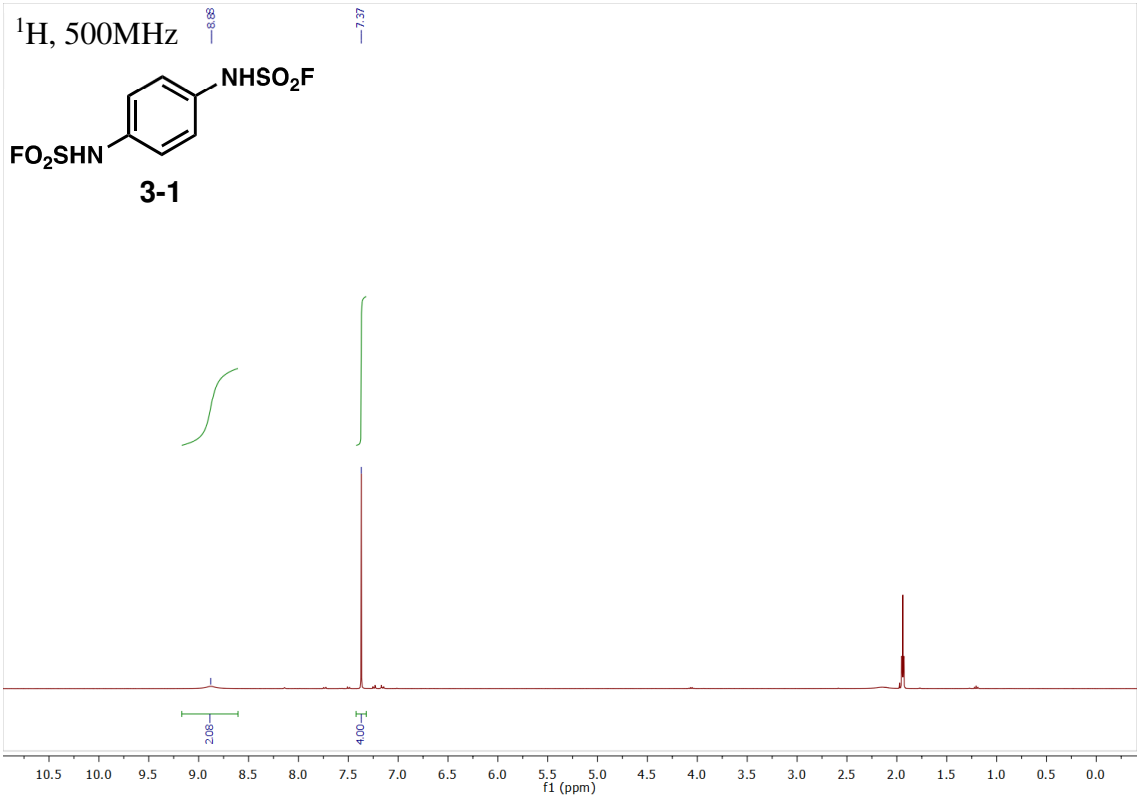

3-15
Transmittance
3500
3000
2500
2000
1500
1000
500
Wavenumber (cm^{-1})


3-16
Transmittance
3500
3000
2500
2000
1500
1000
500
Wavenumber (cm^{-1})

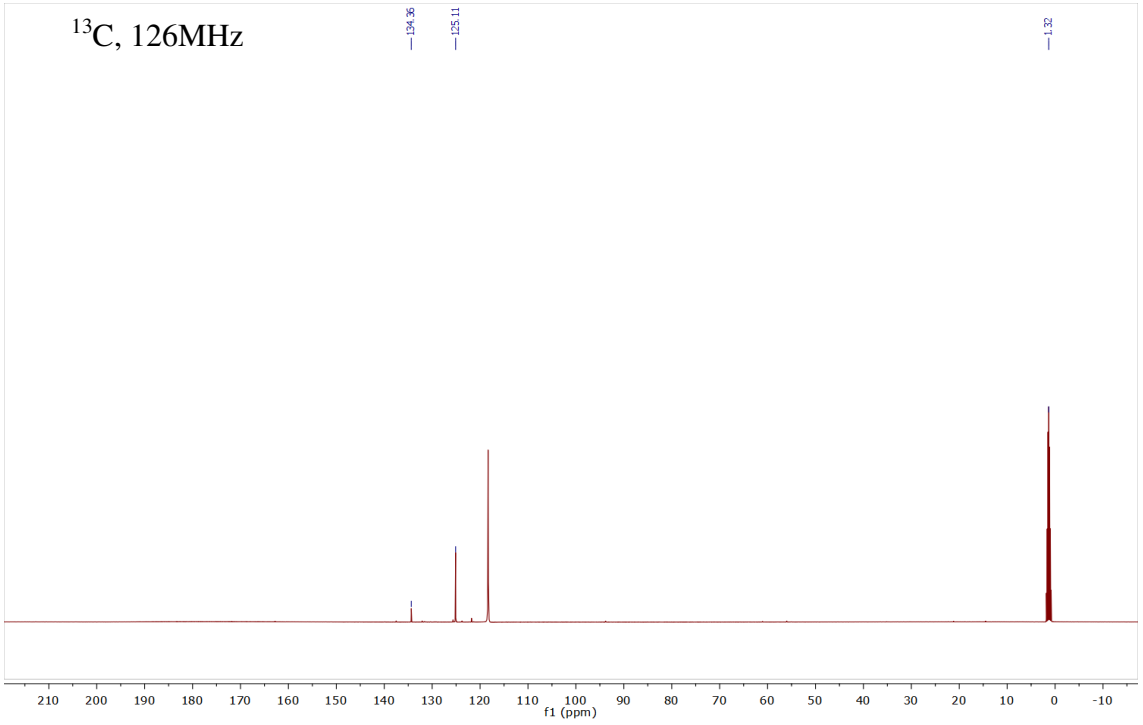

3-17
Transmittance
3500
3000
2500
2000
1500
1000
500
Wavenumber (cm-1)

3.4.9 NMR Spectra of Novel Compounds

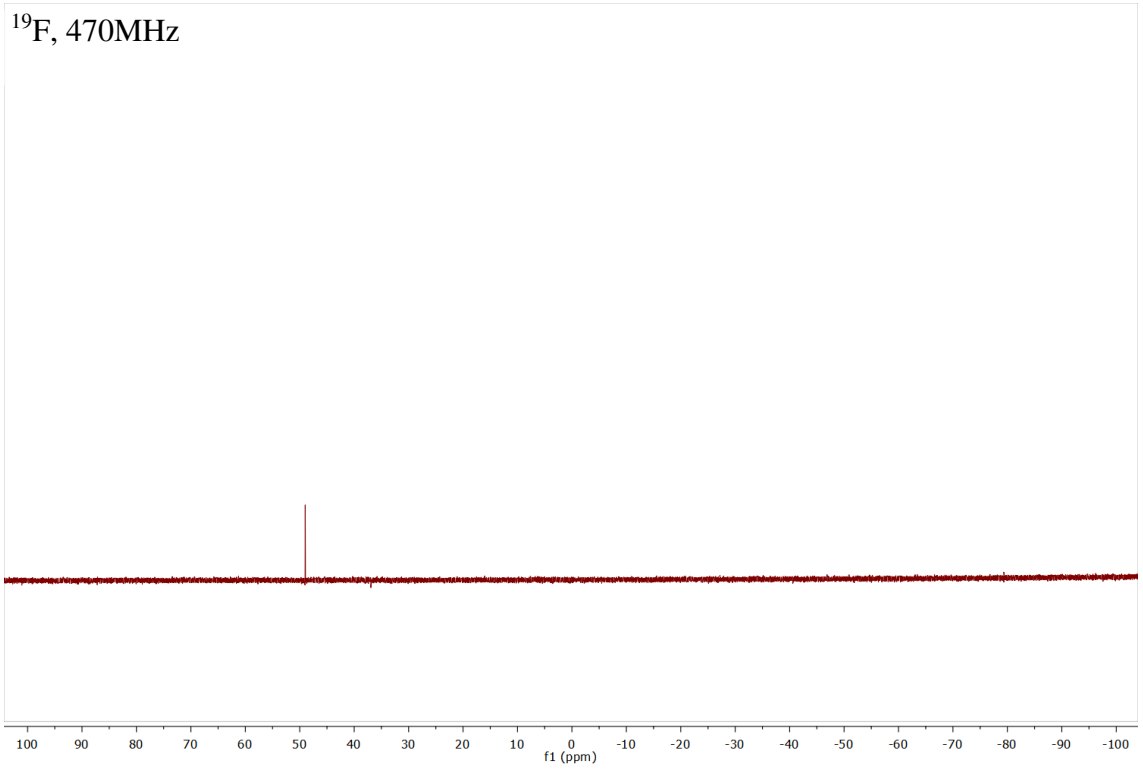
NMR Spectra of 1,4-Phenylenebis(sulfamoyl fluoride) (**3-1**) (CD_3CN)



^{13}C, 126MHz

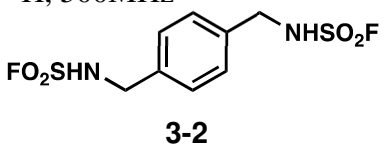


^{19}F, 470MHz



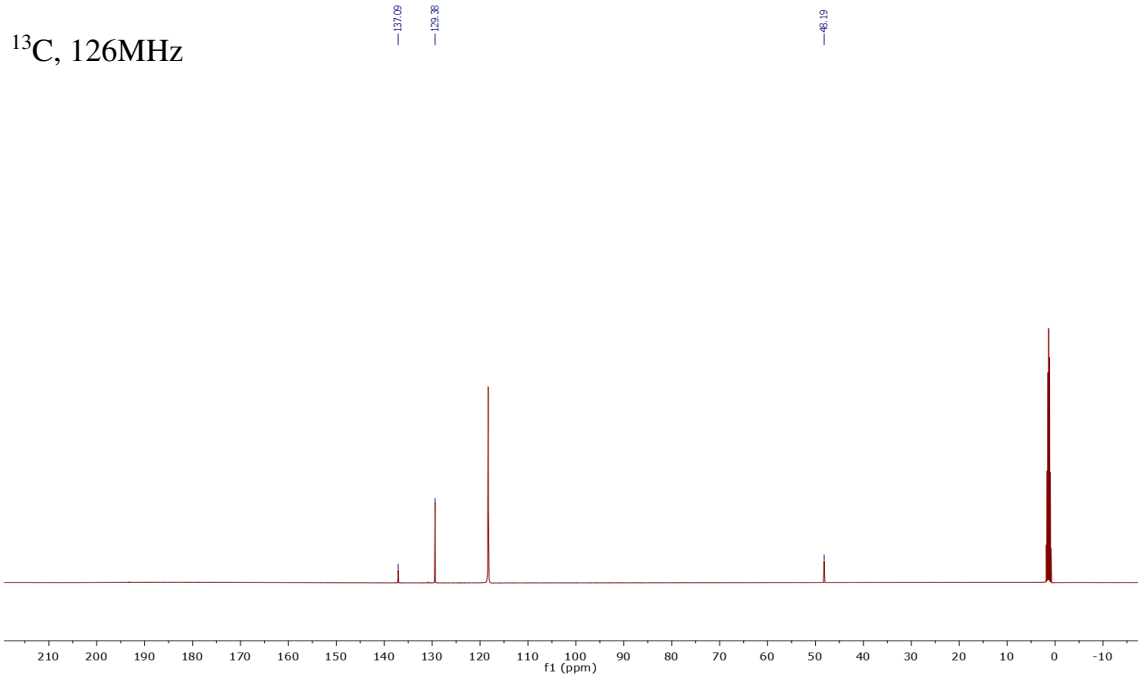
NMR Spectra of (1,4-phenylenebis(methylene))bis(sulfamoyl fluoride) (**3-2**) (CD_3CN)

^1H, 500MHz

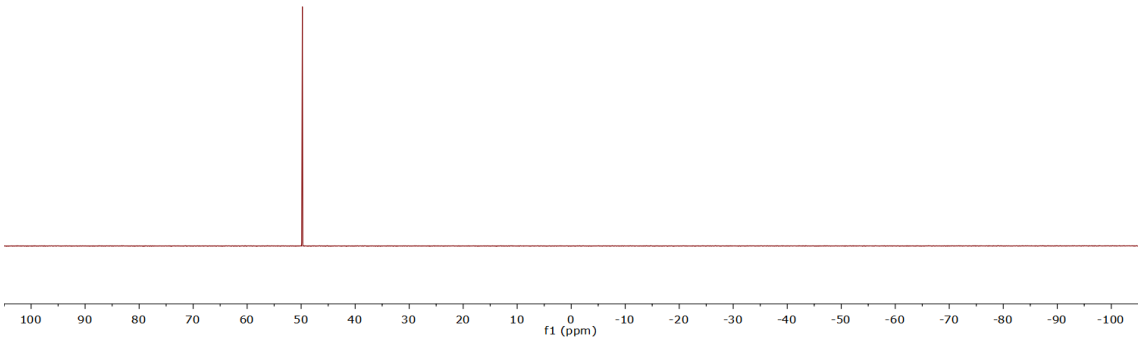


3-2

^{13}C, 126MHz

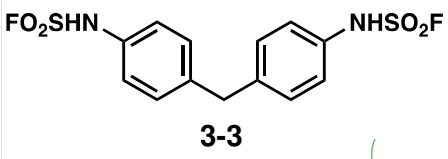


^{19}F, 470MHz



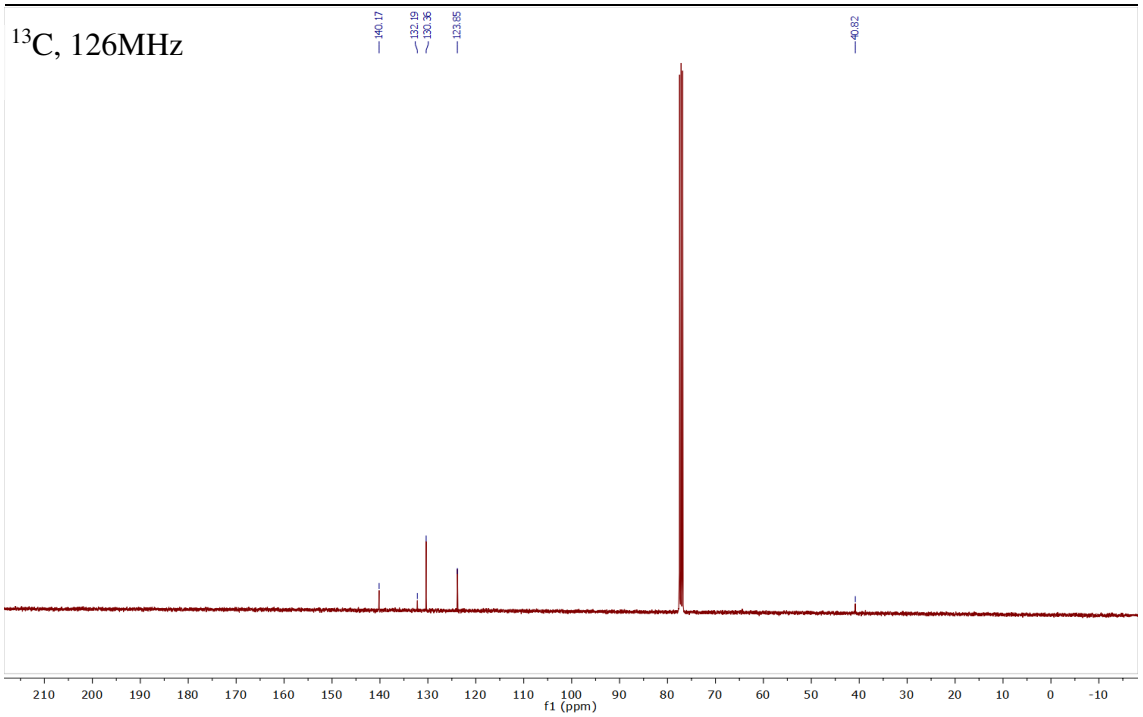
NMR Spectra of (Methylenebis(1,4-phenylene))bis(sulfamoyl fluoride) (**3-3**) ($CDCl_3$)

^1H, 400MHz

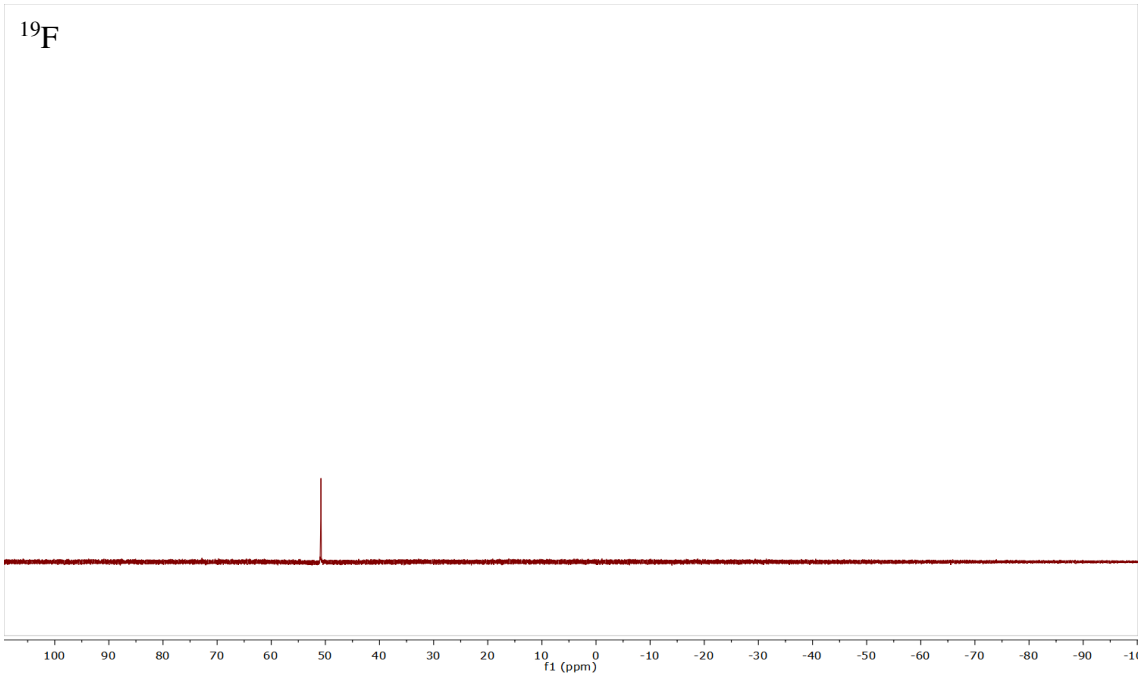


3-3

^{13}C, 126MHz



^{19}F

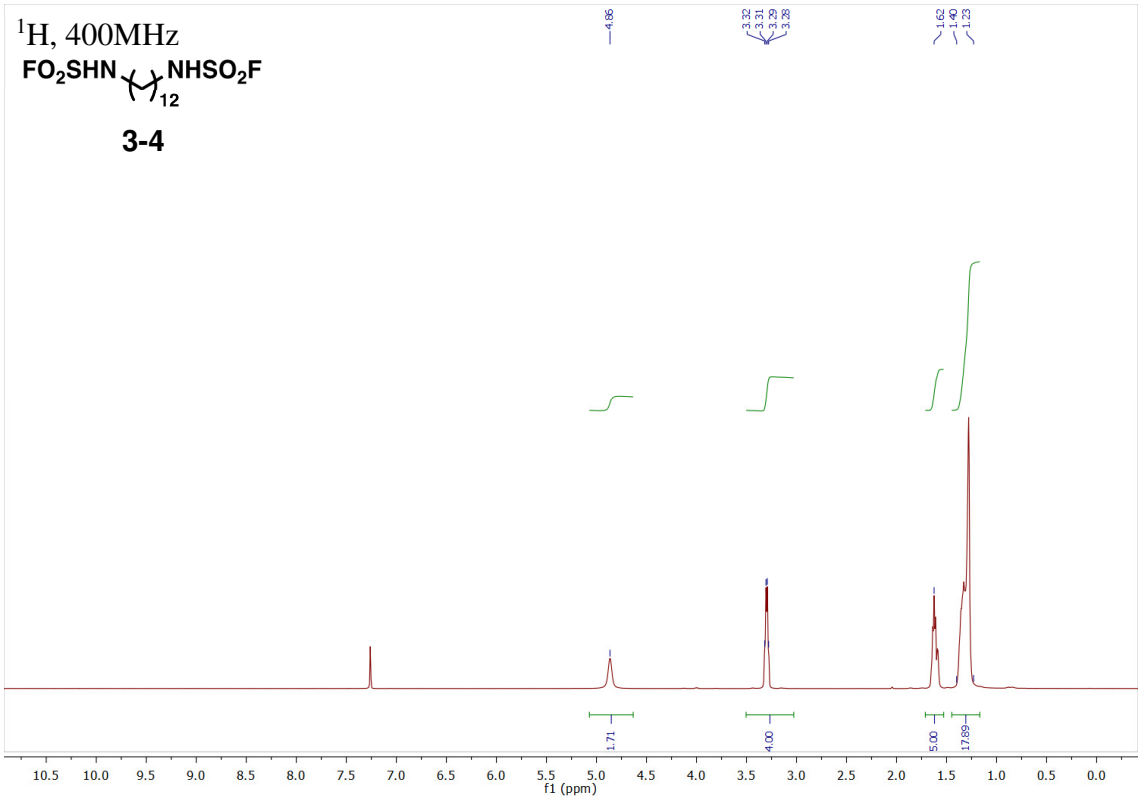


NMR of Dodecane-1,12-bis(sulfamoyl fluoride) (**3-4**) ($CDCl_3$)

