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Syntheses of Polymers with Dendrimer Architecture

by

Coromoto Martínez

A thesis submitted to the Faculty of Graduate Studies and Research in partial fulfillment of the requirements for the degree of Doctor of Philisophy

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To:

my mother and son

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Synthesis of polymers with dendrimer architecture

by Coromoto Martínez

Abstract

Cascade poly(aryl ether) containing aryl sulfide or aryl sulfone groups, and aryl fluoride terminal functionality, were synthesized. Four generations of the dendrimers were prepared. The divergent initiator core method was employed, using 4,4'-difluorodiphenyl sulfone, as the core precursor, and a relatively high molecular weight phenol as the monomer. The strategy is based on an activation/condensation sequence that involves oxidation of the aryl sulfide group and the displacement of the activated aryl halide moiety by a phenolate ion. The aryl halide was activated by a sulfone group formed by oxidation of a sulfide group.

Optimum conditions for the condensation reaction utilized a very active metal carbonate, such as cesium carbonate, in conjunction with magnesium hydroxide or calcium carbonate which removes some of the fluoride ions formed. The phenolate was generated *in situ* from an organic carbonate, thus eliminating the usual dehydration step. NMR characterization indicated that the reactions were almost quantitative and MALDI-TOF-MS confirmed those results up to the third generation. No reaction intermediates were detected. Imperfections in some molecules of the dendrimers, formed by reaction of the core precursors with an impurity present in the phenol, were also identified.

Simultaneously, aryl halide-terminated and phenol-terminated hyperbranched poly(ether sulfone)s were prepared by the polycondensation of A_2B monomers via a one-pot approach. Syntheses were developed for all the new monomers required. The main advantage of this method is its simplicity, which allows rapid access to large amounts of hyperbranched polymers. Molecular weights and viscosities were controlled by the concentration of the monomer and temperature of the reaction. The best conditions were obtained when the condensation agent was a mixture of Cs_2CO_3 and $Mg(OH)_2$ and the displaced halide was a fluoride.

Synthèse des polymères avec architecture dendritique

par Coromoto Martínez

Sommaire

Des poly(éther d'aryle)s dentritiques contenant le sulfure d'aryle ou la sulfone d'aryle et un groupement aryle fluoré ont été synthétisées. Quatre générations dendritiques ont été préparées. La méthode d'initiateur divergent du noyau a été employée, utilisant le difluordiphénylsulfone comme précurseur et un composé phénolique de masse molaire relativement élevée. La stratégie fut basée sur une séquence d'activation/condensation qui requiert l'oxydation du groupement sulfure d'aryle et le déplacement de l'halogène par le phénolate. L'aryle fluoré est activé par le groupement sulfone qui se forme par l'oxydation du sulfure.

Des conditions optimisées pour la réaction de condensation ont montré l'utilité d'un carbonate comme le carbonate de césium en conjonction avec l'hydroxyde de magnésium (ou le carbonate de calcium) pour enlever efficacement une partie des ions de fluorures libérés lors de la réaction. Le phénolate est généré *in situ* à partir d'un carbonate organique, éliminant ainsi l'étape de déshydratation. La caractérisation par RMN indique que les réactions sont presque quantitatives et la spectroscopie de masse MALDI-TOF confirme ces résultats jusqu'à la troisième génération. Aucun intermédiaire de réaction n'a été détecté. Des imperfections dans les molécules dendritiques se forment lors de la réaction des précurseurs avec un impureté présente dans le phénol.

Simultanément, des poly(éther sulfone)s hyperbranchés terminés par des halogénures d'aryle et l'hydroxyphényle ont été préparés par polycondensation des monomères du type A_2B. Des synthèses ont été développées pour tous les monomères requis. L'avantage majeur de cette méthode est la simplicité qui permet ainsi un accès facile à des quantités importantes de polymères hyperbranchés. Les masses molaires et les viscosités sont contrôllés par les concentrations des monomères et la température de la réaction. Les

meilleures conditions ont été obtenues lorsque l'agent de condensation était une mélange de Cs_2CO_3 et $Mg(OH)_2$ et l'halogénure était le fluor.

Contributions to original knowledge.

Interest in macromolecules with dendrimer architecture has increased steadily during recent years. Their syntheses have received worldwide attention in both academic and industrial laboratories due to their promising properties and potential new applications. Synthetic strategies using both convergent and divergent methodologies have been used to produce over twenty families of dendrimers. However, in most cases only small amounts of these materials have been prepared and the characterization of higher generations is often difficult.

One of the contributions of this research is the development of a method to synthesize cascade poly(aryl ether)s with aryl sulfide or aryl sulfone groups, and aryl fluoride terminal functionality. The divergent initiator core method is used employing 4,4'-difluorodiphenyl sulfone as the core precursor and a relatively high molecular weight phenol as the monomer. The strategy is based on an activation/condensation sequence that involves oxidation of the aryl sulfide group and the displacement of the activated aryl halide moiety by a phenolate ion. The aryl halide is activated by a sulfone group. This is the first time, to our knowledge, that this specific sequence has been used to synthesize cascade polymers.

This research started using the pre-formed sodium salt of a bis(aryl chloride) phenol for the condensation reaction. An exploratory work on the effect of the temperature on the condensation reaction was also carried out. The method used is successful for the synthesis of the first generation of dendrimers. The second generation can also be formed but the reaction is not complete. The sodium phenolate and/or the aryl chloride is not active enough to force the condensation reactions to be quantitative.

In the second part of this project we used a higher rate condensation reaction employing the pre-formed salt of a bis(fluoro aryl) phenolate. The iterative sequence is easily carried out and produces, in high yield, the first generation poly(aryl ether) dendrimer. However, the reaction is incomplete in the synthesis of the second generations of these dendrimers with formation of a small amount of high molecular weight byproducts. The displacement of fluorides instead of chlorides permits the formation of crude products with lower polydispersities and made the reaction cleaner. The use of the sodium phenolate is postulated as the major limitation in the synthesis of the higher generations.