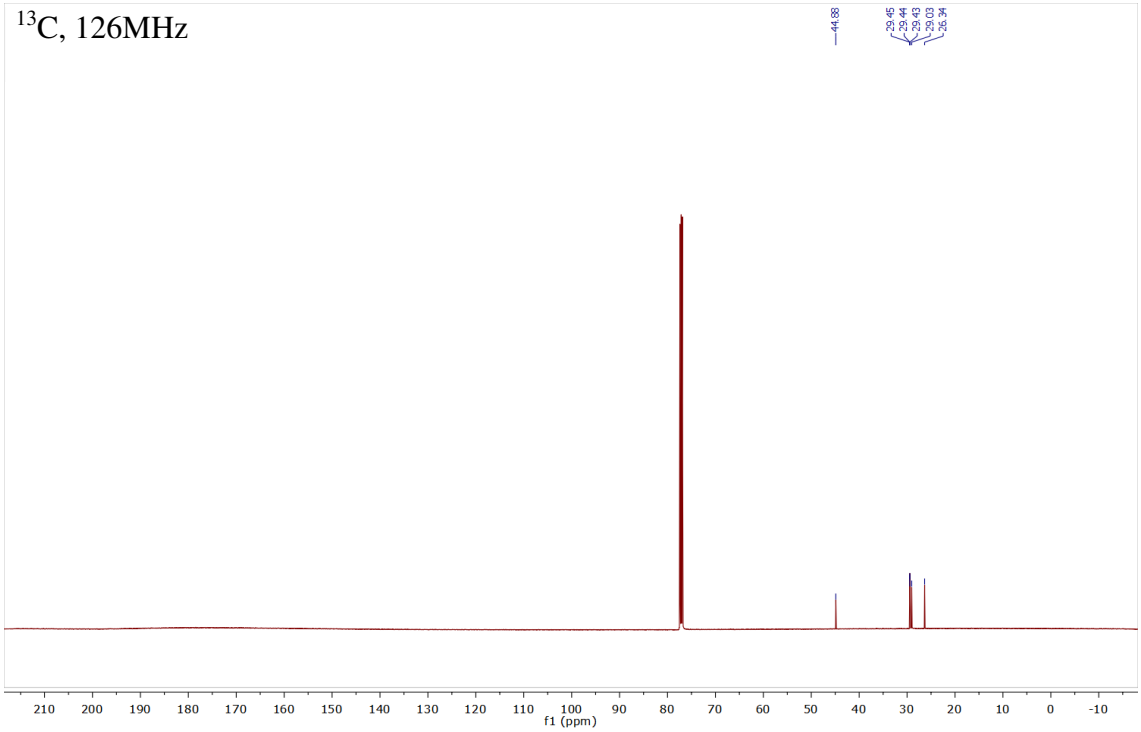
^1H, 400MHz

$FO_2SHN(CH_2)_{12}NHSO_2F$

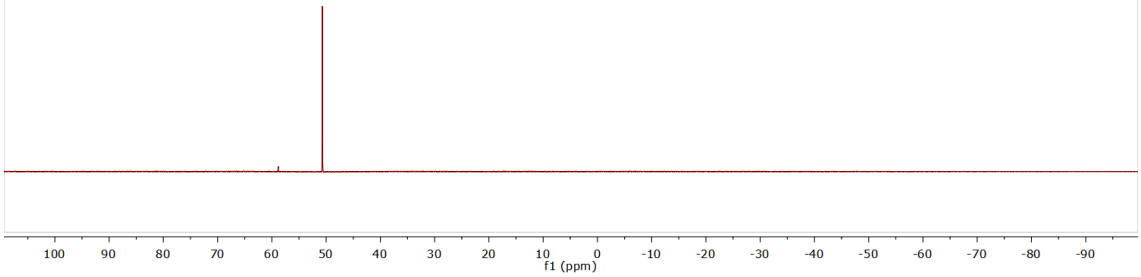
3-4



^{13}C, 126MHz

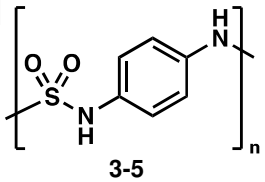


^{19}F, 470HMz



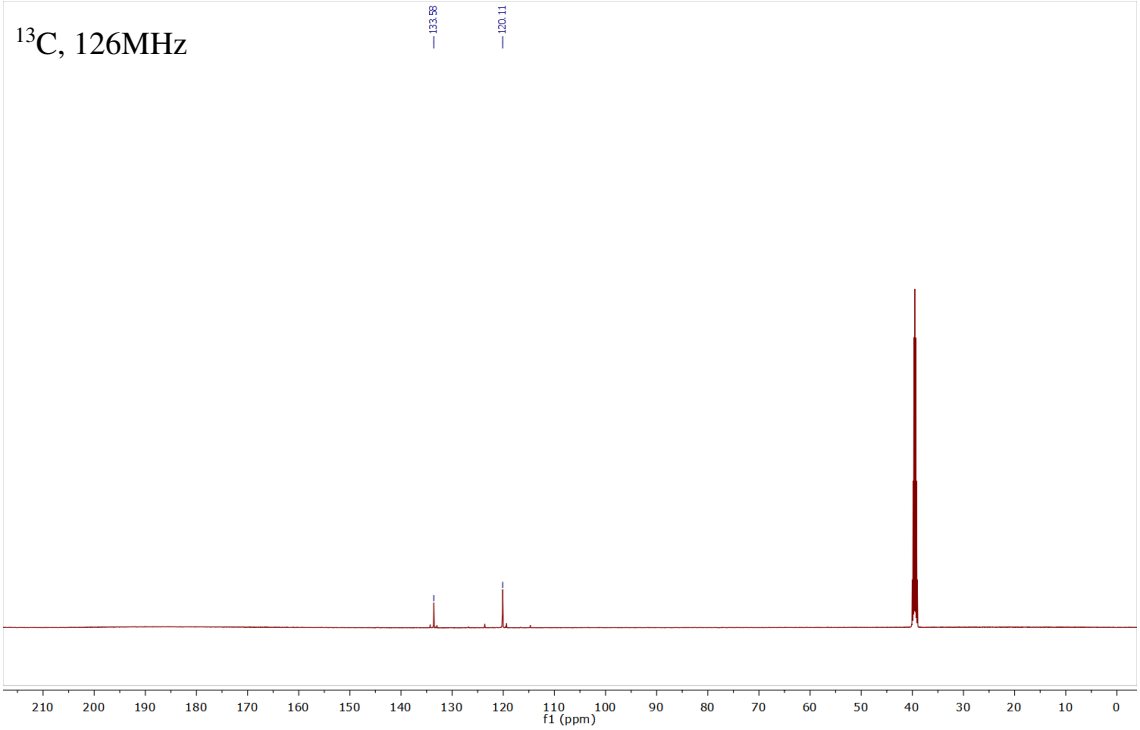
NMR Spectra of polysulfamide **3-5** (d_6-DMSO)

^{1}H, 500MHz



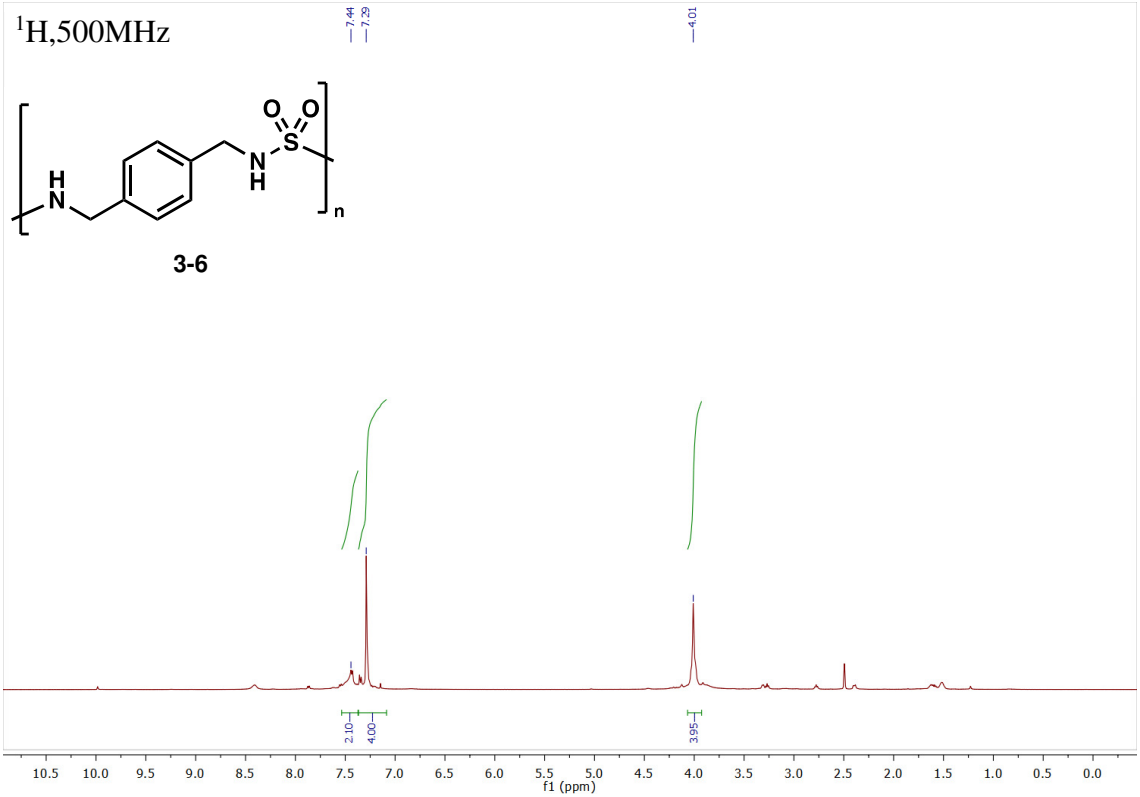
3-5

^{13}C, 126MHz



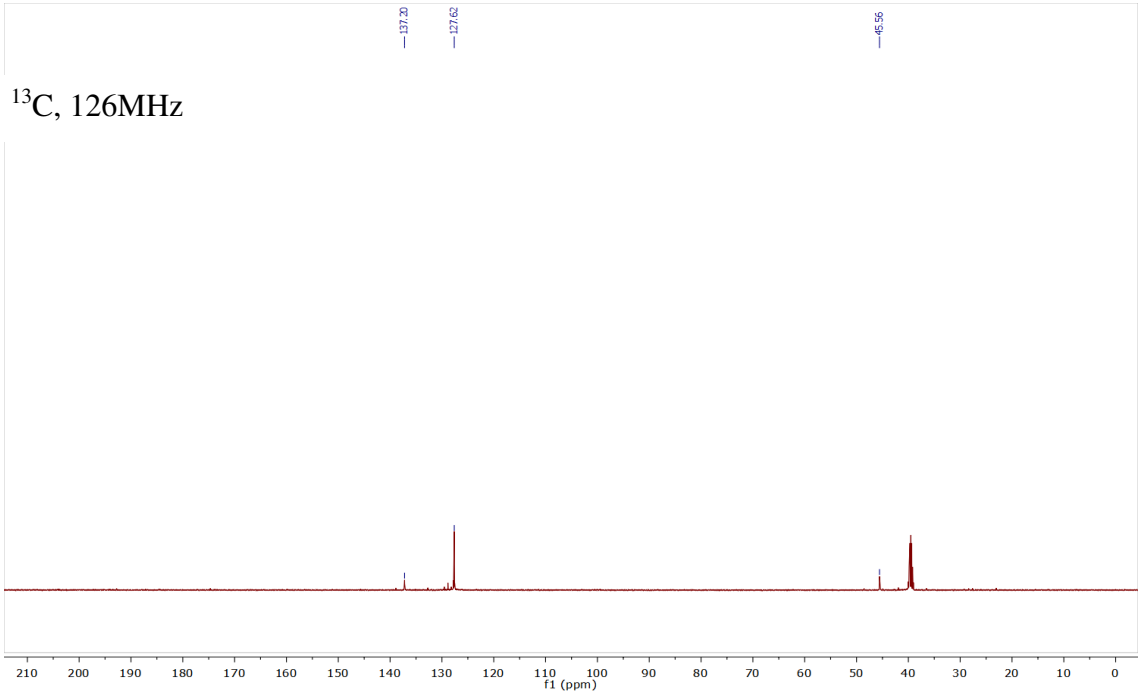
NMR Spectra of polysulfamide **3-6** (d_6-DMSO)

^{1}H,500MHz



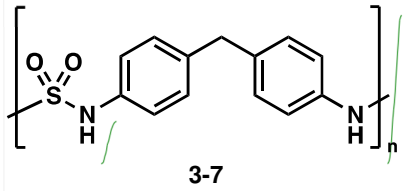
3-6

^{13}C, 126MHz



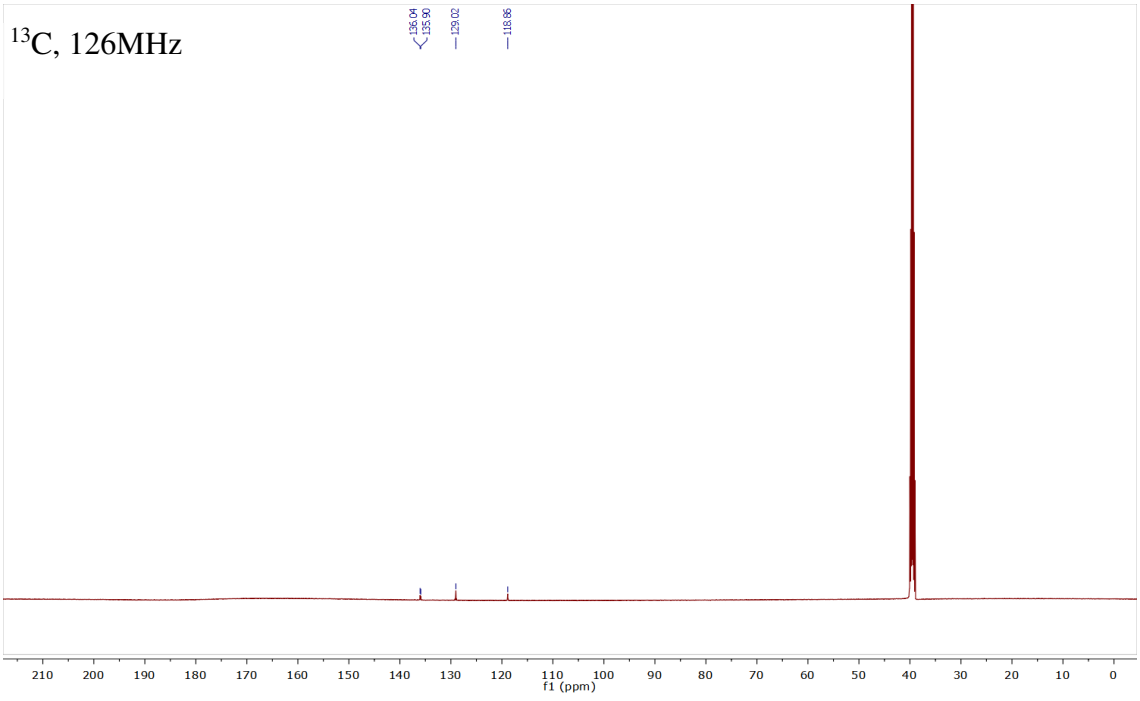
NMR Spectra of polysulfamide **3-7** (d_6-DMSO)

^{1}H, 500MHz

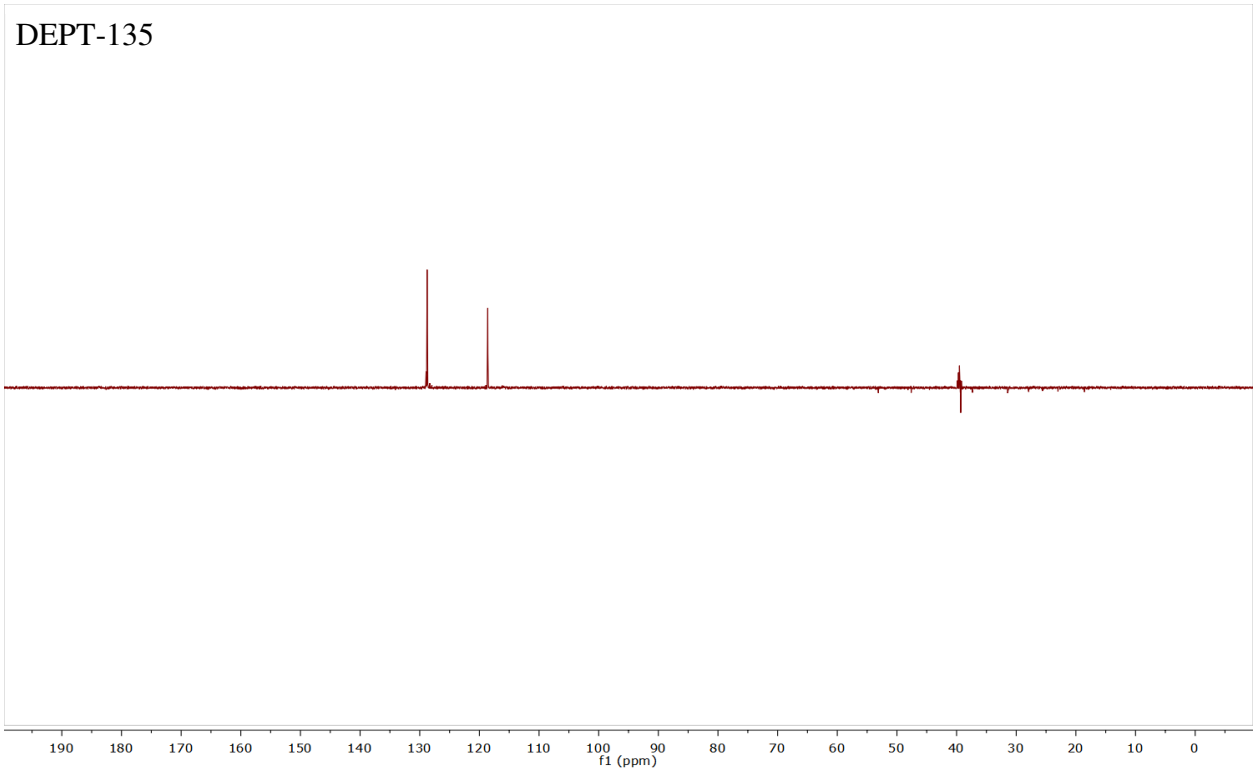


3-7

^{13}C, 126MHz

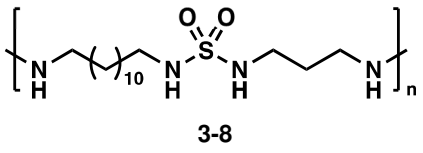


DEPT-135


190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

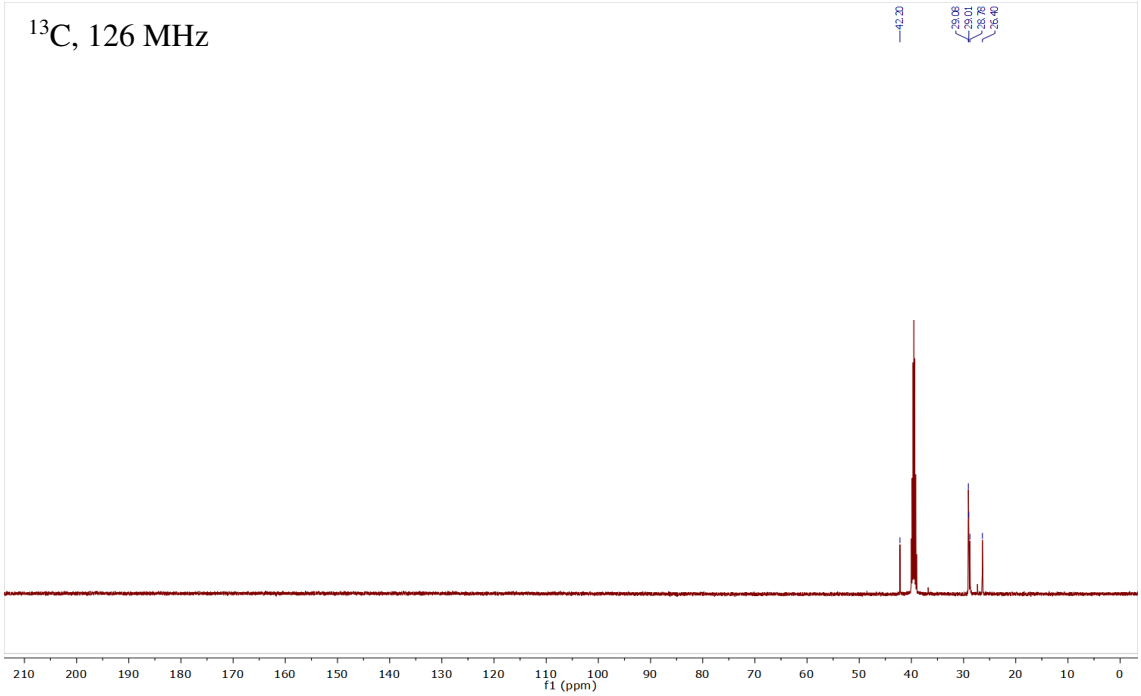
NMR Spectra of polysulfamide **3-8** (d_6-DMSO)

^{1}H, 500MHz

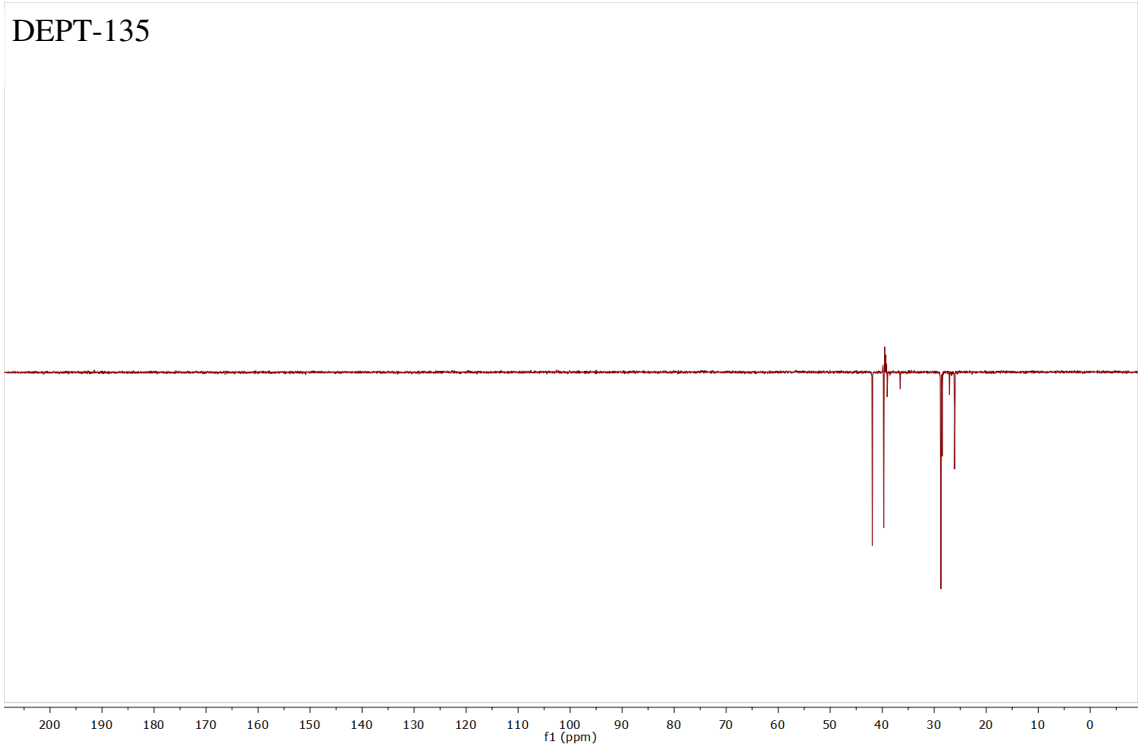


3-8

^{13}C, 126 MHz

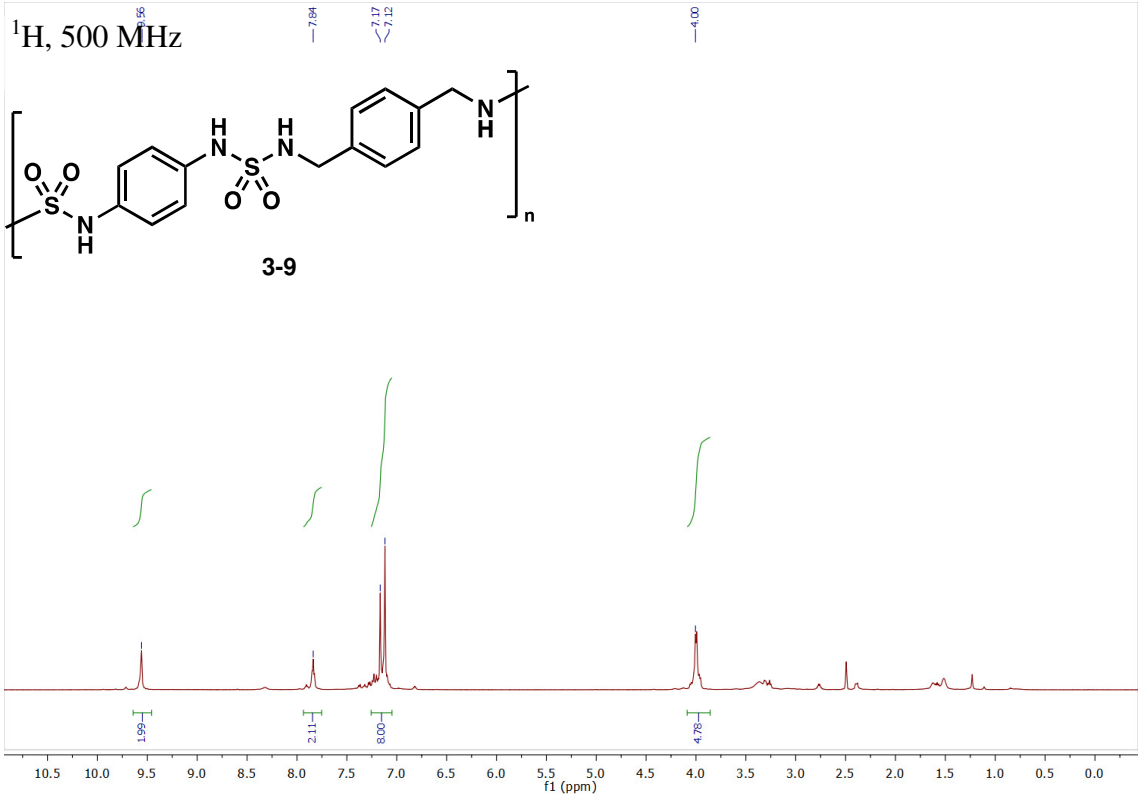


DEPT-135


200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

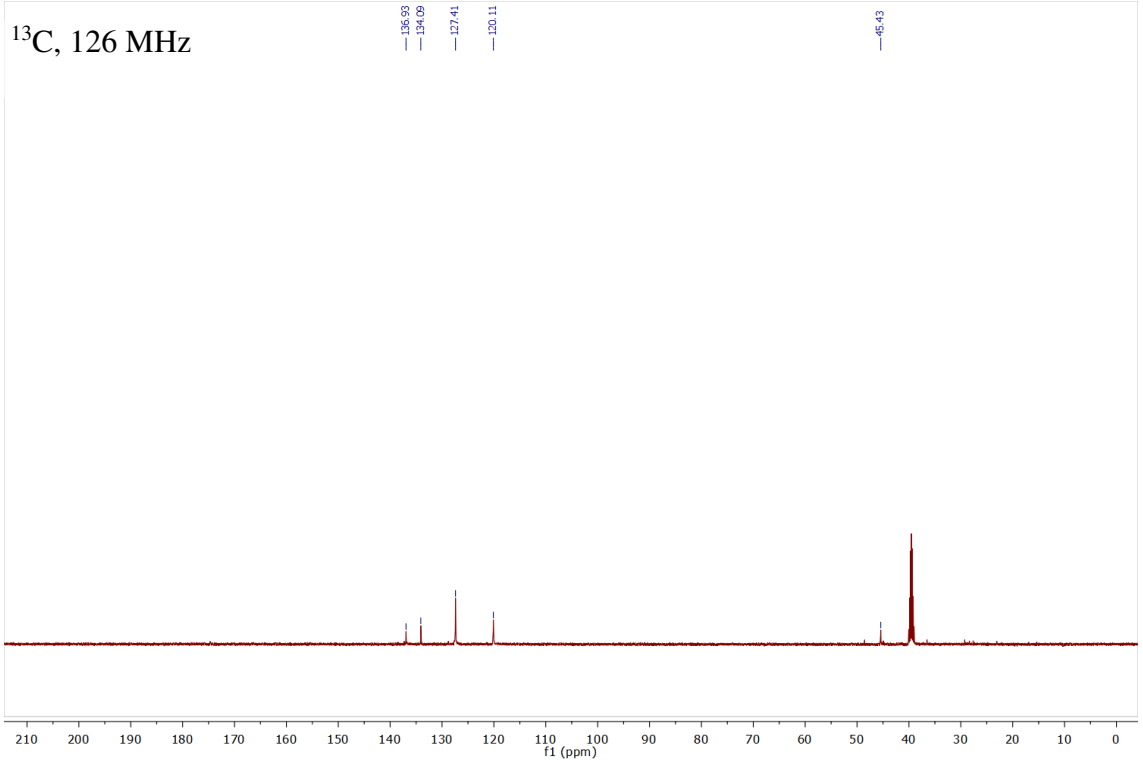
NMR Spectra of polysulfamide **3-9** (d_6-DMSO)

^{1}H, 500 MHz



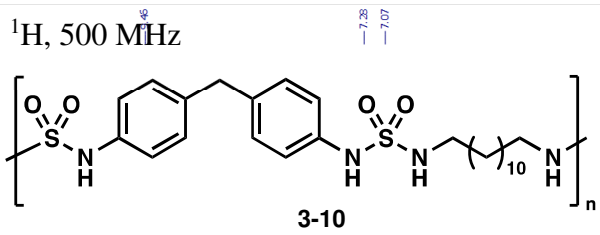
3-9

^{13}C, 126 MHz



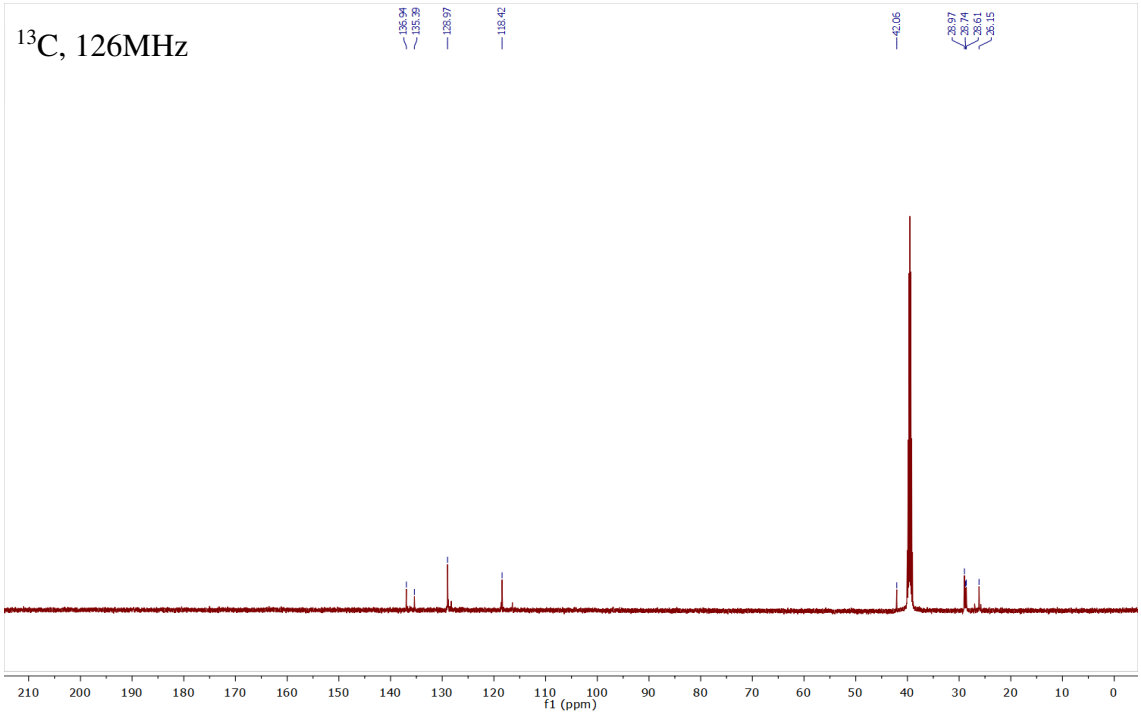
NMR Spectra of polysulfamide **3g** (d_6-DMSO)

^{1}H, 500 MHz

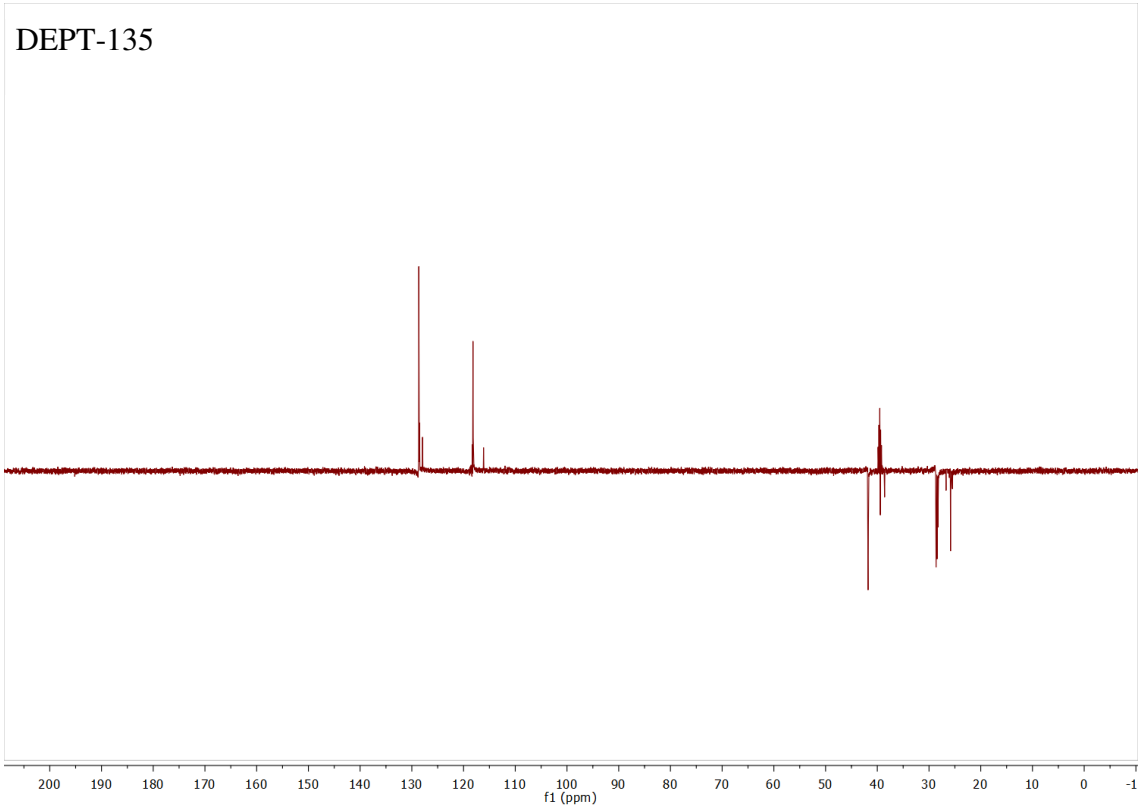


3-10

^{13}C, 126MHz

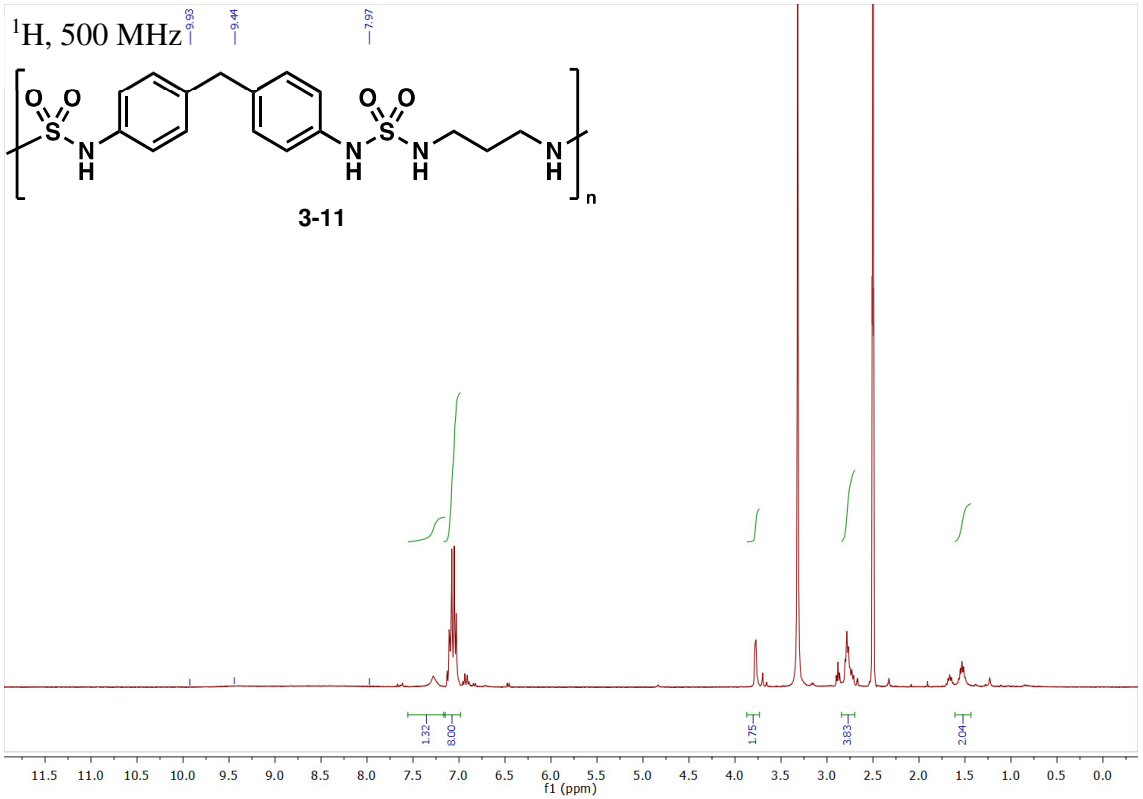


DEPT-135


200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

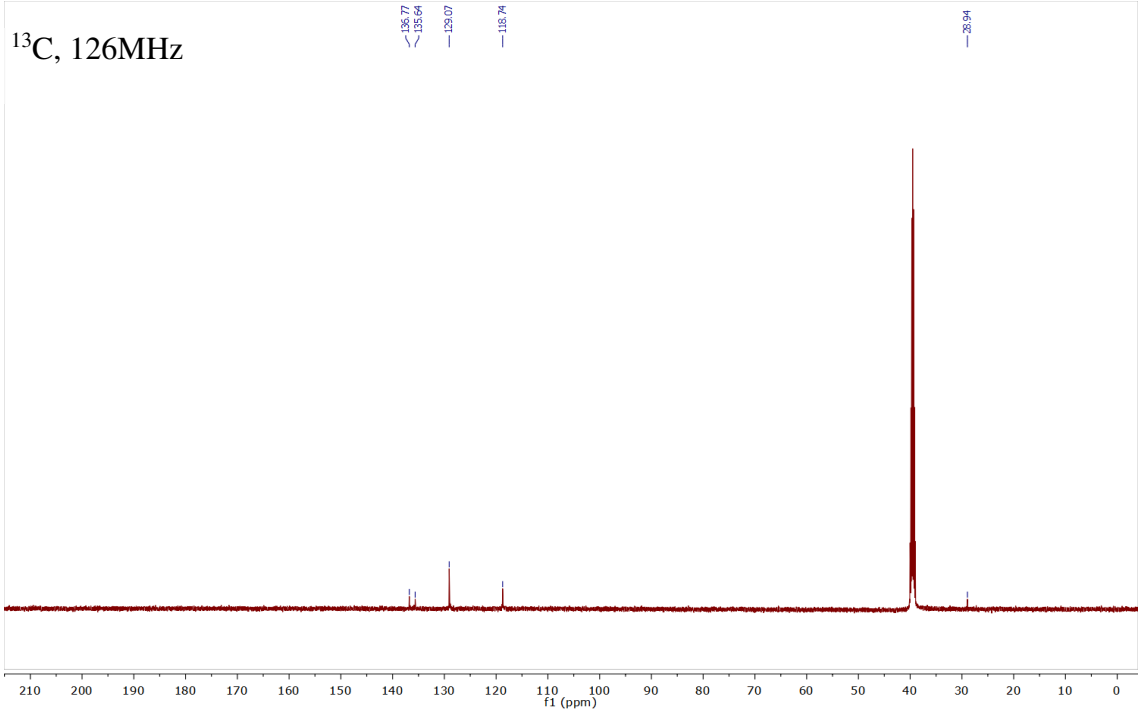
NMR Spectra of polysulfamide **3-11** (d_6-DMSO)