During the last stage of this project the condensation reaction was carried out using a masked bis(fluoro aryl) phenol and mixtures of metal carbonates and metal hydroxides. The strategy included: a) control of the concentration of fluoride in the reaction medium, by using alkaline earth cations such as calcium or magnesium, b) use of a more active nucleophilic polycondensation agent such as Cs_2CO_3 along with the metal hydroxides, and c) employment of a masked bisphenol to allow rapid generation of the phenolate ion *in situ* without the usual dehydration step. Alkaline earth cations can remove fluoride ions from the reaction mixture as insoluble metal fluorides. Several combinations of metal carbonates and metal hydroxides under different reaction conditions were used: a) alkali metal (Cs, K) carbonates and calcium carbonate, b) potassium hydroxide and calcium hydroxide, and c) cesium carbonate and alkaline earth metal (Ca, Mg) hydroxides.

NMR characterization indicated that the reactions were almost quantitative and MALDI-TOF-MS confirmed those results up to the third generation. No reaction intermediates were detected. Imperfect molecules in the dendrimers which appear to be form by reaction of the core precursors with an impurity present in the phenol, were also identified.

The best conditions for the synthesis of the dendrimers have been found when combinations of $CaCO_3$:Cs_2CO_3 and $Mg(OH)_2$:Cs_2CO_3 are used. In general the best conditions are: a) slight excess of basic equivalents (metal carbonate, metal hydroxide) with respect to organic carbonate; b) around 30 % molar excess of $CaCO_3$ or $Mg(OH)_2$ to

Cs_2CO_3, and c) about 0.9 mol of cesium per mol of organic carbonate. The use of argon instead of nitrogen is preferable. The use of only K_2CO_3 is clearly unsatisfactory.

Simultaneously, aryl halide-terminated and phenol-terminated hyperbranched poly(ether sulfone)s were prepared using the one-pot approach and A_2B monomers. The project included the synthesis of all the new monomers required. The main advantage of this method is its simplicity, which allows rapid access to large amounts of hyperbranched polymers. The molecular weights and viscosities of the polymer are directly affected by the concentration of the monomer and temperature of the reaction. Mixture of Cs_2CO_3 and $Mg(OH)_2$ in combination with fluoroaryl monomers are preferable. MALDI-TOF-MS and NMR characterization are in agreement with the proposed structure for the hyperbranched polymers. In addition, MALDI mass spectrometry allows the identification of the termination reaction in these polymerization systems which appears to be an internal cyclization. The terminal phenolic groups of the poly(aryl ether sulfone)s were readily functionalized, in almost quantitative fashion, confirming the accessibility of the chain ends.

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Glossary of abbreviations and symbols

Å	Angstrom (1 x 10^{-8} cm)
COSY	Correlated spectroscopy
CPK	Corey-Pauling models
D	Dendrimer
DMAc	N,N-Dimethylacetamide
DMSO	Dimethylsulfoxide
FTIR	Fourier transform infrared
G	Generation
GDS	Genealogically directed synthesis
HPLC	High pressure liquid chromatography
l	Branch cell segment length
LALLS	Low angle laser light scattering
MALDI-TOF-MS	Matrix-assisted laser desorption ionization time-off-flight mass spectrometry
mp	Melting point
Mw	Weight average molecular weight
Nb	Multiplicity of the monomer
Nc	Multiplicity of the core precursor
NMP	N-Methylpyrrolidinone
NMR	Nuclear magnetic resonance
MS	Monosubtituted product
OC	Organic carbonate
PAMAM	Poly(amido amine) dendrimer
PD	Polydispersity

ppm	Part per million
SEC	Size exclusion chromatography
Tg	Glass transition
THF	Tetrahydrofuran
Z	Terminal groups

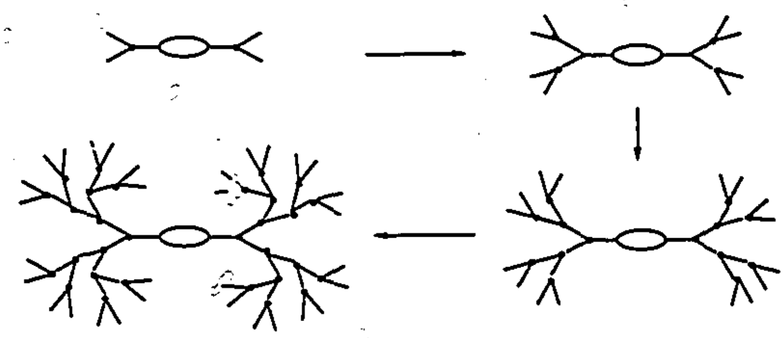
Chapter 1

General introduction.

1.1 Introduction.

There is a growing interest in macromolecules with architectures that differ from the classical linear polymers since new polymer architectures may exhibit unusual behavior and possess properties that differ from those of linear materials. (1) One family of macromolecules which has attracted considerable attention is dendritic polymers (Scheme 1.1). Researchers have referred to this class of polymers by trivial class names such as arborols, silvanols, dendrimers, molecular fractal, hyperbranches, which were coined to reflect the tree-like branching of these molecular structures. (2)

Scheme 1.1



Tomalia (3) introduced the term genealogically directed synthesis, GDS, to refer generically to synthetic strategies directed toward these molecules. Genealogically directed syntheses are those synthetic strategies which involve a sequence of chronological steps wherein critical intermediates involved in the sequence function as radial templates upon which subsequent structural components are introduced in some chronological order. As a consequence, important molecular information can be chronological designed into the final structure. Biological examples of this "information flow" strategy are DNA replication as well as DNA transcription to RNA followed by translation to produce proteins.

Using simple reagents and procedures, the GDS strategy has been used to successfully produce over twenty different families of dendrimers based on classical repeat units and monomers (also called: branch cell reagents or building blocks).

The covalent architectures obtained from GDS can be systematically controlled by stepwise reiterative reaction sequences (generations). For example, starburst dendrimers were produced using the following method:

1. Start with a core precursor possessing N_c reactive sites .

2. Choose a reaction sequence so that each of the N_c reactive sites adds monomer B possessing new N_b ($N_b > 1$) reactive sites (thereby introducing multiplicity) to obtain dendrimer D_1 of generation 1.

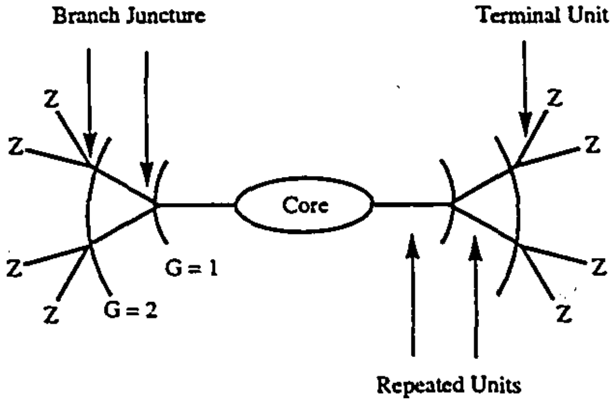
4. Use some type of strategy that ensures that B reacts with all reactive sites of the core precursor, but that no reaction occurs at the new reactive sites on B of dendrimer D_1.

5. Define an iterative sequence involving addition of new monomers to the molecule Di of generation i to form a new dendrimer D_{i+1} of generation i + 1.

As shown in Scheme 1.2, starburst dendrimers possess three major architectural features: a core, interior zones containing cascading tiers of repeated units, and an exterior or surface region of terminal units attached to the outermost generation. Each of the branches which emanated from the core has been call a dendron (Greek term) due to the similarity to a tree. In this example, $N_c = N_b = 2$.

Both the core multiplicity, N_c, and the branch-juncture multiplicity, N_b, directly affect the number of terminal functional groups, Z, the number of repeated units, N_{ru}, and the molar mass of the dendrimer, M, as a function of generations, G.

Scheme 1.2



These values can be predicted mathematically for this ideal example in accordance with the following expressions:

$$Z = N_c\,(N_b)^G$$

$$N_{ru} = N_c[(N_b)^G\ -\ 1)]/\,(N_b - 1)$$

$$M = M_c + \{M_{ru}N_c[(N_b)^G\ -\ 1]/\,(N_b - 1)\} + M_t\,N_c(N_b)^G$$

Where M_c, M_{ru}, and M_t are the molar masses of the core, repeat units, and terminal units, respectively.

According to this description, starburst dendrimers are simple assemblies of dendrons attached to a common initiator core, or a variety of initiators cores in the same molecule.

1.2 Dendrimer systematic nomenclature.

The increasing diversity of functionalities and design of dendritic materials made the need for a systematic nomenclature for dendritic polymers manifestly apparent. The application of current nomenclature rules to these molecules has several disadvantages. The names rapidly increase in length with successive generations and the core and branch multiplicity, and in addition the number and type of functional moieties are not obvious.

G. R. Newkome(2) proposed a systematic nomenclature to represent cascade polymers. They defined cascade (dendritic) polymers as discrete, highly branched monodisperse polymers that possess branching patterns described by a mathematical progression.

For example, according to this nomenclature the name for the third generation poly(aryl ether) dendrimer shown in Scheme 1.3 is: 24-Cascade: ethane[3-1,1,1]:(5-(2-p-phenyl-2-oxaethyl)-1,3-phenylene):(5-(2-oxaethyl)-1,3-phenylene)^2:(2-oxaethyl)benzene.

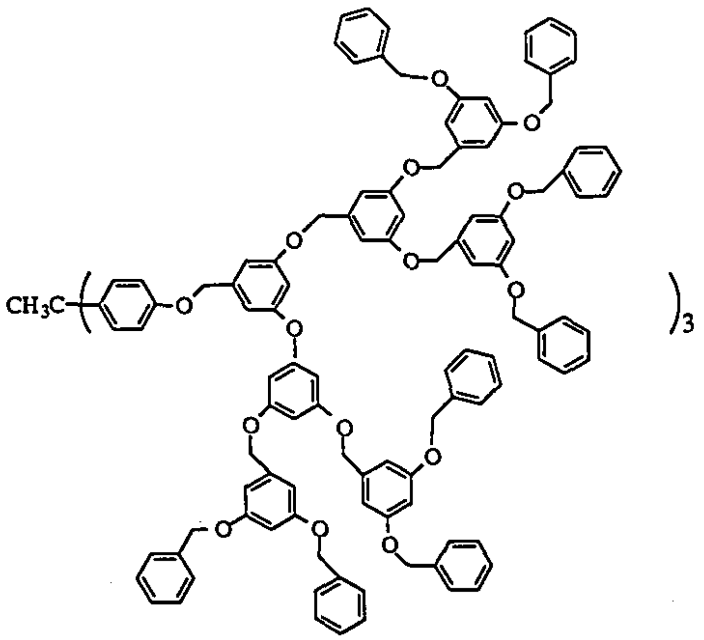
The name was derived using the following general terminology:

Z - Cascade: Core [N_c] : (Repeated Unit A)^n : (Repeated Unit B)$^{n'}$: Terminal Unit

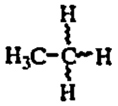
The use of this nomenclature requires the identification of the core, repeated units and terminal units. The number of terminal units, Z, the multiplicity of the core, N_c, the number of layers of repeated unit A, n, and the number of layers of repeated unit B, n', are also indicated.

The different structural fragments are also given in Scheme 1.3, with their respective names. This structure contains one layer of repeated unit A, two layers of repeated unit B, and 24 terminal units. The multiplicity of the core is 3 and three branches are generated from the carbon designated number one in the core.