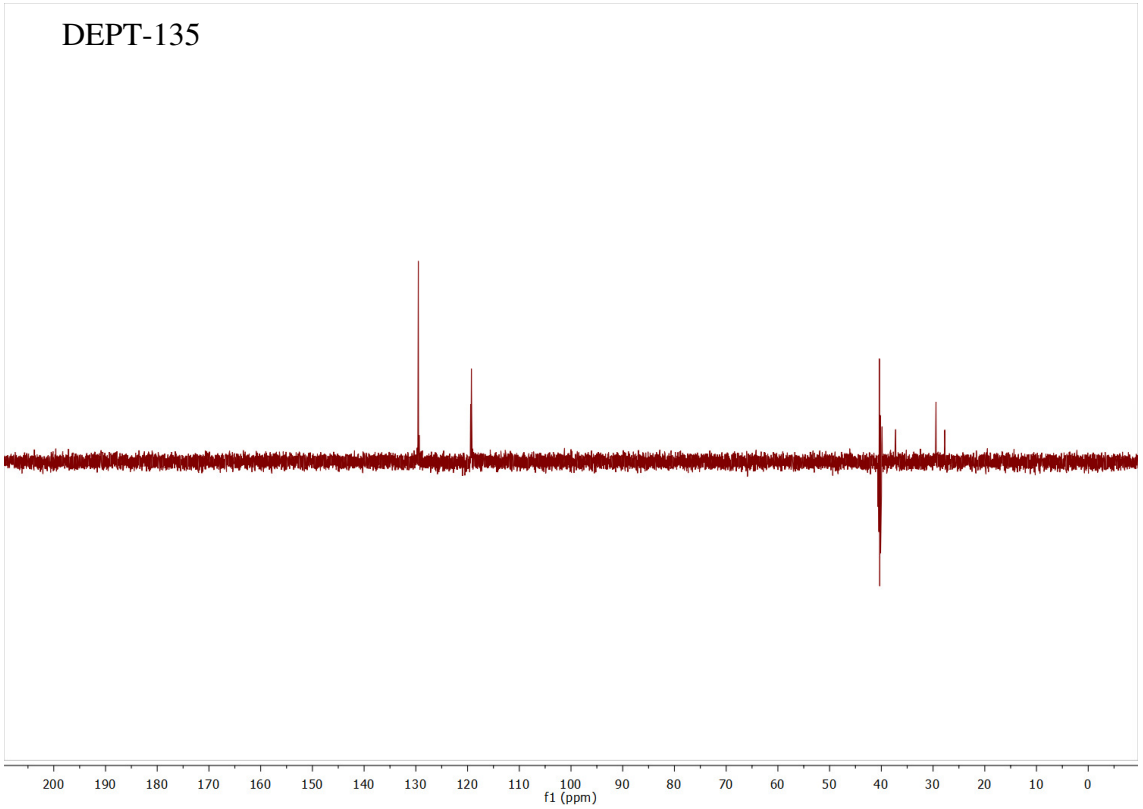
^{1}H, 500 MHz



3-11

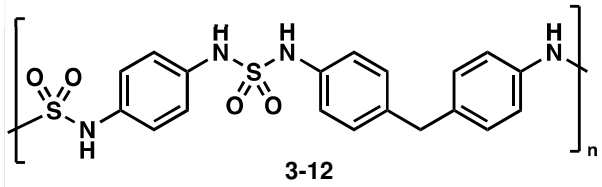
^{13}C, 126MHz




DEPT-135
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

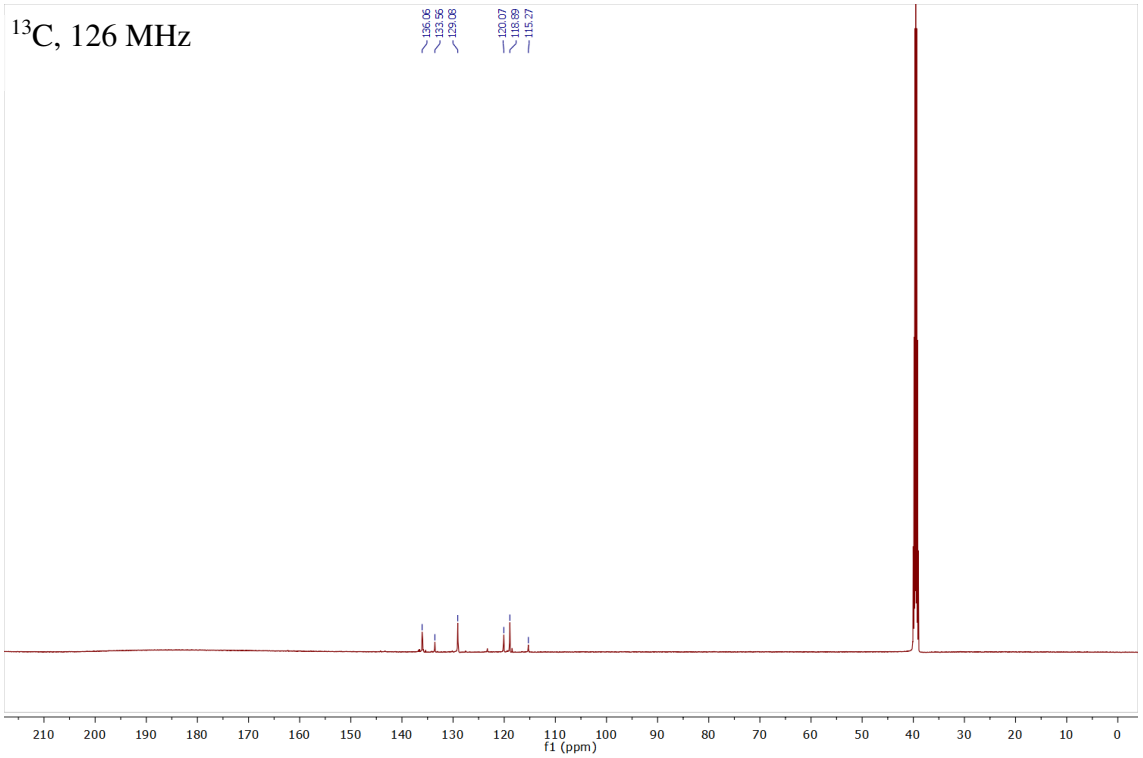
NMR Spectra of polysulfamide **3-12** (d_6-DMSO)

^{1}H, 500MHz

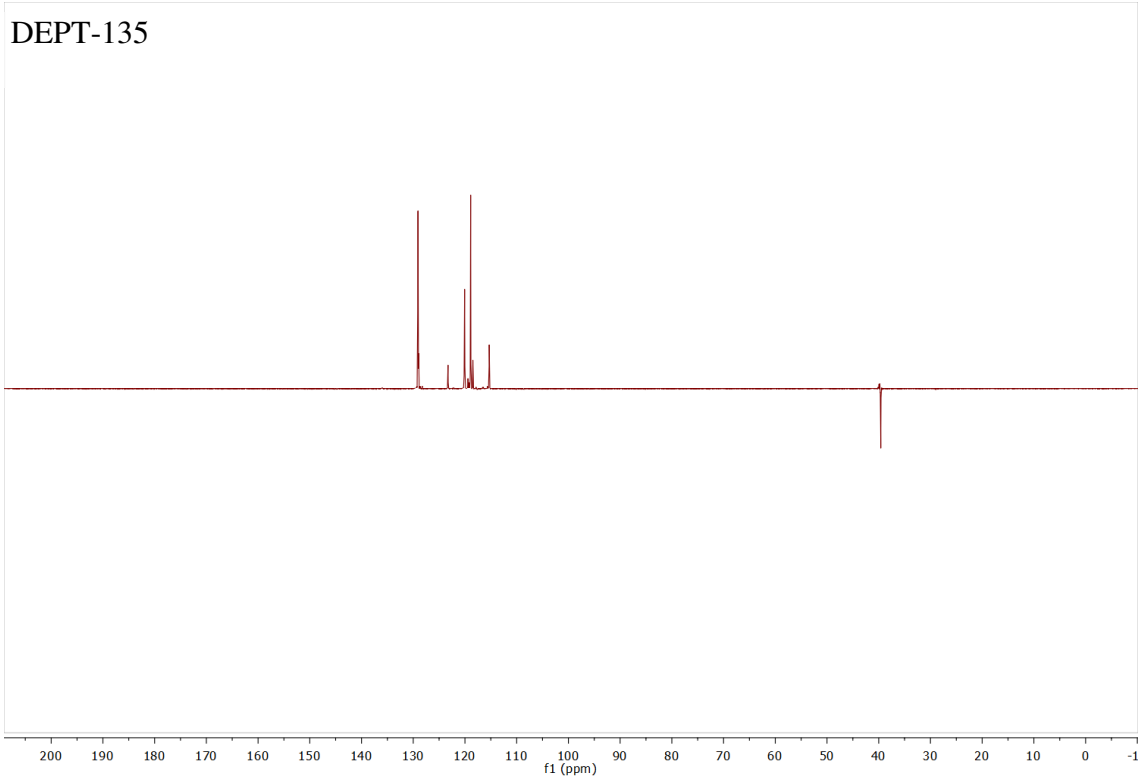


3-12

^{13}C, 126 MHz



DEPT-135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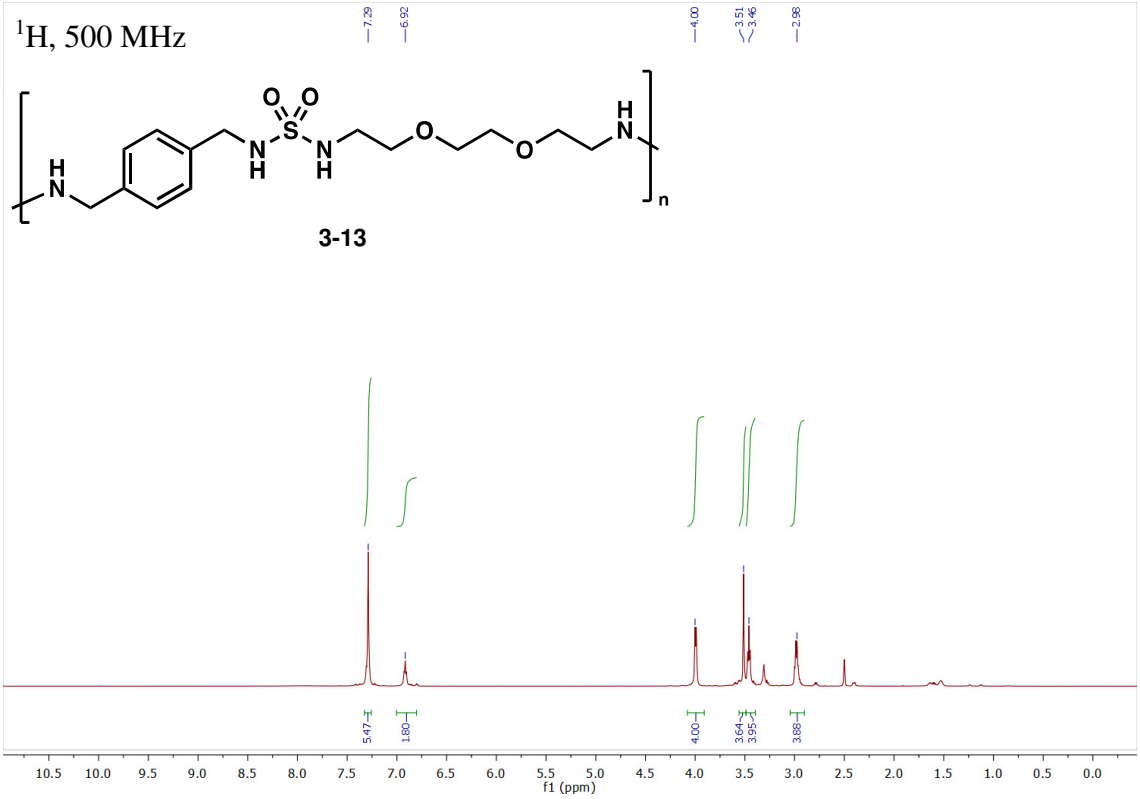
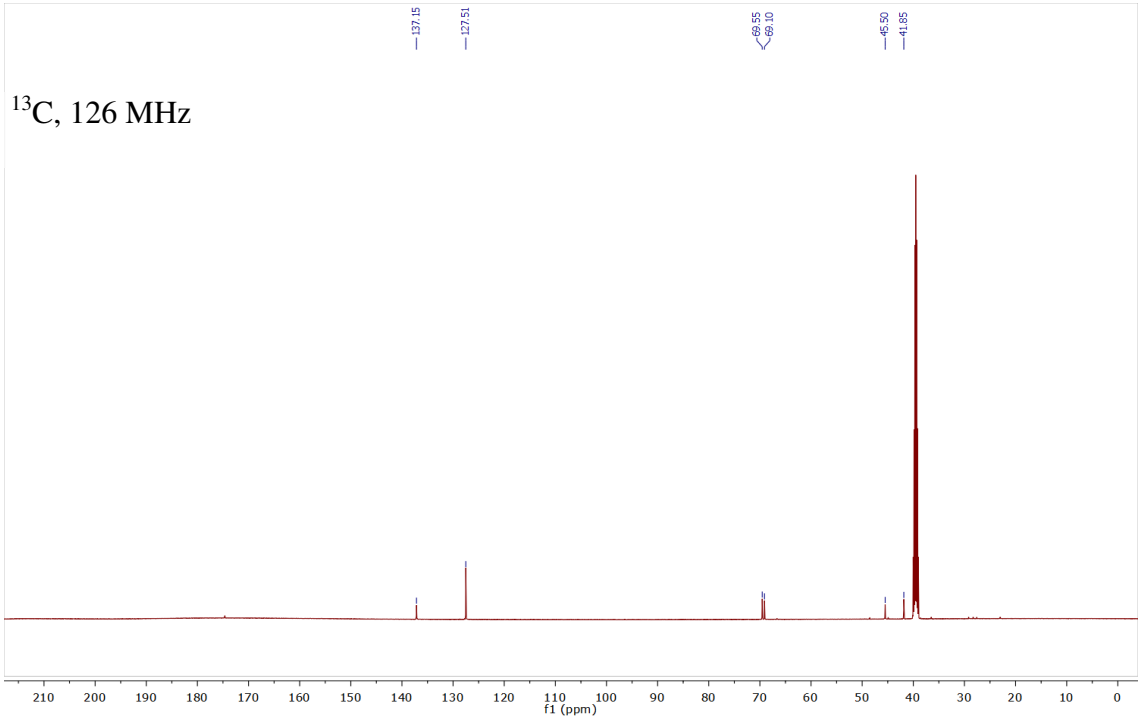
NMR Spectra of polysulfamide **3-13** (d_6-DMSO)

^{1}H, 500 MHz



3-13

^{13}C, 126 MHz



NMR Spectra of polysulfamide **3-14** (d_6-DMSO)

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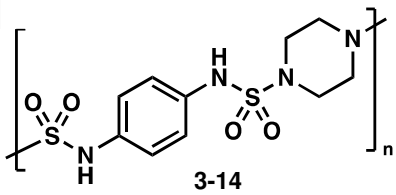
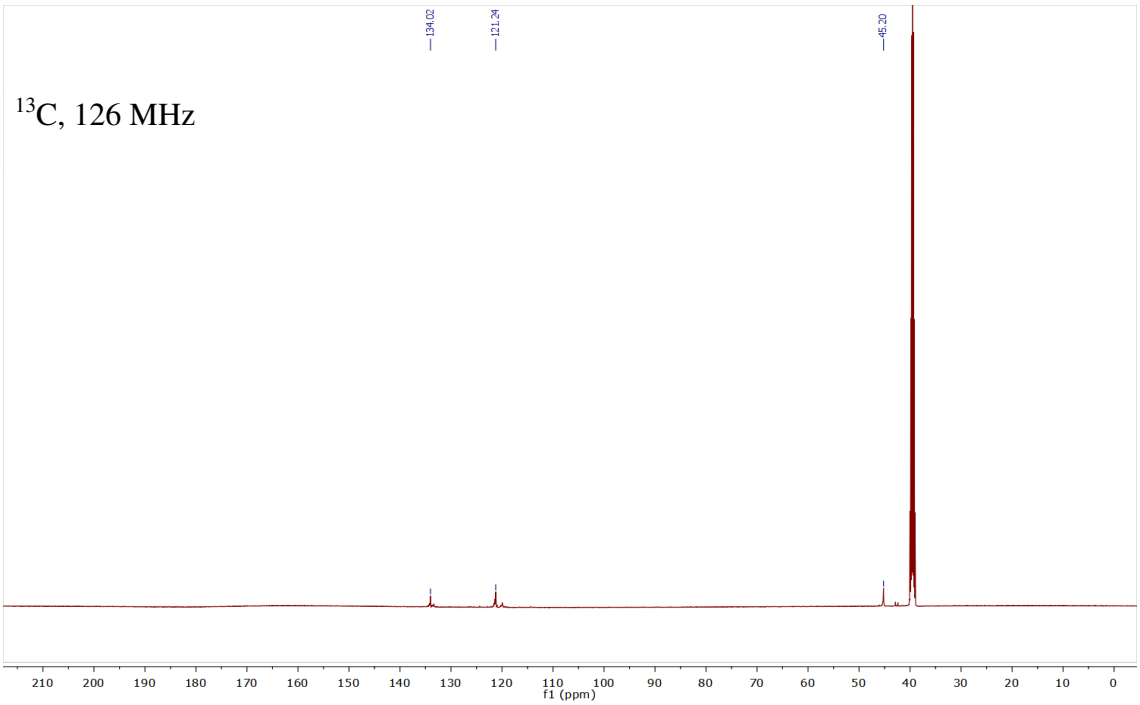


3-14

^{13}C, 126 MHz



NMR Spectra of polysulfamide **3-15** (d_6-DMSO)

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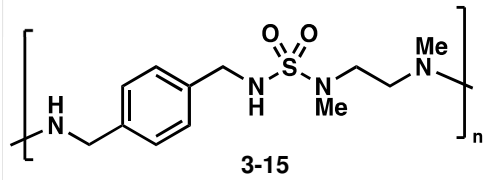
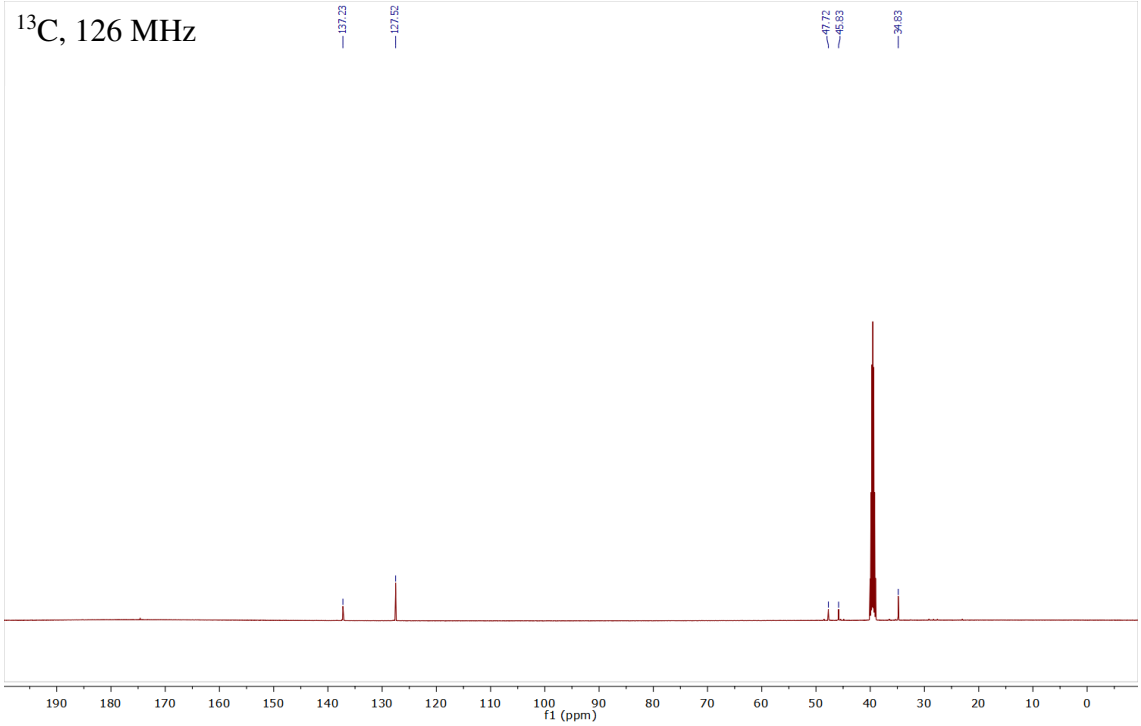


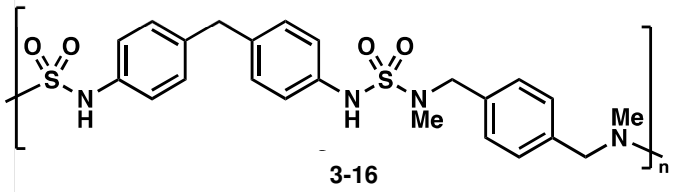
3-15

^{13}C, 126 MHz



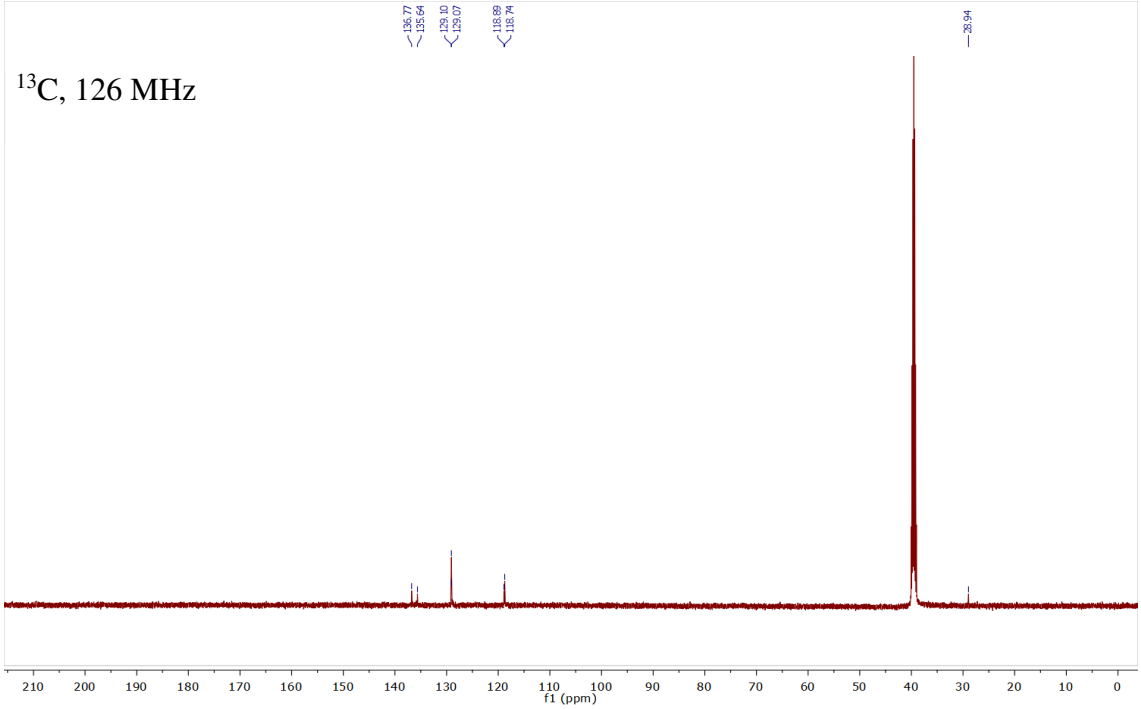
NMR Spectra of Polysulfamide **3-16** (d_6-DMSO)

^{1}H, 500 MHz

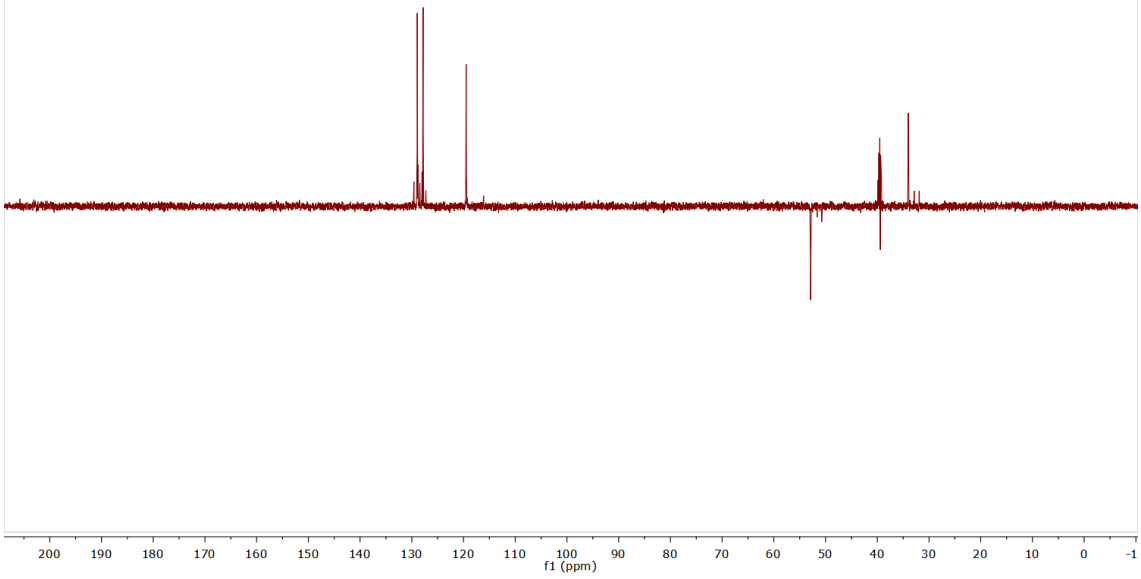


3-16

^{13}C, 126 MHz



DEPT-135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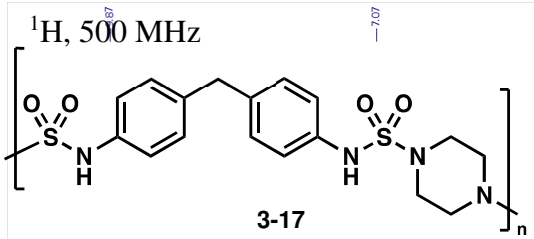
f1 (ppm)

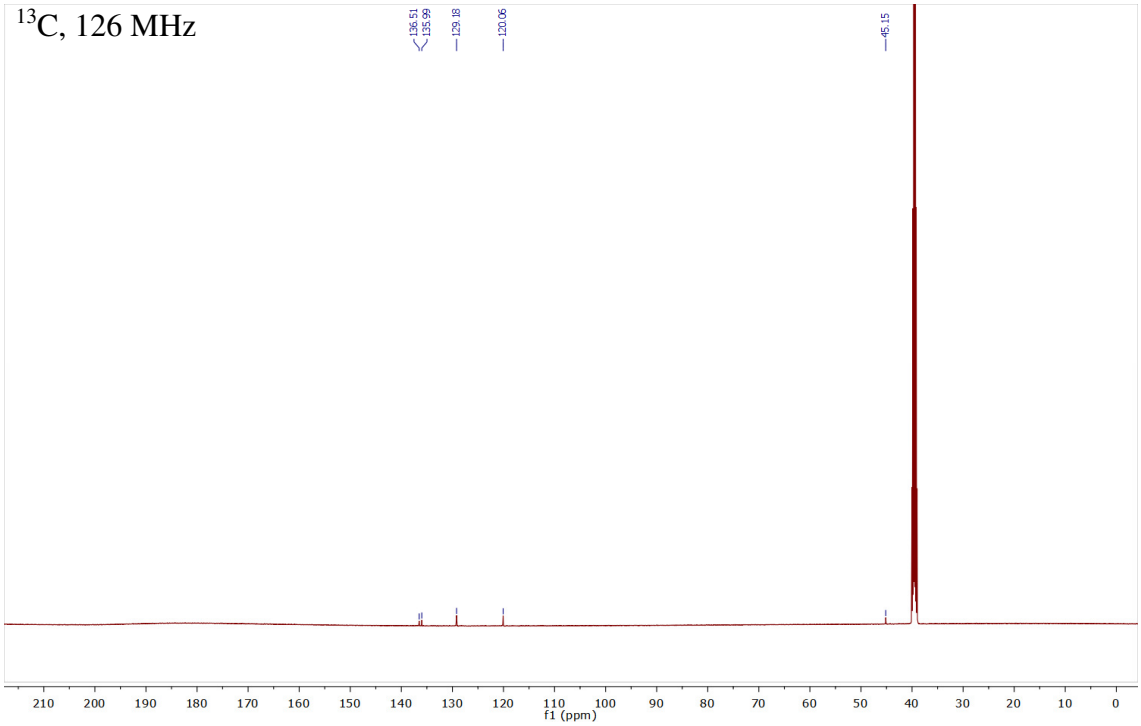
NMR Spectra of Polysulfamide **3-17** (d_6-DMSO)

^{1}H, 500 MHz

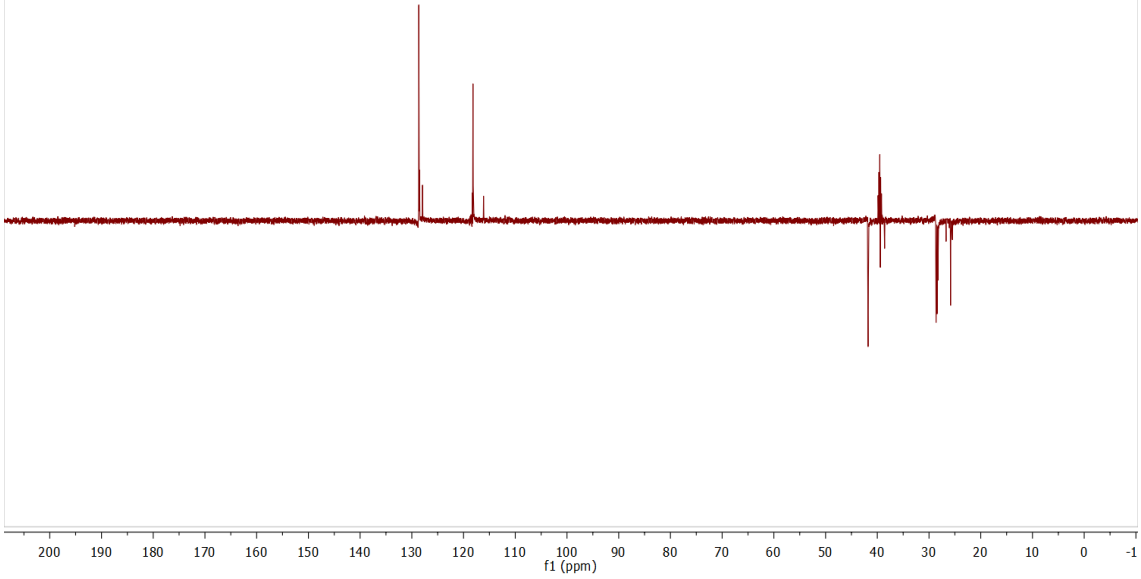


3-17

^{13}C, 126 MHz



DEPT-135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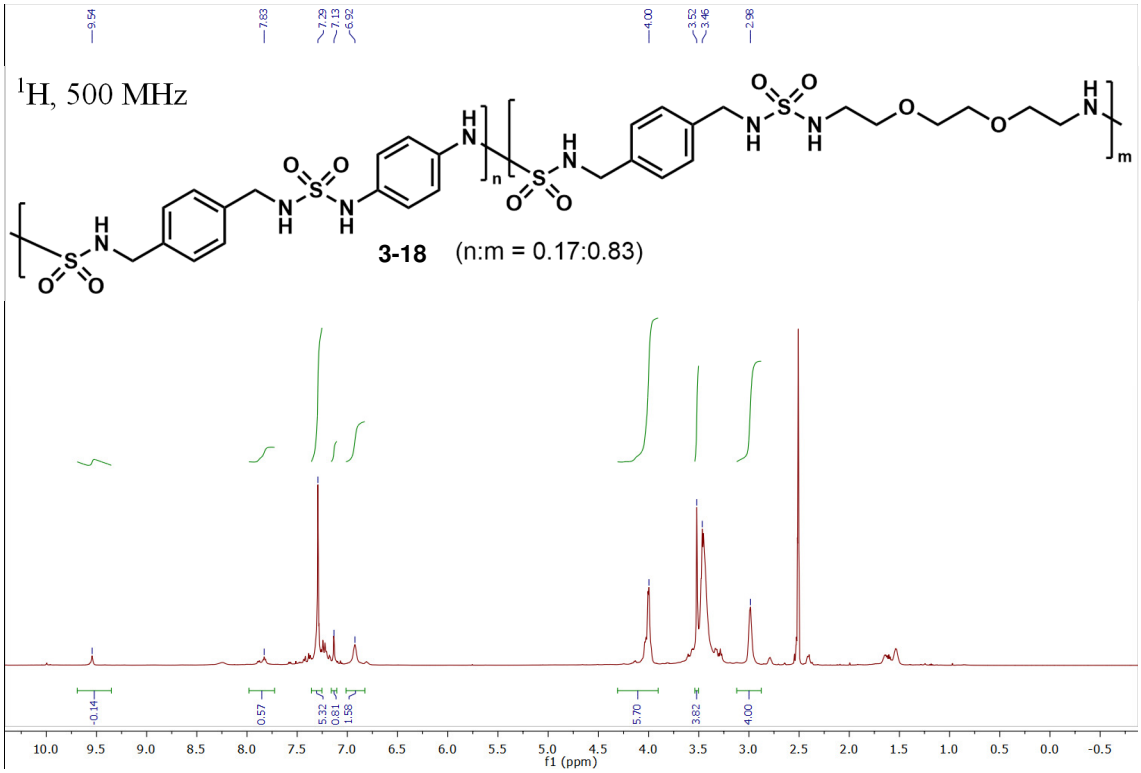
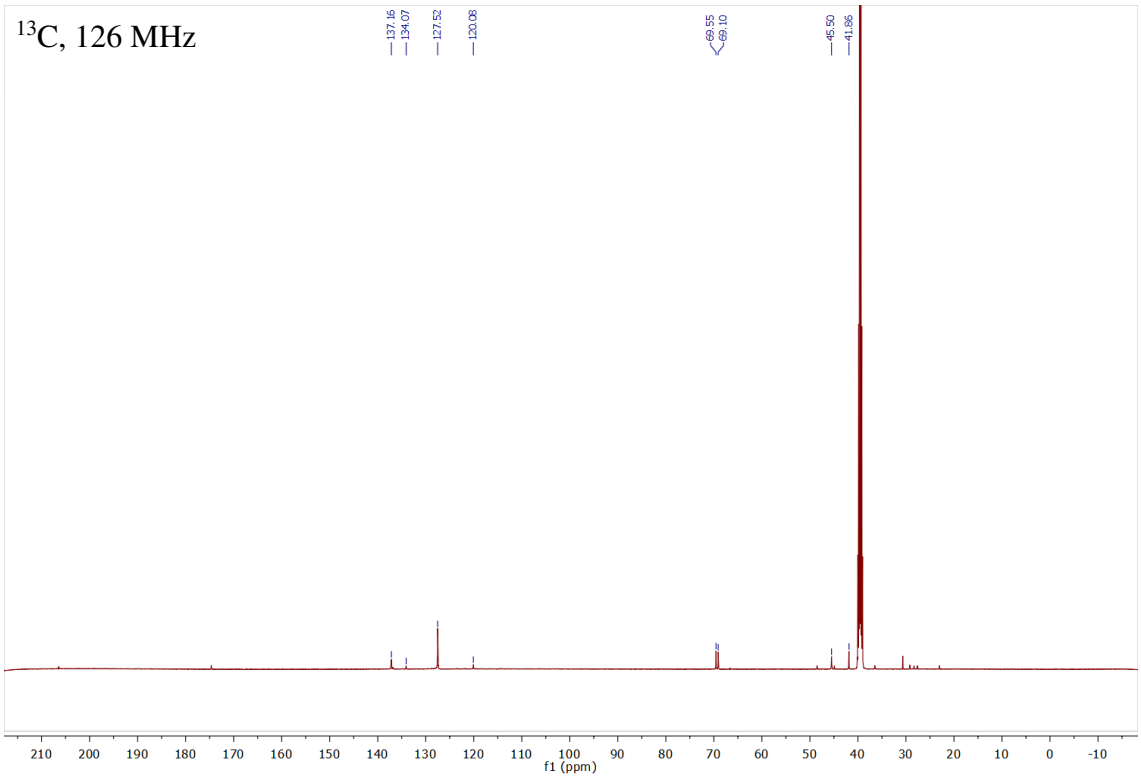
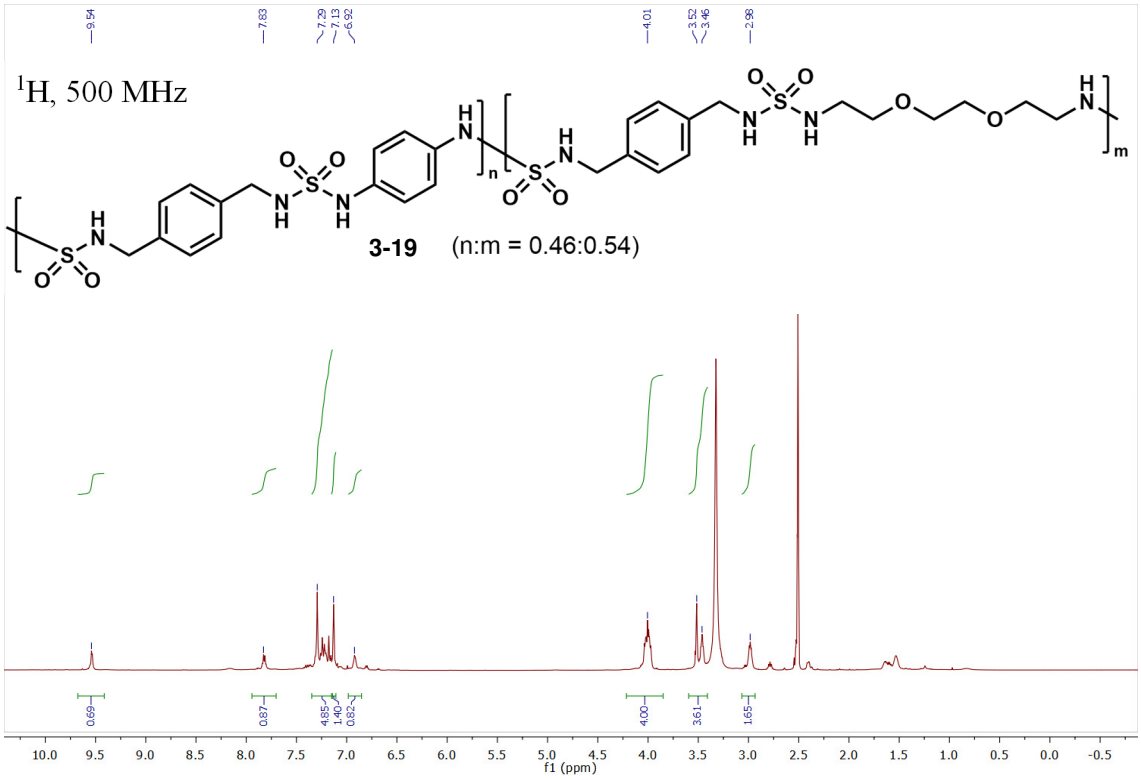
f1 (ppm)