Scheme 1.3

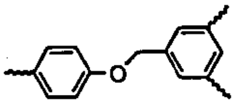


Third generation poly(aryl ether) dendrimer

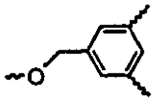


$$H_3C-\overset{H}{\underset{H}{C}}-H$$

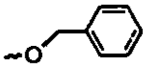
Core Precursor: ethane



Repeated Unit A: 5-(2-p-phenyl-2-oxaethyl)-1,3-phenylene



Repeated Unit B: 5-(2-oxaethyl)-1,3-phenylene



Terminal Unit: (2-oxaethyl)benzene

$$Z = 24,\ N_c = 2,\ n = 1,\ n' = 2$$

1.3 Dendrimer synthesis.

We will use the term dendrimer to describe starburst dendrimers, cascade polymers, arborols, silvanols, dendrons, and hyperbranched polymers.

Different strategies for dendrimer construction have been reported. (3, 4) They are:

a) *divergent dendron method*, which may involve either controlled sequencing techniques or uncontrolled propagation methods for the synthesis of dendrons,

b) *convergent dendron method*, for the synthesis of dendrons,

c) *exponentially convergent growth dendron methods* , for the synthesis of dendrons,

d) *divergent dendron/divergent anchor method*, for the synthesis of dendrimers using a core precursor,

e) *convergent dendron/divergent anchor methods*, for the synthesis of dendrimers using a core precursor, and

f) *divergent initiator core method*, for the synthesis of dendrimers using a core precursor.

In general, one can design and articulate the total construction of a dendrimer based on the choice of strategies used. For example, use of preformed dendrons allows one to differentiate sectors or hemispheres in the final dendrimer structure. On the other hand, if the dendrimers are produced directly by proliferating divergently from a core, it is possible to produce dendrimers containing differentiated radial infrastructures.

1.3.1 Divergent controlled dendron method.

This method has been employed for the synthesis of dendrons and it requires that the dendron grows from its focal point to the outside direction. If suitable functional groups are introduced in the focal point, these moieties may be used to subsequently anchor multiples of these groups to a core precursor.

Vogtle (5) reported some of the first examples of this method of synthesis. Several low molecular weight (< 1,000) dendrons were produced possessing either amine or cyano-functionalized surfaces.

Poly(amido amine) dendrons, PAMAM, have been synthesized by Tomalia. (6) Different initiator molecules were used and submitted to sequential Michael addition reactions with methyl acrylate followed by reaction with an excess of ethylene diamine to construct *in situ* branch cells. The resulting dendrons have a functional group at their focal point. Subsequent tethering of these dendrons around various cores allowed them to synthesize quadrant or hemispherically differentiated new dendrimers. Within this poly(amido amine) series it was generally noted that beyond the fourth or fifth generations the focal point became so sterically congested that coupling with the core precursors was substantially more difficult.

Newkome has produced poly(amido alcohol) (7) and poly(amido acid) (8) dendrons. They refer to these series as unidirectional arborols. They are a special example of a dendron series possessing radially oriented heterogeneous generations since the branch cells were derived from different monomers. There are some other examples in the literature utilizing this approach. (9, 10)

1.3.2 Divergent uncontrolled dendron method.

Flory (11) first suggested the possibility of forming highly branched, tree-like networks by polymerization of A_nB type monomers, where n is greater than one and functional group A can only react with B. Very early reports described them as polycondensates, consisting of broad molar-mass distribution materials with randomly branched topologies. Recent examples of this type of polymerization have involved A_2B type monomers. In general, the final hyperbranched polymers are substantially more polydisperse than products from the controlled divergent method with branching ranging from 50 - 75%.

Bochkarev (12) has recently described the anionic polymerization of $HM(C_6F_5)_3$, where M = Ge, Si, or Sn with $N_c = 1$ and $N_b = 3$. Most noteworthy is the germanium system, where they have obtained molecular-mass ranges of approximately 100000 - 170000.

Completely aromatic, hyperbranched polyphenylenes with aryl halide terminal groups were synthesized from A_2B type monomers by Kim and Webster. (13) These dendrimers were obtained as brittle, non-film forming materials. They were soluble in many organic solvents and thermally stable up to 550°C. Branching efficiencies were estimated to be approximately 70% by ^{13}C NMR. Kim also reported the synthesis of hyperbranched poly(phenylene ether)s and poly(aryl amide)s. (14)

Fréchet (15) has reported the synthesis of hyperbranched poly(aryl ester)s with hydroxyl terminal groups, by the thermal self-condensation of 3,5 bis(trimethylsiloxy)benzoyl chloride. They (16) also reported the synthesis of hyperbranched polymers using 5-(bromomethyl)-1,3-dihydroxybenzene.

Mathias (17) has produced hyperbranched poly(siloxysilanes) by the self-hydrosilation of A_3B type monomers and Miller (18) synthesized hyperbranched polymers with aryl fluoride end groups.

Some other examples of the synthesis of hyperbranched polymers can be found in the literature. (19)

1.3.3 Convergent dendron method.

Nearly simultaneously two groups namely: Fréchet (20) at Cornell University and Neenan and Miller (21) at A.T. & T. Bell Labs, introduced a new method for constructing dendrons which they refer to as the *convergent method.* The synthesis begins at what will become the periphery of the final dendron and proceeds inwardly to the focal point. Dendrimer growth is designed to occur via a limited number of reaction sites.

Advantages offered by this approach include the involvement of a very limited number of reactive sites for each generation of growth which makes the purification easier.

However, as the size of the dendrimer increases the focal functional group might become sterically encumbered. This can limit the size of the macromolecules that may be prepared by the convergent method.

Fréchet (20) completed the synthesis of a series of poly(aryl alkyl ether) dendrons based on the use of 3,5-dihydroxybenzyl alcohol as the branch cell reagent. They produced six generations of dendrons. The nominal molecular weight of the sixth generation was 13542 g/mol. These reactive dendrons were converted to new dendrimers by allowing them to react with various core precursors.

In a second dendritic series, Fréchet (22) selected 4,4-bis(4-hydroxyphenyl)pentanol as the branch cell reagent for construction of a more flexible dendron. These functionalized dendrons were coupled to various core precursor to produce new dendrimers.