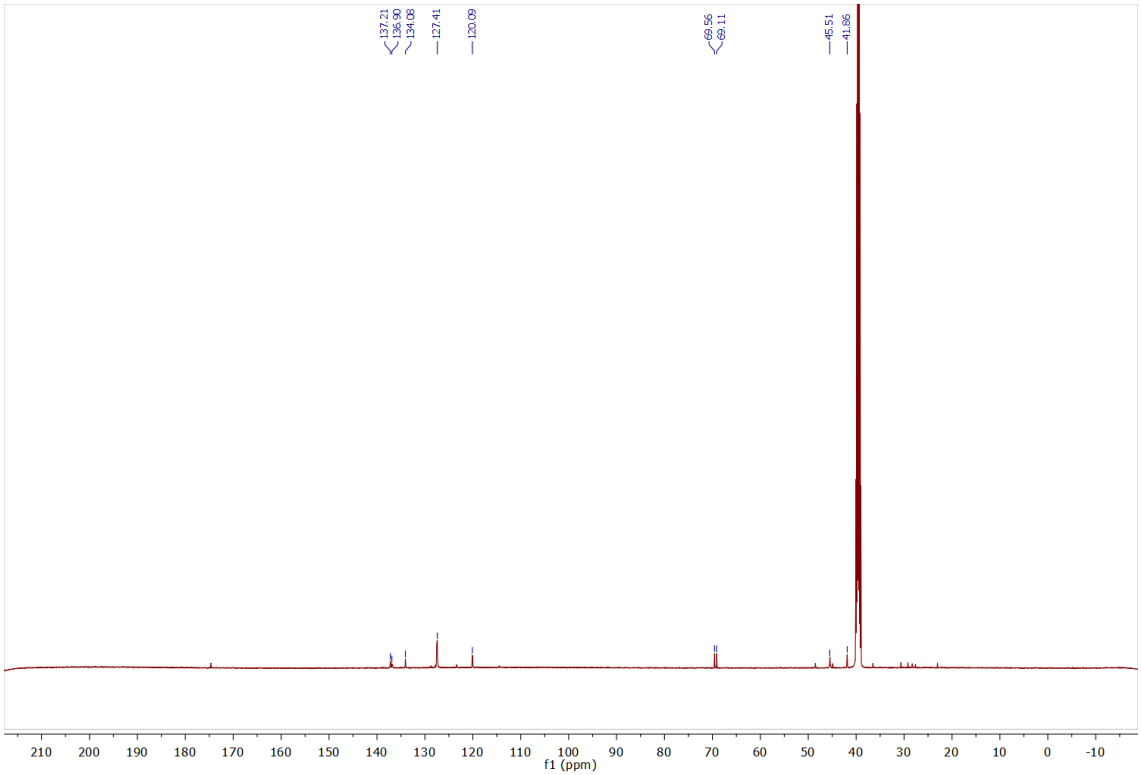
NMR Spectra of Polysulfamide **3-18** (d_6-DMSO)





NMR Spectra of Polysulfamide **3-19** (d_6-DMSO)





3.4.10 Calculating T_g for Polymers 3-18 and 3-19

Predicted T_g values for copolymers **3-18** and **3-19** were determined using the Fox equation:

Equation 3-1: $$\frac{1}{T_{g,mix}} = \sum \frac{\omega_i}{T_{g,i}}$$

Using the experimental T_g values obtained for **3-9** (T_g = 170 °C) and **3-13** (T_g = 46 °C)

Table 3-2. Predicted vs. experimental T_g values for copolymers **3-18** and **3-19***

Polymer	***m:n***	**ω_m**	**ω_n**	**Predicted T_g (°C)**	**Experimental T_g (°C)**
3-18	**0.2:0.8**	**0.18**	**0.82**	**53**	**62**
3-19	**0.5:0.5**	**0.47**	**0.53**	**70**	**88**

*Adapted with permission from the Royal Society of Chemistry (*Ibid.*)

The theoretical Tg of each polymer was significantly lower than the experimental Tg determined through DSC analysis. These discrepancies are likely the result of intermolecular interactions such as hydrogen bonding between polymers.

3.5 References

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CHAPTER IV

SYNTHESIS OF AB TYPE MONOMERS

In the field of condensation polymerization, the simplest way to increase the molecular weight of a polymer is to synthesize an AB-type monomer. This eliminates a major hurdle in the perfection of step-growth polymerization: the stoichiometric balance of AA and BB type monomers. When two monomers are used in a step-growth polymerization, the Carothers equation expands to[1]:

Equation 4-1: $DP_n = (1 + r)/(1 + r - 2rp)$

Where the new variable r is the stoichiometric ratio of the two monomers. Thus, whenever there is an excess of one of the involved monomers, the degree of polymerization begins to decrease. This is why the degree of polymerization in step-growth polymerization is highly dependent on the purity of the monomers used. However, by placing both functional groups involved in the polycondensation on the same molecule, the stoichiometric balance of the monomers is automatically 1:1 (r = 1), and the degree of polymerization becomes dependent on the degree of monomer conversion as in the ideal case mentioned previously. Therefore, in an attempt to maximize the molecular weight of the sulfamides obtained, work began on the synthesis of an AB-type monomer. This monomer would contain both the amine and sulfamoyl fluoride functionalities essential to SuFEx coupling.

Since there was already a point of comparison in the form of polymers **3-5** and **3-6**, initial work began on the synthesis of AB-type monomers derived from amines *p*-phenylenediamine and *p*-xylenediamine. The general plan for these two amines (Figure 4-1) was to first protect one of the amino groups with a Boc functional group. The resulting compound could then be reacted with the fluorosulfonylating reagent **2-7** to transform the remaining unprotected amine to a sulfamoyl fluoride. This asymmetrically substituted diamine would act as a bench-stable precursor to a polysulfamide. The Boc group would not be removed until polymerization was desired to prevent the monomer from autopolymerizing over time.

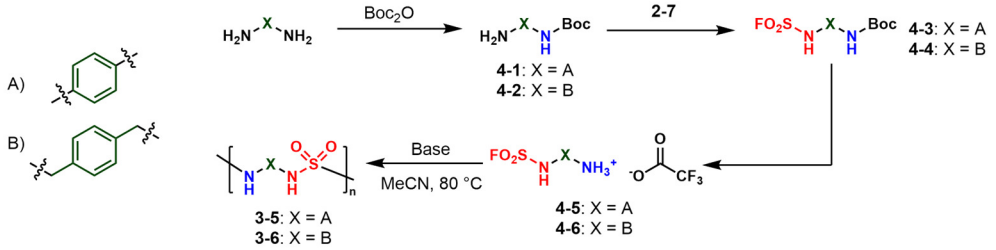


Figure 4-1. Synthetic scheme for the AB polymerization of polysulfamides

The Boc protection step has been previously covered by many previous studies, and proceeded without incident aside from some poor yields. Likewise, the now familiar fluorosulfonylation step with reagent **2-7** also proceeded smoothly. The only difference in procedure came in the purification step, where column chromatography was immediately performed with no aqueous workup due to concerns with premature cleaving of the Boc group by aqueous acid. In total, two monomers were successfully synthesized using this method, **4-5** and **4-6**.

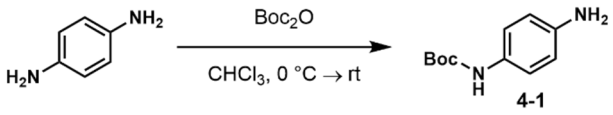
The deprotection reaction was performed using an excess of trifluoroacetic acid (TFA) in DCM at room temperature. A color change in the reaction mixture indicated a near-instantaneous deprotection. After removing the solvent and any excess TFA, leaving behind the trifluoroacetate salt of the deprotected monomer, acetonitrile and base were directly added to start polymerization. For monomer **4-6**, the polymerization proceeded smoothly, producing polymers of molecular weights similar to those obtained through AA-BB polymerization (M_n = 3.1 kg/mol, $Đ$ = 1.67). While the lack of an increase in molecular weight was somewhat disappointing, it was still interesting to show that polysulfamide formation could still occur through this avenue of synthesis.

Interestingly, the AB monomer based on *p*-phenylenediamine, **4-5** did not produce a polymer when subjected to the same procedure. Instead, the solid material isolated from the reaction mixture was completely water soluble, and dissolved in saturated ammonium chloride solution, unlike the polymer synthesized through AA/BB polymerization. The NMR of this material was not very enlightening, showing what appears to be a diverse mixture of aromatic materials. Believing unremoved TFA to be the culprit for this lack of polymer formation, the intermediate deprotected AB monomer was isolated. This proved to be rather simple, requiring only a simple aqueous extraction from distilled water. This provided the intermediate, which appeared to be uncontaminated by NMR. However, after treating this compound with pyridine at 80 °C, the same water-soluble product as before was the result. For a full discussion of the findings from this reaction, see section 4.2.4. Needless to say, this study of the synthesis and application of AB monomers is by no means complete, and the reaction conditions are still in the process of optimization.

4.1 Experimental

4.1.1 Synthesis of mono-Boc protcted diamines

Synthesis of N-(*tert*-butoxycarbonyl)-1,4-phenylenediamine (4-1)

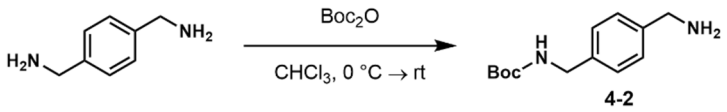


Compound **4-1** was prepared according to literature procedure.[2] To a solution of *p*-phenylenediamine (1.08 g, 10.0 mmol. 3 equiv) and K_2CO_3 (511 mg, 3.70 mmol, 1.2 equiv) in THF (10 mL) was added Boc_2O (720 mg, 3.30 mmol, 1 equiv) dropwise over 30 min. The reaction mixture was stirred at room temperature for 15 h. The reaction mixture was transferred to a separatory funnel and diluted with H_2O (20 mL). The mixture was extracted with DCM (3 x 20 mL). The organic fractions were combined and washed with brine (1 x 20 mL) before drying over $MgSO_4$ and concentrating *in vacuo* to obtain an orange solid. This solid was purified through column chromatography (SiO_2, 35:65 EtOAc:hexanes) to obtain the title compound as a yellow solid (674 mg, 98%). The spectroscopic data for this compound were identical to those reported in the literature.[2]

^{1}H NMR (d_6-DMSO, 400 MHz) δ: 8.77 (s, 1H), 7.06 (d, J = 8.2 Hz, 2 H), 6.46 (d, J = 8.2 Hz, 2 H), 4.72 (s, 2 H), 1.44 (s, 9 H) ppm.

^{13}C NMR (d_6-DMSO, 100 MHz) δ: 153.0, 143.8, 128.4, 120.1, 113.8, 78.0, 28.1 ppm.

Synthesis of N-(*tert*-butoxycarbonyl)-4-(aminomethyl)benzylamine (4-2)



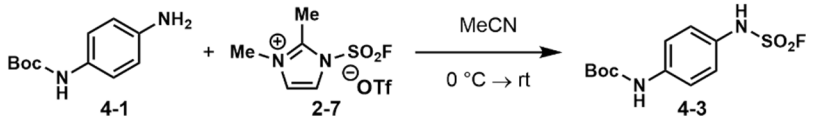
Compound **4-2** was prepared according to literature procedure, with some alterations.[3] To a solution of *p*-xylylenediamine (1.00 g, 7.4 mmol, 2.1 equiv) in $CHCl_3$ (10 mL) cooled in an ice water bath, a solution of Boc_2O (0.77 g, 3.5 mmol, 1 equiv) in $CHCl_3$ (25 mL) was added dropwise over 4 h. The reaction mixture was then brought to room temperature and stirred for 19 h. The resulting mixture was filtered over Celite and washed with cold $CHCl_3$ (25 mL). The filtrate was concentrated *in vacuo* to yield a yellow oil. DCM (25 mL) and H_2O (25 mL) was added to the oil, and the organic layer was isolated. The aqueous layer was extracted with DCM (3 x 15 mL). The organic fractions were combined and dried over $MgSO_4$ before concentrating *in vacuo* to yield a white solid. The solid was purified by column chromatography (SiO_2, 0:10 to 1:9 MeOH:DCM) to obtain the title compound as a white solid (206 mg, 24%). The spectroscopic data for this compound were identical to those reported in the literature.[4]

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.30–7.23 (m, 4 H), 4.83 (br, 1 H), 4.29 (d, J = 5.9 Hz, 2 H), 3.86 (s, 2 H), 1.66 (s, 2 H), 1.46 (s, 9 H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz) δ: 155.9, 142.2, 137.6, 127.7, 127.4, 77.2, 46.1, 44.4

4.1.2 Synthesis of AB-type Monomers

Synthesis of AB monomer 4-3



To a solution of compound **4-1** (400 mg, 1.82 mmol, 1 equiv) in DCM (5 mL) cooled in an ice water bath, compound **2-7** (630 mg, 1.82 mmol, 1 equiv) was added. The reaction was then brought to room temperature and stirred for 3 h. The solvent was removed *in vacuo* to reveal a dark brown solid. The crude material was then purified by column chromatography (SiO_2, 1:2 EtOAc:hexanes) to yield the title compound as a brown solid (476 mg, 85%).

^{1}H NMR (CD_3CN, 500 MHz) δ: 8.58 (br, 1 H), 7.61 (br, 1 H), 7.47 (d, J = 9.0 Hz, 2 H), 7.23 (d, J = 9.0 Hz, 2 H), 1.49 (s, 9 H) ppm.

^{13}C NMR (CD_3CN, 125 MHz) δ: 153.9, 139.9, 129.5, 126.0, 120.2, 80.9, 28.53 ppm.

^{19}F NMR (CD_3CN, 470 MHz) δ: 48.0 ppm.

Synthesis of AB monomer 4-4

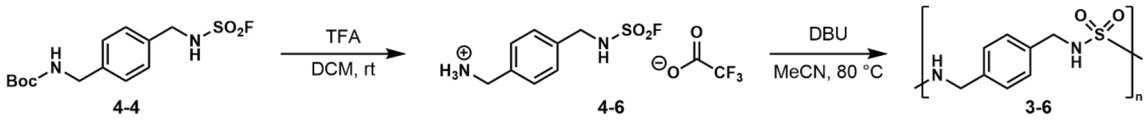
To a solution of compound **4-2** (100 mg, 0.42 mmol, 1 equiv) in MeCN (3 mL) cooled in an ice water bath, compound **2-7** (139 mg, 0.42 mmol, 1 equiv) was added. The reaction was then brought to room temperature and stirred for 3 h. The solvent was removed *in vacuo* to reveal an orange solid. The crude material was then purified by column chromatography (SiO_2, 1:1 EtOAc:hexanes) to yield the title compound as an off-white solid (95 mg, 71% yield).

^{1}H NMR (CD_3CN, 500 MHz) δ: 7.32 (d, *J* = 8.2), 7.28 (d, *J* = 8.2), 7.09 (br, 1 H), 5.79 (br, 1 H), 4.38 (d, *J* = 1.8 Hz), 4.21 (d, *J* = 6.3 Hz), 1.41 (s, 9 H) ppm.

^{13}C NMR (CD_3CN, 125 MHz) δ: 157.1, 141.3, 135.7, 129.1, 128.4, 79.6, 48.4, 44.4, 28.7 ppm.

^{19}F NMR (CD_3CN, 470 MHz) δ: 50.0 ppm.

4.1.3 General Procedure for AB Polymerization (Using 4-4 as an example)



To a solution of **4-4** (20 mg, 66 μmol, 1 equiv) in DCM (1.0 mL), TFA (1.0 mL, excess) was added. The mixture was stirred at room temperature for 30 min. The solvent and excess acid was removed *in vacuo* to yield intermediate **4-6**, which is then used without further purification. The oily residue is then dissolved in MeCN (0.5 mL) and DBU (70 mg, 0.46 mmol, 7 equiv). The reaction mixture is placed in a 80 °C oil bath and stirred for 90 min. The resulting polymer is then precipitated in a centrifuge tube through the addition of Et_2O, until a volume of 15 mL was reached. After centrifuging and removing the

supernatant liquid, the resulting dark orange solid was re-dissolved in DMAc (1 mL) and re-precipitated through the addition of saturated NH_4Cl (aq) until a volume of 15 mL was reached. The solid was then washed with distilled water (2 x 50 mL) and once with isopropanol (50 mL). The polymer was dried *in vacuo* (< 1 mmHg) at 100 ºC for 18 hours to obtain the final polymer as an off-white solid (150 mg). Molecular weight and polymer distribution were determined through SEC.

4.1.4 Results of using 4-3 in the General Procedure

When TFA is added to monomer **4-3**, an immediate color change from dark yellow to bright pink is observed, likely due to the removal of the Boc group from the monomer. After the deprotection step, the remaining oily residue can be mixed with H_2O and extracted with EtOAc to isolate intermediate **4-5** (Figure 4-2). This intermediate retains the *para* substituted aromatic structure expected, and no longer contains the Boc group as indicated by the absence of the peak at 1.49 ppm. The fluorine spectrum of this isolated material contains two signals, one in a similar position to that observed in the starting material, and one corresponding to TFA. Continuing with the general procedure, if **4-5** is dissolved in MeCN at 80 °C and treated with pyridine as a base (7 equiv), after 90 min the reaction mixture will darken. Precipitating in Et_2O will yield a black solid. This solid is soluble in both sat. NH_4Cl and 3.0 M HCl. Examining the NMR of the solid after precipitation in Et_2O shows that the solid bears some similarities to polysulfamide **3-5**, albeit with many other aromatic impurities. The supernatant liquid, when concentrated *in vacuo* appears to contain pyridine, TFA, and oligomers of polymer **3-5** (Figure 4-4). The

peaks present in the supernatant spectrum are farther downfield than those observed in polymer **3-5**, but this is likely due to the presence of pyridine. Based on the integrations, the oligomers have a DP_n of approximately 6.5 (Figure 4-5). It is likely that these smaller oligomers are more soluble in ether, so they are removed from the reaction upon precipitation. The identity of the leftover solid has yet to be determined.

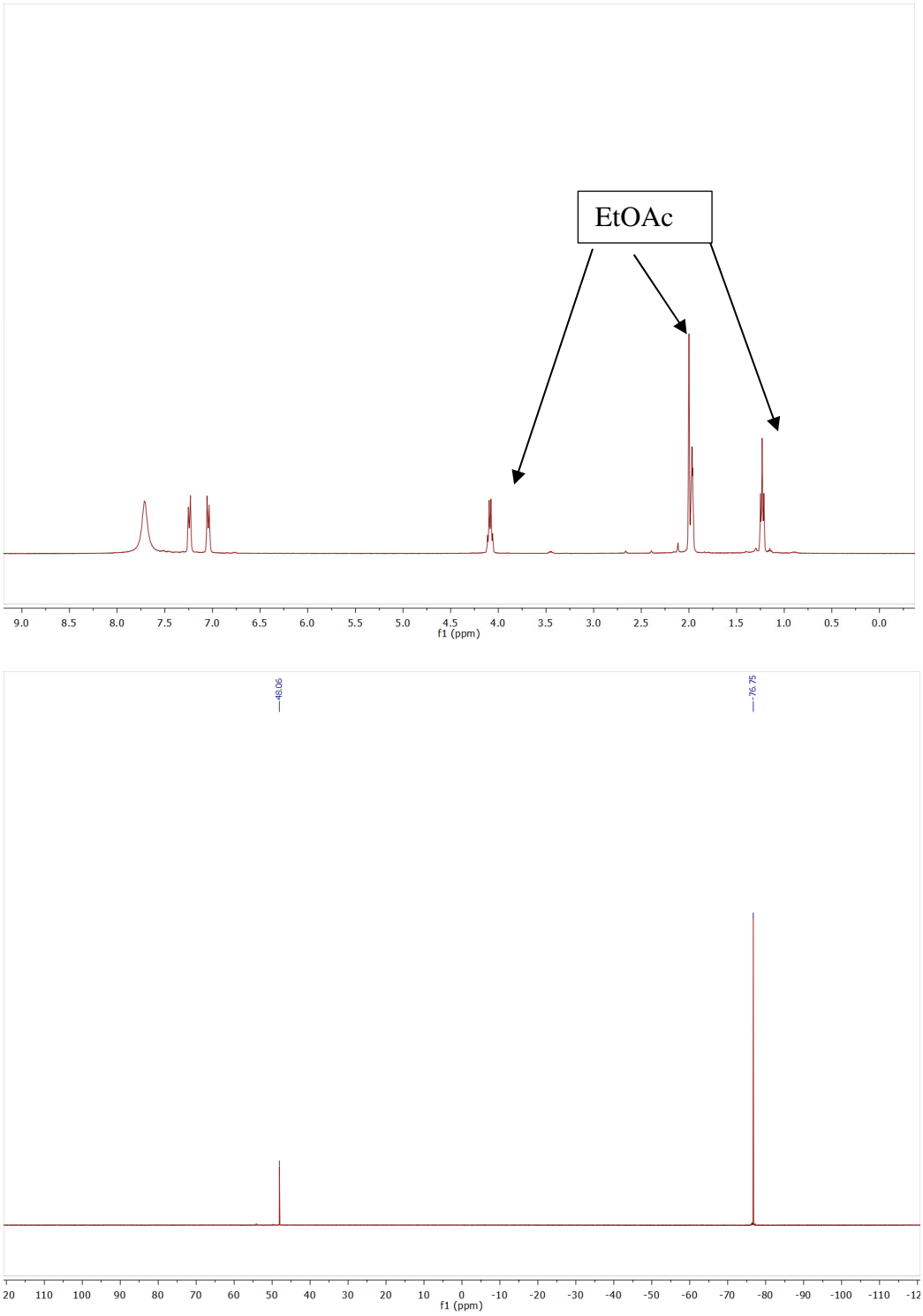


Figure 4-2. Top) ^{1}H-NMR (CD_3CN, 400 MHz) of the crude product obtained after treating compound **4-3** with TFA. Bottom) FNMR (CD_3CN, 376 MHz) of the same material

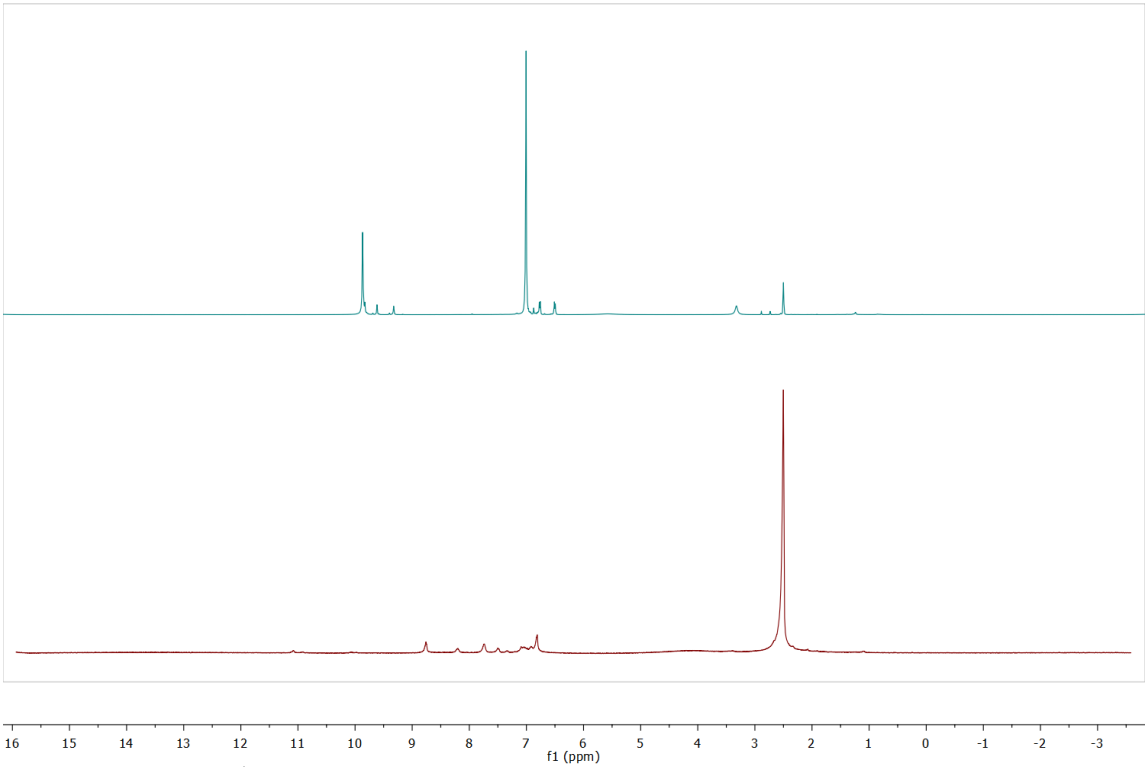


Figure 4-3. Top) ^{1}H NMR (d_6-DMSO, 500 MHz) of polymer **3-5** obtained via AA-BB polymerization. Bottom) HNMR (d_6-DMSO, 400 MHz) of the solid left over after the precipitation of the reaction mixture obtained from the AB polymerization of monomer **4-3**

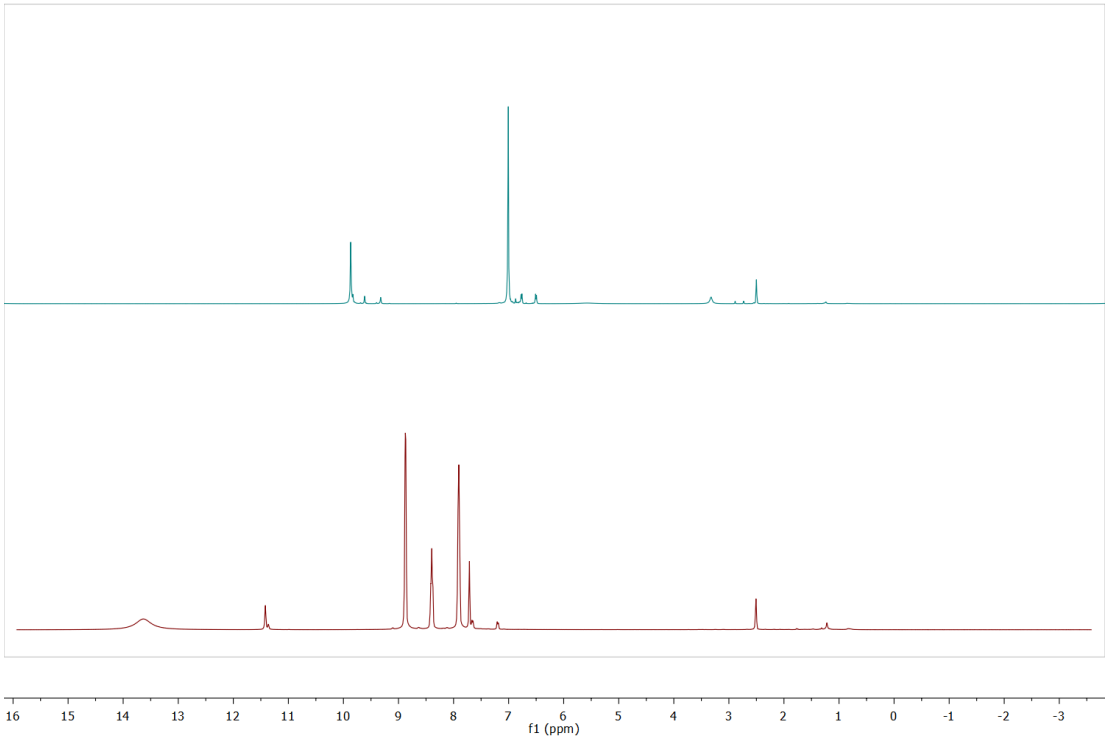


Figure 4-4. Top) ^{1}H NMR (d_6-DMSO, 500 MHz) of polymer **3-5** obtained via AA-BB polymerization. Bottom) HNMR (d_6-DMSO, 400 MHz) of the residue left over after drying the supernatant liquid from the precipitation of the reaction mixture obtained from the AB polymerization of monomer **4-3**

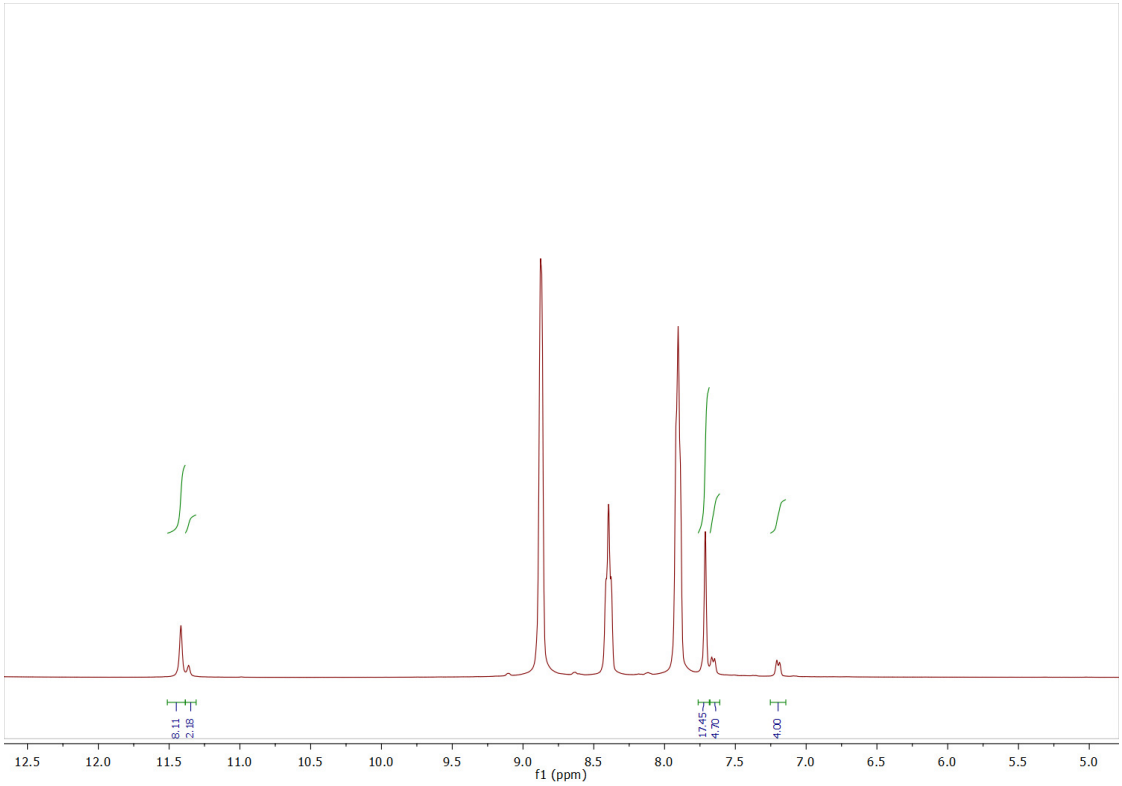


Figure 4-5. ^{1}H NMR (d_6-DMSO, 400 MHz) of the residue left over after drying the supernatant liquid from the precipitation of the reaction mixture obtained from the AB polymerization of monomer **4-3**, highlighting the region from 5.0 to 12.5 ppm. The peaks corresponding to the oligomers have been integrated to determine DP_n.

4.1.5 Characterization Data for Polymer 3-6 synthesized via AB polymerization

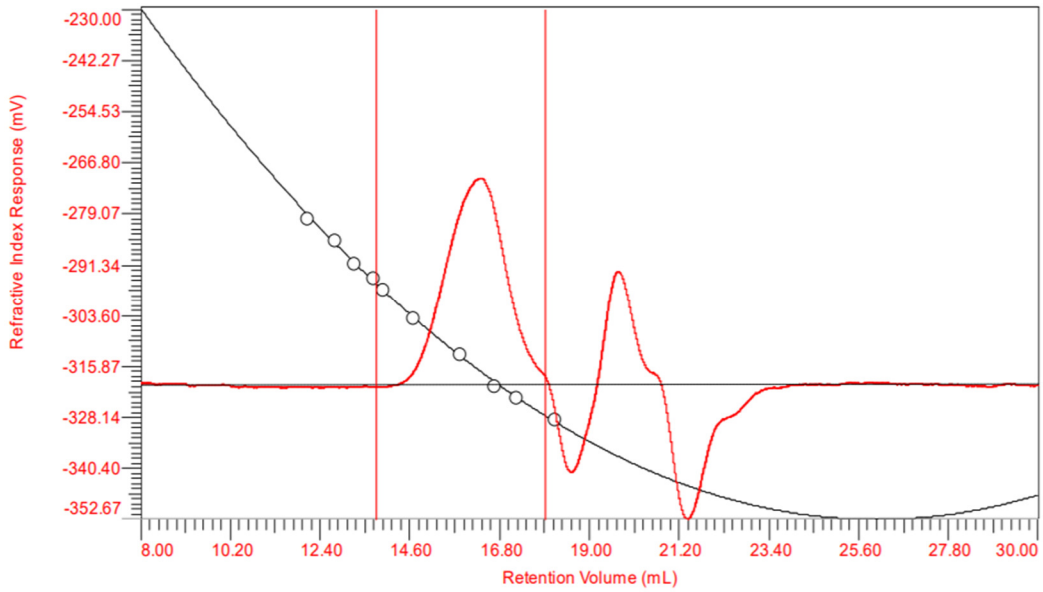


Figure 2-6. SEC trace of polymer **3-6** synthesized using AB monomer **4-4**

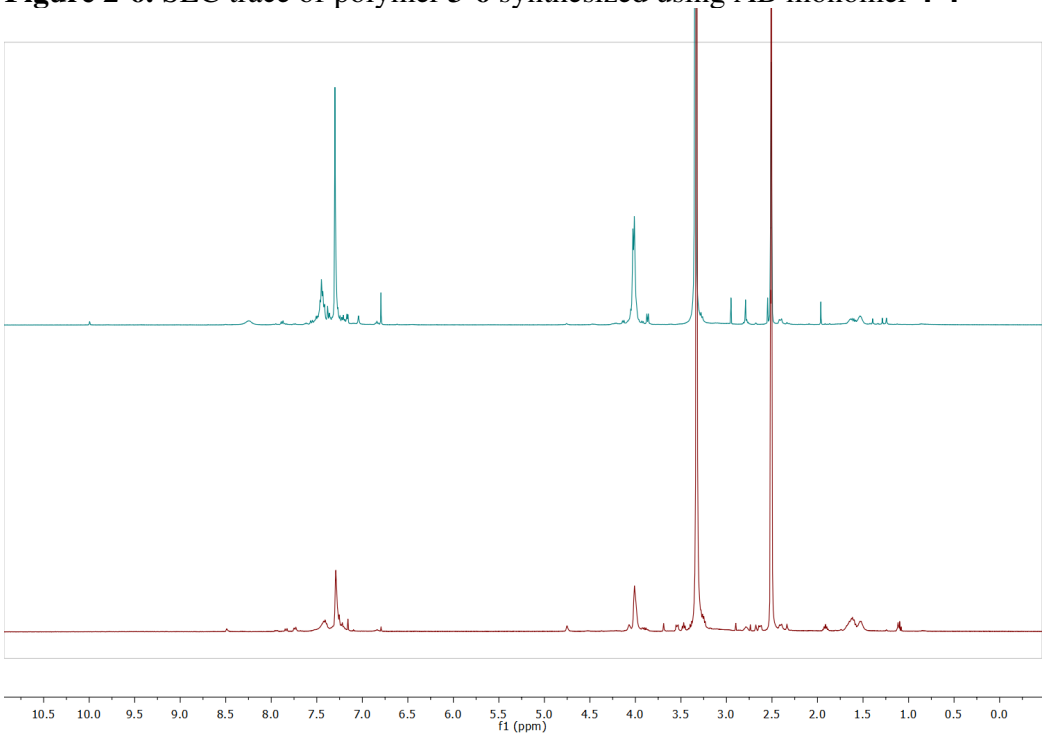
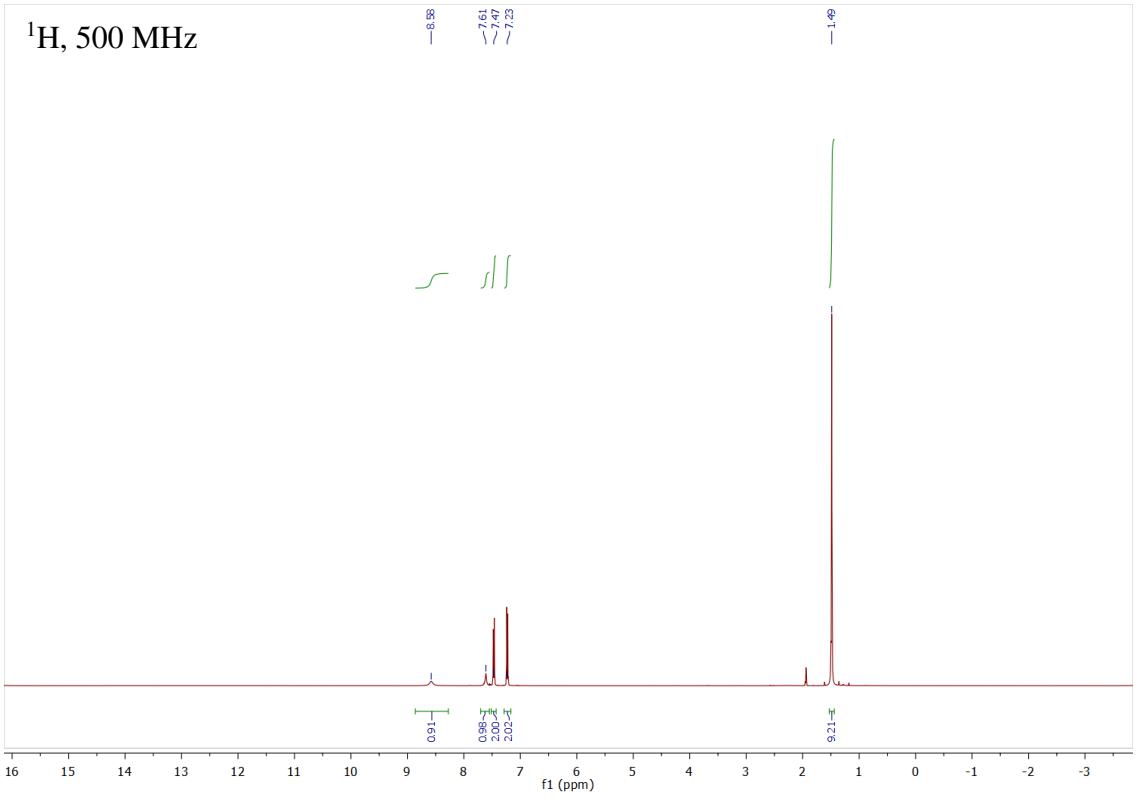


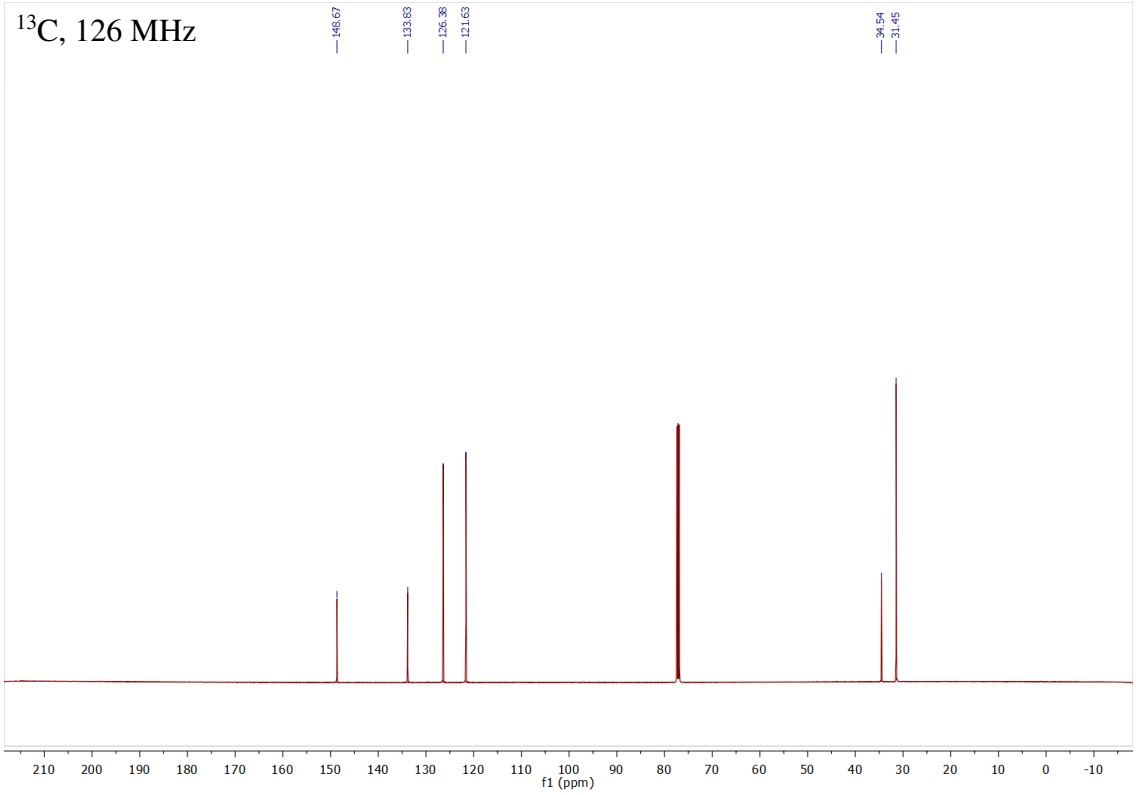
Figure 4-7. Top) ^{1}H NMR (d_6-DMSO, 400 MHz) of polymer **3-6** obtained through AA/BB polymerization. Bottom) ^{1}HNMR (d_6-DMSO, 400 MHz) of polymer **3-6** obtained through AB polymerization.