Miller (23) reported the preparation of poly(aryl ester) dendrons using a convergent iterative sequence consisting of esterification and hydrolysis reactions. They prepared 3 generations of dendrons. He also reported the synthesis of a series of poly(arylene) dendrons possessing extraordinary symmetry and no flexible methylene linkages. (24) These dendrons consist of geometric tiers of aryl groups linked at the 1,3,5-positions, with a reactive boronic acid at its focal point. They prepared two generations of dendrons which were anchored to a core precursor to produce new dendrimers.

Moore (25) reported the successful synthesis of rigid poly(aryl acetylenic) dendrons through the third generation. Damha and co-workers (26) formed a variety of unique oligonucleotide branch cell reagents which were subsequently used to produce RNA or DNA derived dendrons and new dendrimers. Shinkai (27) recently synthesized azacrown ether linked dendrons through the third generation which were used in the construction of dendrimers. Kakimoto synthesized polysiloxane (28) and poly(aryl ether keto) (29) dendrons through the fourth generation.

1.3.4 Exponentially convergent growth method.

Moore (4) has reported the synthesis of a third generation (225-mer) phenylacetylene monodendron that has been characterized by MALDI mass spectrometry (39972 Da). By this process, the number of repeated units per dendrimer accumulate in according with a double exponential function in terms of generation. Monomers of the type $A_p(B_p)_n$ are required, where p means that the corresponding functional group has been protected.

The synthesis of the first generation involves the selective removal of the protected group on A_p to give $A(B_p)_n$ monomers, selective removal of the protecting groups in B_p to give $A_p(B)_n$ monomers and subsequent coupling of the two intermediate monomers in proper stoichiometric ratio. The same general procedure is repeated for the synthesis of the higher generations, using the new dendron instead of monomer $A_p(B_p)_n$. The monodendrons maintain a single A_p group at their focal point. The number of peripheral groups, Z, is obtained from the following expression:

$$Z = (N_b \exp 2) \exp G$$

where N_b is the number of groups B in the monomer.

This scheme offers advantages similar to those of the double stage convergent method (22) but has the additional advantage that the anchoring dendron grows concomitantly with the peripheral dendron producing high molecular weight dendrimers in a few generations. However, a pair of orthogonal protecting groups (rather than one) is required and the number of generations that can be obtained is apparently limited.

1.3.5 Divergent dendron/divergent anchor method.

Tomalia has synthesized a variety of PAMAM dendrimers by first preparing dendrons functionalized at their focal points. (6) The synthesis was less effective after the fifth or sixth generation presumably due to steric congestion surrounding the dendron focal point functional group. They also used dendrimers as anchoring core precursors.

1.3.6 Convergent dendron/divergent anchor method.

In this strategy, dendrons are functionalized at their focal point and then used as reagents to react with appropriate multifunctional core precursors to produce the desired dendrimers. Dendrimers synthesized by this approach have been reported almost exclusively by Fréchet (20) and Miller. (21, 23, 24, 30) This approach has been used successfully to produce at least four different types of dendrimer families which include poly(aryl ester), poly(arylene), poly(aryl alkyl ether), and poly(aryl azacrown ether) dendrimers.

The Fréchet group has selectively introduced differentiated hemispheres in the dendrimer which allows the control of dendrimer surface functionality. (31) They also demonstrated a two stage dendrimer synthesis by preconstructing a lower generation dendrimer using the convergent dendron/divergent anchor method, and coupling preformed dendrons to this multifunctional dendrimer core precursor. (117)

Shinkai (27) synthesized dendrimers through the second generation.

1.3.7 Divergent initiator core method.

Using this approach, dendrimers are produced directly by proliferating divergently from a core. This synthetic strategy requires very high yield syntheses as well as efficient workup procedures for purification of the dendrimers. A major advantage offered by this approach is that the steric bulk of the monomer is usually much lower than that of the dendron. This allows one to advance to higher generations by iterative reaction sequences before the cascade dense-packing occurs.

Tomalia has synthesized starburst poly(amido amine) dendrimers, PAMAM. (6, 32, 33) Successful synthesis of highly branched dendrimers through generation 11 have been completed. They also reported the synthesis of polyether dendrimers (34, 35) through the third generation with hydroxyl-terminal groups and poly(ethyleneimine) dendrimers. (32, 36) In the last synthesis, the defect levels become progressively higher and divergence from branch ideality becomes substantial as one approaches generations 4 and 5, and especially generation 6. CPK models indicate that ideally branched generation 6 is forbidden due to dense packing as described and predicted by de Gennes. (37)

A unique class of structures referred to as iptycenes has recently been reported by Hart. (38) These architectures represent the first example of all-hydrocarbon dendrimer prototypes. Astruc and co-workers (39) have described hydrocarbon dendrimers possessing organometallic cores (Fe, Co).

Some polythioether dendrimers have been also synthesized. (32, 35) This dendrimer series contains thioether linkages in the interior with hydroxyl surface groups. The dendrimer family was successfully proliferated through the third generation.

Newkome and co-workers (40) have described the synthesis of poly(amido alcohol) dendrimers. These dendrimers are a special example of a heterogeneous series. They possess branch cells derived from different monomers. A second generation dendrimer was obtained by advancement through an alkylation stage and amidation step.

An iteration sequence has been developed by these workers which involves introduction of spacer groups which produces a longer branch cell segment length. They prepared dendrimer families with several combinations of core precursors and monomers. (41) A dendrimer series possessing an all-hydrocarbon interior and up to 36 surface carboxylic acid groups (second generation) exhibited very interesting unimolecular micelle properties. These products have been shown to form host-guest complexes with various hydrophobic guest molecules. Newkome refers to these products as "micellanes". (42)

Hall (43) produced a low-molar mass series of poly(aryl amine) dendrimers and Engel (44) reported several poly(phosphonium) dendrimers in which ionic sites were incorporated at both the core precursor as well as the branch juncture.

Masamune (45) was the first to report the synthesis of silicone dendrimers. This group was successful in proliferating the dendrimer structure out to the fourth generation to give molecular weights of greater than 14000. It should be note that the surface of these silicone dendrimers are coated with -Si-H groups, thus rendering them amenable to further chemical modifications.

Kakimoto(46) reported a series of polysiloxane dendrons. Using protection/deprotection schemes, a dendron was prepared possessing 24 phenylsilyl groups.

Roovers (47) has reported a high yield iteration sequence leading to the synthesis of poly(carbosilane) dendrimers. Reiteration ultimately leads to a fourth generation dendrimer possessing as many as 64 silicon chloride or vinyl surface groups.

Meijer and de Brabander den Berg (48) synthesized polypropyleneimine dendrimers through the fifth generation with 64 nitrile groups at the outer tips of the branches and molecular weight of 7000.

1.4 Dendrimer characterization.

Dendrimer structure determination requires a variety of analytical methods for unequivocal characterization. Different methods has been used to characterized these materials: elemental composition, mass spectrometric fragmentation patterns, molecular weights of the different generations, polydispersities, interior and end groups analysis, and structure and dimension determinations.

Techniques such as low-angle laser light scattering (LALLS), vapor phase osmometry, electrophoresis, conventional mass spectrometry (electron and chemical ionization), fast atom bombardment mass spectrometry, laser desorption mass spectrometry and electrospray mass spectrometry have been used for mass characterization.

Size exclusion chromatography (SEC) and SEC coupled with LALLS, electron microscopy, atomic force microscopy, scanning tunnel microscopy and capillary electrophoresis have been used to study the homogeneity of the samples.

Infrared and NMR spectroscopy give valuable information about the nature of the interior and end groups and structure of these molecules.

Intrinsic viscosity measurements, SEC, computer-assisted molecular simulations, comparison with CPK models, and atomic force microscopy, among others, have been used to determined the dimensions of the dendrimers.

Some examples of these characterization methods are given in a paper by Fréchet. (49)

In the case of PAMAM dendrimers, intermolecular coupling, intramolecular cyclization and branching defects have been identified. ^{13}C NMR spectroscopy and electrospray mass spectrometry were used to identify them.

A branch defect is a consequence of an incomplete reaction in which a functional group remains unreacted. During advancement to the next generation, the unreacted functional group may react. The consequence of such an event is that the molecules formed from that imperfect structure are one generation retarded in branch-cell development compared to those obtained from the symmetrical structures.

The structure of a molecule that results from a sequential, reiterative process must reflect its unique history of preparation. Tomalia (3) described a procedure to infer the synthesis history of a sample from its isomeric composition using a statistical procedure. According to them, examination of the product distribution of a given sample should provide an insight into the history of the sample preparation, with the average molecular weight giving an overall measure of the efficiency of the conversion and the shape of the curve an indication of the mass/isomer distribution. This was accomplished by comparison of a statistical model of a material with branching defects with measured distributions by electrospray ionization mass spectroscopy. The deconvoluted mass spectrum of the fifth generation suggests the presence of at least 16 components in the sample. They observed the molecular mass of the perfect fifth generation dendrimer plus signals corresponding to the different intermediates of the reaction as well as intramolecular cyclization products. This work leads to the conclusion that the efficiency of reaction for the synthesis of PAMAM materials must be between 97-98% for each step.

Branch defects contribute in a minor way to dendrimer polydispersities but intermolecular coupling and species derived from unremoved propagating reagents are major contributors.

The iterative branching process must at some point lead to severe steric crowding either at the molecule surface or throughout the volume of the molecule. De Gennes and Hervet (37) predicted a dendrimer surface congestion in PAMAM dendrimers using a simple mathematical equation. This relationship predicts that for a higher generations G, the surface area per group, Z, becomes increasingly smaller and experimentally approaches the cross-sectional area or Van der Waals dimensions of the surface group Z. The generation G thus reached is referred to as "dense-packed generation". An ideal cascade growth without branch defects is possible only for those generations preceding this dense-packed stage. It gives rise to self-limiting dendrimer dimensions, which are a function of the branch cell segment length, l, the core multiplicity, N_c, the branch cell juncture multiplicity, N_b, and the steric dimensions of the terminal group Z. Larger values of l delay this congestion, whereas, larger N_c and N_b values and larger Z dimensions hasten it. The tacit assumption in their calculation is that the branches become elongated as the molecule grows with the branch ends lying on the surface of the molecule throughout all stages of growth.

Lescanet (50) simulated starburst molecules by a kinetic growth method, and the results show significant differences from those previously predicted (37). The most significant of these differences is that the ends of the branches at a given generation are not on the surface but may be buried within the molecule. Monte Carlo calculations on dendrimers, reported by Mansfield, (51) gave similar results.

The congestion can be the cause of sterically-inhibited reaction rates and stoichiometric changes, and contributes to the differentiation of dendrimer branch cells during the advancement to higher generations. A comparison of spin-lattice relaxation times, T_1, for interior and surface carbon atoms shows that although the T_1 values for the interior carbons remain relatively constant with increasing generations, the T_1 values for the surface carbons decrease dramatically. (52) In general T_1 values for the terminal carbons were higher than those of the interior carbons. The surface of an ideal PAMAM dendrimer of generation 10-11 would be extraordinarily dense and congested. The mobility of the terminal groups, indicated through studies of relaxation times, suggests more available area. Therefore, either the number of terminal groups must be much lower than that attributed to the 2% growth failure rate, or the conformation must be such that all of the terminal groups do not reside at the surface. This would be consistent with a folding back of terminal groups into the interior of the molecule as has been suggested (50, 51). Such conformations would be subject to volume, rather than surface area, limitations.

If radial differences in concentration, or solvation, were present in the dendrimers such that the segmental mobility of the structure varied significantly, measurable changes in T_1 and T_2 would be expected. The method employed for this evaluation was determination of deuterium NMR relaxation times as a measure of molecular motion (53). The results were similar to those found above. (53) The differences between the relaxation times of the deuterium in the interior layers were not great enough to confirm the existence of gradients within the dendrimer.