4.1.6 NMR Spectra of Novel Compounds

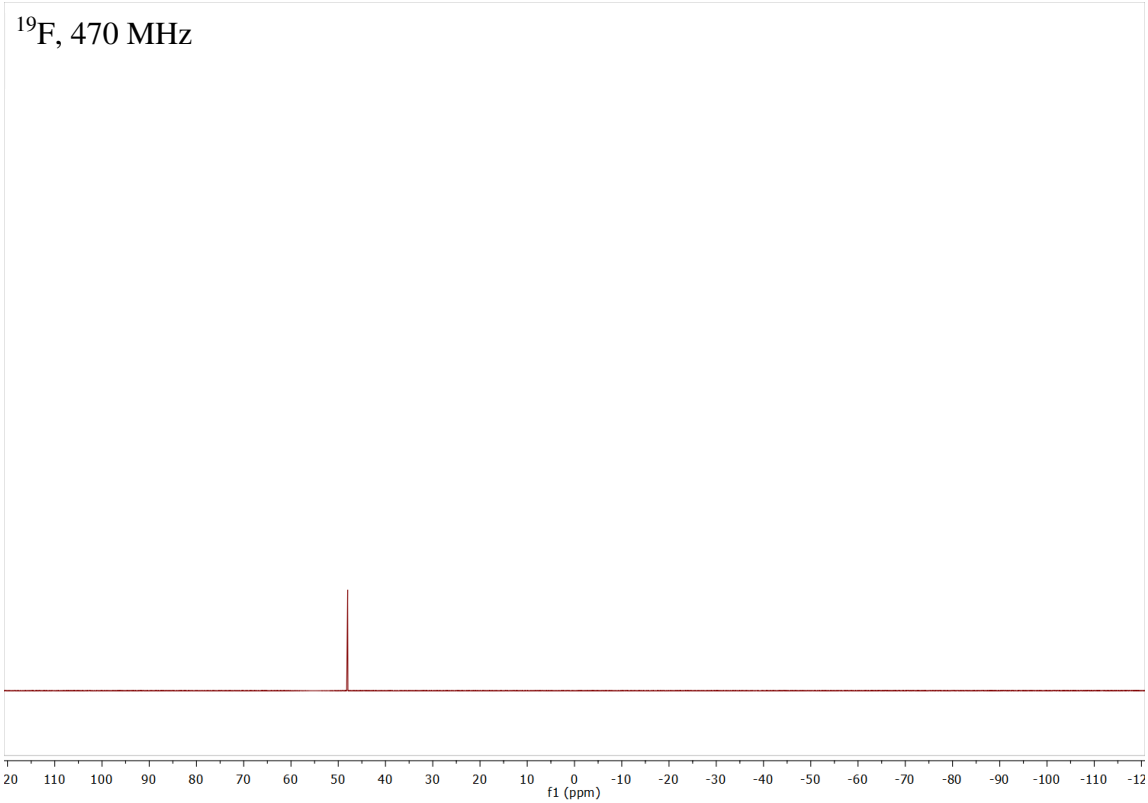
NMR Spectra of AB Monomer **4-3** (CD_3CN)



^{13}C, 126 MHz

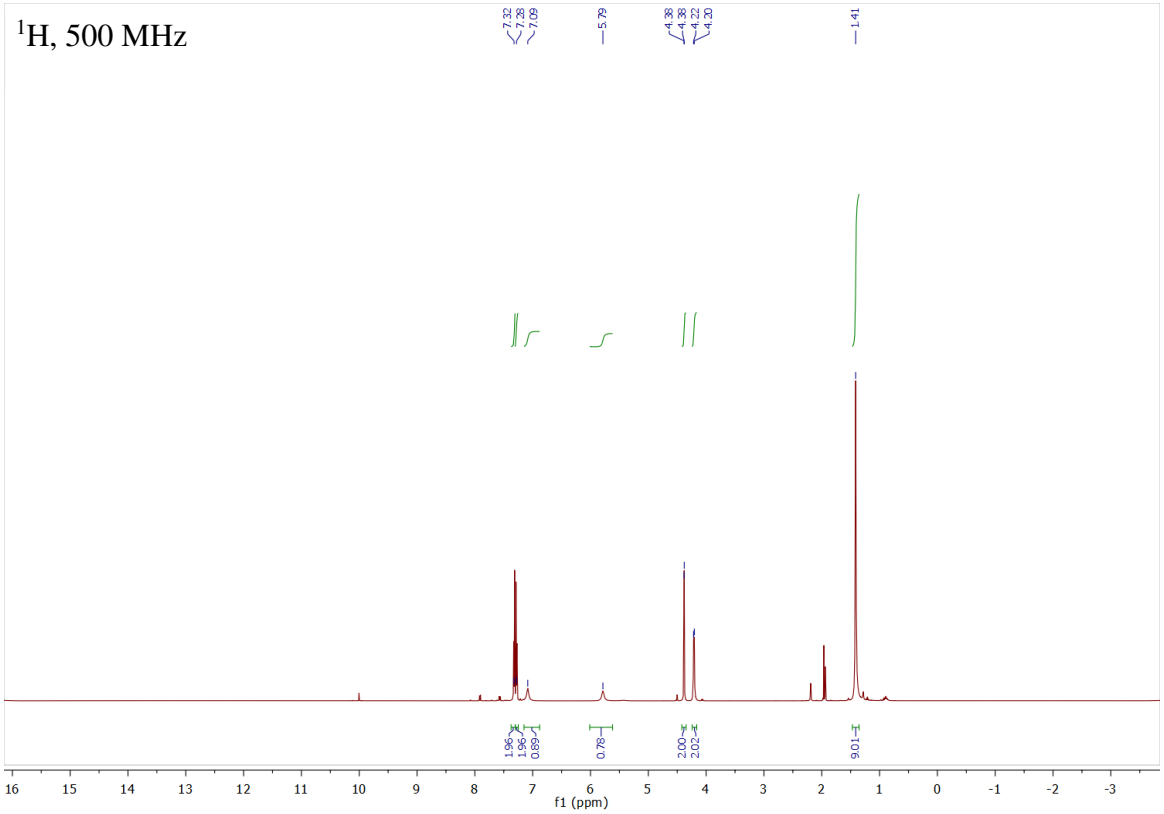


^{19}F, 470 MHz

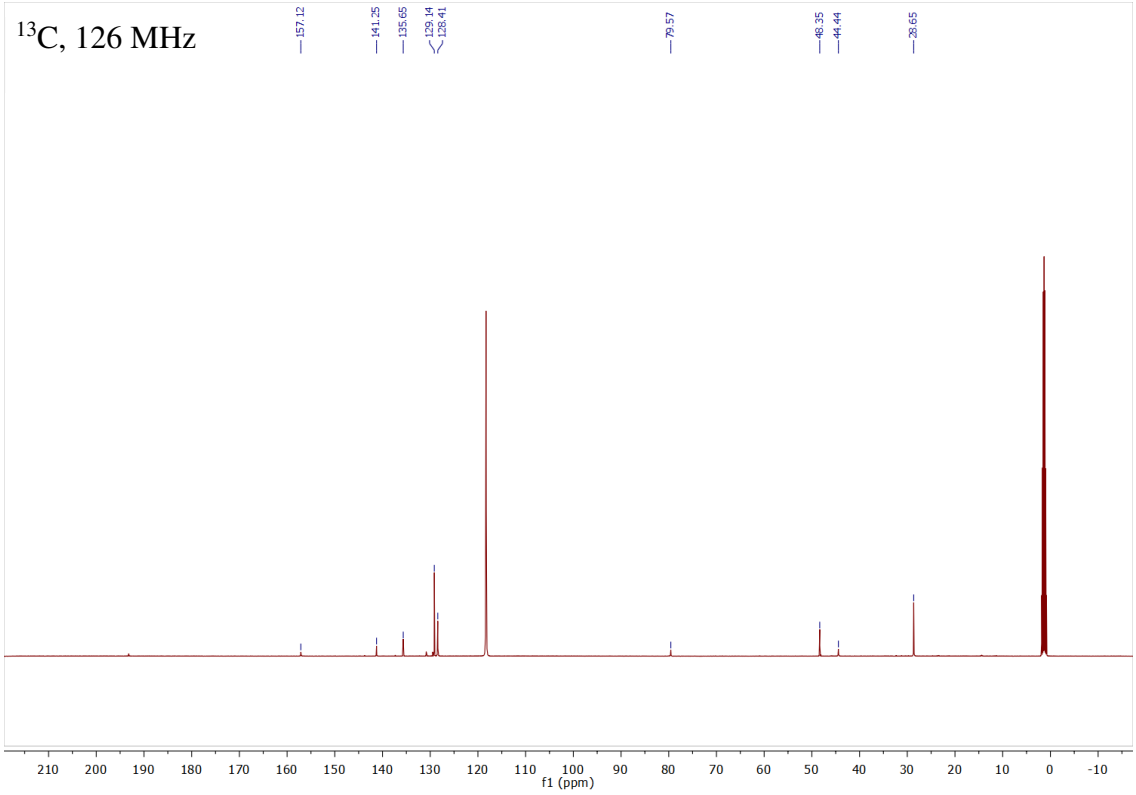


NMR Spectra AB Monomer 4-4 (CD_3CN)

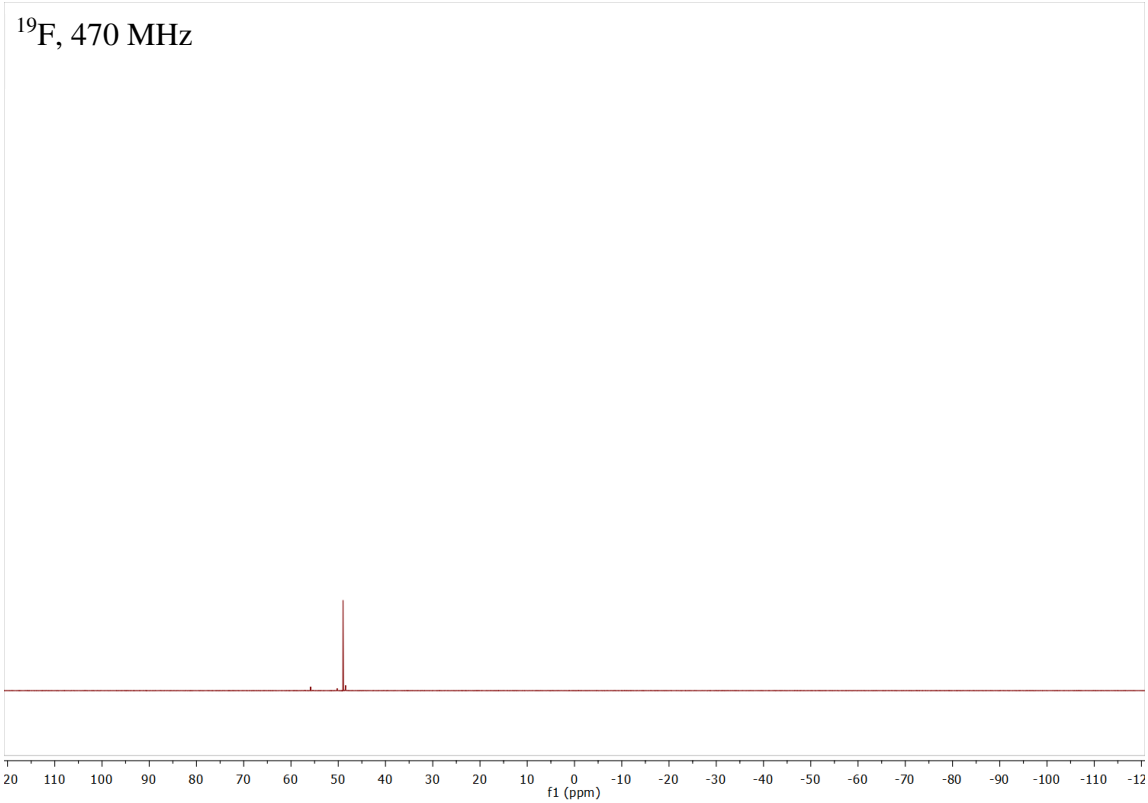
^1H, 500 MHz



^{13}C, 126 MHz



^{19}F, 470 MHz



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CHAPTER V

CONCLUSIONS

This dissertation covers the development of a method for the synthesis of polysulfamides through SuFEx chemistry. This synthetic method stands apart from previous syntheses of polysulfamides in that the conditions used are mild and the molecular weight of the resulting polymers are considerably higher. The ability to synthesize an AA type monomer allows for more precise stoichiometric control over the polymerization, and thus raises the molecular weight of the resulting polymers. The material properties of these polysulfamides were examined using a variety of characterization techniques, such as SEC, FTIR, TGA, DSC, and powder XRD. This synthetic method can act as a base for the synthesis of a diverse array of polysulfamides, along with other sulfur(VI)-containing polymers going forward.

In Chapter II, the synthesis of primary sulfamoyl fluorides was examined first. Sulfuryl fluoride, along with two crystalline alternatives were investigated. Overall, it was found that an imidazolium-based reagent was the most efficient and consistent reagent out of the three. This reagent could install an -SO_2F group on primary, secondary, aromatic, and aliphatic amines with little in the way of side reactions, giving access to a wide range of amines for study. After establishing the best sulfonylating reagent, the coupling reaction between sulfamoyl fluorides and amines to form sulfamides was optimized. It was found that secondary sulfamoyl fluorides are significantly less reactive, due to the inability to form an azasulfene intermediate. Therefore, the scope of this study was narrowed to just

primary aromatic and aliphatic amines. The ideal solvent, base, and temperature was found for the coupling reaction. A kinetic study was also run to determine the required reaction time for the coupling reaction. While the coupling of primary sulfamoyl fluorides to amines was optimized, conditions still need to be found for similar couplings with secondary sulfamoyl fluorides. Multiple synthetic methods have been discovered for the coupling of secondary sulfamoyl fluorides and amines. These aforementioned methods need to be tested for efficacy in solvents more preferential for polysulfamide formation before fully substituted polysulfamides can be synthesized.

In Chapter III, the synthesis and properties of polysulfamides were examined. The first synthetic method attempted was an AA-BB type step-growth polymerization. A wide array of bis(sulfamoyl fluoride) monomers were synthesized and then coupled to a robust library of diamines. This allowed for a broad examination of the thermal and material properties of these polymers to be examined. It was found that the T_g of these polymers can be tuned based on the monomer blend used in general agreement with the Fox equation. Through powder XRD, it was found that these polymers can adopt structures of varying crystallinity depending on monomer composition. Similarly, it was found that through FTIR, the hydrogen-bonding character of each polymer could be assessed. As of writing, no real mechanical studies have been conducted on these polymers, mostly due to the limited scale the polymerizations were conducted on. With a synthetic method for polysulfamide formation now established, work can now begin on large (<1 g) syntheses in order to generate enough polymer to conduct rheological and mechanical tests. These tests would help further establish the intramolecular forces at work in this relatively

understudied class of polymer. It was also found that, at least in entirely aromatic polysulfamides, prolonged exposure to acidic conditions at elevated temperatures allows for the controlled hydrolytic degradation of a polysulfamide back into its constituent diamines. If conditions for the controlled degradation of aliphatic polysulfamides can be uncovered, a system of monomer recycling can be established.

In Chapter IV, the synthesis of AB-type monomers for polysulfamide formation were synthesized. One aromatic and one aliphatic AB monomer were synthesized containing both the sulfamoyl fluoride functional group along with a Boc-protected amine. While the aliphatic monomer underwent deprotection followed by polymerization as expected, the aromatic monomer has had some difficulty polymerizing. It is possible that either the highly activated aromatic ring of the deprotected monomer, the base used, or the temperature of the reaction could have contributed to the failure of this aromatic AB monomer to polymerize. The reactivity of this monomer needs to be examined more fully in order to control the reaction and produce the desired polysulfamide. Additionally, there are many other commercially available diamines and dianilines that can act as candidates for AB monomer formation.

APPENDIX A

REAGENT AND ANALYTICAL INFORMATION

A.1 Reagent Information

All reactions were carried out under ambient atmosphere unless otherwise stated. Reagents were purchased at the highest commercial quality and used without further purification unless otherwise stated. DBU was purified by vacuum distillation with potassium hydroxide and stored over 4 Å molecular sieves under nitrogen atmosphere. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogenous material, unless otherwise stated. Reactions were monitored by thin-layer chromatography carried out on 250 µm SiliCycle SiliaPlate™ silica plates (F254), using ultraviolet light as the visualizing agent and an acidic solution of *p*-anisaldehyde and heat, ceric ammonium molybdate and heat, a basic solution of potassium permanganate and heat, or an acidic solution of ninhydrin and heat as developing agents. Flash silica gel chromatography was performed using SiliCycle SiliaFlash® Irregular silica Gel (60 Å, particle size 43–063 µm). Polymers were isolated using an Eppendorf Model 5804 Centrifuge and dried using a VWR Model 1410 vacuum oven.

A.2 General Analytical Information

SEC of polymer samples was performed using two systems: Visotek TDA302 and GPCmax with refractive index and dual-angle light scattering detectors with two columns, I-MBHMW and I-MBLMW, in series at a flow rate of 0.5 mL/min and a EcoSEC Elite®

HLC-8420GPC with refractive index detector and column TSKgel® SuperAWM-H at a flow rate of 0.2 mL/min. DMAc with 0.5% LiCl was used as the eluent in both systems. M_n, weight-average molecular weights and $Đ$ were calculated from refractive index chromatograms against poly(methyl methacrylate) standards. ^{1}H NMR spectra were recorded on 2 Bruker Avance NEO 400 MHz and a Bruker Avance 500 MHz; ^{13}C spectra were recorded on a Bruker Avance 500 MHz and a VNMRS 500MHz; ^{19}F spectra were recorded using a Varian Inova 500 MHz instrument and calibrated by a solution of $CFCl_3$ in $CDCl_3$ (@ 0.65 ppm ^{19}F NMR). All ^{1}H and ^{13}C proton-decoupled spectra were calibrated using residual protonated solvent as an internal reference ($CDCl_3$ @ 7.26 ppm ^{1}H NMR, 77.16 ppm ^{13}C NMR; CD_3CN @ 1.94 ppm ^{1}H NMR, 1.32 and 118.26 ppm ^{13}C NMR; d_6-DMSO @ 2.50 ppm ^{1}H NMR, 39.52 ppm ^{13}C NMR). The following abbreviations were used to explain NMR peak multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. High-resolution mass spectra (HRMS) were recorded on an Agilent LC/MSD TOF mass spectrometer by electrospray ionization time-of-flight reflection experiments. Melting points were recorded on a Fisher-Johns 13-144 melting point apparatus and are uncorrected. Thermogravimetric analysis (TGA) was performed on a TA Instruments TGA 5500 Thermogravimetric Analyzer or an Instruments Q500 Analyzer. Typically, samples were heated at 10 °C/min to 600 °C under nitrogen. Data were processed using Universal Analysis 2000 for Windows software. Differential scanning calorimetry (DSC) was performed using a TA instrument DSC 2500. Samples were prepared in aluminum pans and were analyzed using the following heating program: −50 °C to 5 °C below decomposition temperature at 10 °C/min, cooling to −50

°C at 10 °C/min, and heating again from −50 °C to 5 °C below decomposition temperature at 10 °C/min. The data were processed using TA Instruments TRIOS for Windows software. All reported T_g's were taken from the second heating cycle. FT-IR spectra were acquired using an Agilent Cary 630 FTIR in the attenuated total reflectance mode. All plots and spectra (SEC, DSC, TGA, XRD, and FTIR) were produced using raw instrumental data and Wolfram Mathematica version 12.1, unless otherwise noted.