It has been found that plots of intrinsic viscosity, density, surface area per group Z, and refractive index as a function of generation show a maxima or minima at the fourth or fifth generation, paralleling computer-assisted molecular-simulation predictions. (32, 54)

The intrinsic viscosities increase in a very classical fashion as a function of molar mass but decline beyond the fifth generation, presumably because of surface congestion which would reduce optimun surface-solvent interactions. The dendrimer density minimizes between fourth and fifth generation, then begins to increase due to increasingly larger exponential accumulation of surface groups as a function of generation. Since refractive indices are related directed to density parameters, their values should minimize and parallel the above density relationship.

1.5 Reactions, properties, and applications of dendrimers.

The dendrimer surface cells not only provide steric protection to its interior, but can also potentially function as primary molecular recognition sites for external reagents and solvents. For example, well-developed dendrimers with very hydrophobic interiors and hydrophilic surfaces are water-soluble (e.g., polyether dendrimers) whereas dendrimers with hydrophilic interiors and hydrophobic surfaces are hydrocarbon-soluble (e.g., PAMAM dendrimers).

Different procedures have been used to modify the dendrimer surface. For example, chelation, (32, 55) introduction of optically active groups, (6) and modification of the solubility of the dendrimer.

Fréchet has reported several modification procedures for the poly(aryl ether) dendrons and dendrimers in which the synthesis was based on 3,5-dihydroxybenzyl alcohol. For example, synthesis of copolymers with linear and dendritic blocks, (56) metalation by superbases, (57) synthesis of a dendritic fullerene, (58) and synthesis of dendrimers containing a solvatochromic chromophore at their focal point (59) have been reported.

Moore has produced copolymers of stiff dendritic macromolecules and linear flexible chains. (60)

Newkome has reported a study on the pH dependence of hydrodynamic radii of acid terminated dendrimers, (61) the introduction of alkyne groups in the structure of the dendrimers and subsequent reaction with a cobalt complex (62), and the use of core precursors containing ruthenium atoms. (63)

In Italy, a team of researchers at the University of Pisa, Messina, and Bologna, (64) has been using luminiscent and redox-active transition-metal complexes as monomers to build dendrimers. These metal-complex monomers have interesting photophysical and electrochemical properties. For example, the Ru_{22} complex is luminescent, it strongly absorbs visible and ultraviolet light, and it can be reversibly oxidized and reduced. They can potentially be used as photochemical molecular devices, that is, as antennas for harvesting light in solar energy conversion devices, or as multi-electron-transfer catalysts.

Tomalia's group (64) converted linear nylon-6 into a star-branched form and found that this reduces the viscosity of the melt by a substantially 30%, without changing its other properties. This reduced viscosity makes the dendritic nylon easier to be injection-molded.

Inoue (65) reported the synthesis of a porphyrin covalently encapsulated into a huge dendritic cage. The dendritic cage served as a barrier for the access of a large fluorecence quencher molecule, but behaved as a trap for vitamin K_3 which is a smaller fluorescence quencher molecule.

Kim and Webster (13c) used their hyperbranched polyphenylenes as multifunctional initiators to preparer star polymers and they studied the rheology behavior and thermal stability of mixtures of hyperbranched polyphenylenes with polystyrene.

Miller and Neenan (64) are exploring the physical properties of hyperbranched poly(aryl ether)s, analogs of linear poly(aryl ether)s, a common class of engineering plastics. They expect them to have properties quite distinct from their linear counterparts, in terms of ease of processing, rheological behavior, thermal stability, and mechanical behavior. They have proved to be more soluble than the linear analogs which are used in high-strength and high-temperature applications.

One of the many indications that dendrimers can have practical uses has recently come from the laboratory of D. A. Tomalia and that of J. R. Baker, Jr., of the University of Michigan Hospital and, separately, from the laboratory of F. C. Szoka, Jr., of the University of California in San Francisco. (66) They found evidence that dendrimers might one day be valuable in gene therapy, as vehicles for bringing DNA sequences into cells. The DNA-transporting structures they fashioned resembles clusters of proteins called histones. In the human body, nuclear DNA is found wrapped around such clusters. These dendrimers are so close in shape and size to a histone cluster that DNA wraps around them just as it does around the natural protein complex. The structure of dendrimers can be designed to home in on specific target cells. For example attaching certain substances, particularly sugar and protein groups, to dendrimer surfaces causes these polymers to adhere more favorably to some cell membranes than with others.

G. van Koten and his group at Utrecht University in the Netherlands identified another potential application for dendrimers. (66) In many manufacturing processes, chemical plants must use a catalyst to enhance the efficiency of certain reactions. The outside of a dendrimer can be covered with many catalytic sites, so that one dendrimer might induce a large number of reactions. These dendrimer typically readily dissolve in the reaction mixture.

The ability to attach substances that can serve as catalysts or biosensory agents to the surface of dendrimers has attracted the attention of the U.S. Army Research Laboratories. Tomalia , in collaboration with H. Dupont Durst and his colleagues there, are studying the possibility of using dendrimers to detect dangerous biological or chemical agents in the environment. (66)

For the first time, at DSM in the Netherlands in cooperation with Germany's Freiburg University, polypropyleneimine dendrimers are being made in multikilograms lots, and samples soon will be going to laboratories and enterprises around the world (48) to be tested for different applications, such as adhesive improvers, viscosity modifiers, agriculture, perfumes and pharmaceuticals. Some theoretical treatments and molecular dynamics simulations (50, 52) indicated that the large dendritic molecules should be capable of forming an outer barrier or shell, that restricts access to the interior of the molecule and that 50% of the internal volume is a "solvent-filled void". The intramolecular spaces in the dendrimers might be used to harbor agrochemicals, drugs, or fragrances, for instance, to be released slowly as required.

1.6 Strategy and goals.

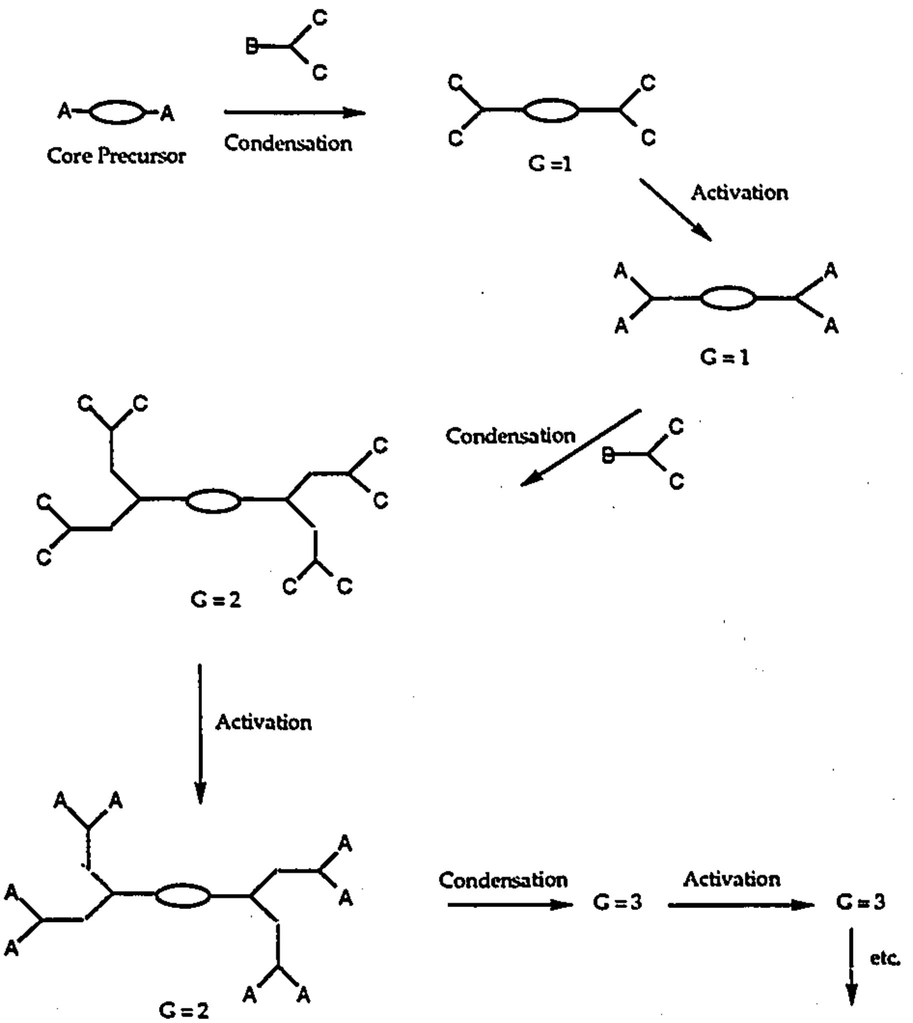
We proposed to synthesize two different types of multifunctional macromolecules: a) symmetrical poly(aryl ether) dendrimers using the *divergent initiator core method* based on a condensation/activation sequence and b) unsymmetrical poly(aryl ether) dendrons employing the *divergent uncontrolled method* based on a condensation polymerization reaction.

We expected that our dendrimers would possess the high terminal functionality characteristic of hyperbranched structures, which gives them interesting potential applications, along with the high thermal stability and hydrolytic resistance chracteristic of linear poly(aryl ether)s.

The divergent initiator core method proposed, is described in Scheme 1.4. There are two basic units for the construction of the dendrimers, the core precursor and the monomer. The core precursor contains two functional groups, which are represented by A. A dendritic branch will grow from each of the two functional groups. The monomer has two different functional groups, depicted as B and C. It is not only required that both functions B and C cannot coreact but also that function C must not react with function A. In the first step each A of the core precursor reacts with B of the monomer (condensation reaction) to form a symmetric unit with 2 times the number of C groups. Then in an activation step (oxidation reaction) each function C is converted to A.

Scheme 1.4

Divergent initiator core method



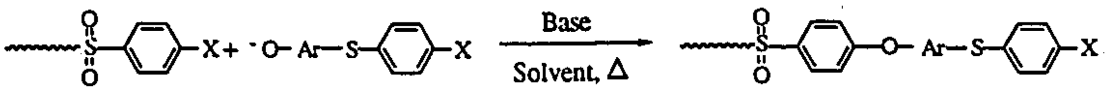
The resulting first generation product is used as a new core precursor and the reactions of the first generation are repeated to yield the second generation product. The higher generations are made in the same manner. All reactions involved in each growth step should be quantitative, since incomplete reactions or side reactions will cause structural defects and/or by-products. The purity of each generation is very important for the subsequent growth of starburst dendrimers.

The condensation and activation reactions we proposed to use are the displacement of a halide (Cl or F) by a phenolate and the oxidation of an aryl sulfide moiety to produce an aryl sulfone group (Scheme 1.5), repectively. They have proved to be very convenient methods for forming aryl ether linkages and sulfone groups. The advantages of these reactions in the dendrimer synthesis are their high yield and minimal side reactions, provided an optimum good system is selected and the reaction conditions are well controlled.

Scheme 1.5

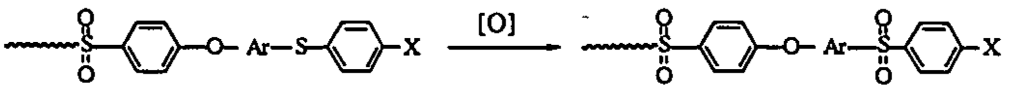
"Condensation"

Nucleophilic displacement of halogen



"Activation"

Oxidation of sulfide to sulfone



X = Cl, F

We proposed a similar condensation reaction for use in the synthesis of the hyperbranched poly(aryl ether) dendrons. The divergent uncontrolled method is a faster route to obtain highly branched structures, however the polymer structures obtained have defects. The preparation of similar dendrimers by these two methods will allow us to compare properties of symmetrical and unsymmetrical dendrimers.

1.6.1 Chronological development of our research.

We initially began our research with the synthesis of a potentially inexpensive, high molecular weight dihalide monomer with aryl chloride terminal units for the preparation of poly(aryl ether) dendrimers. Pre-formed sodium phenolate was used in these reactions. Nuclear magnetic resonance, NMR, and size exclusion chromatography, SEC, characterization suggested incomplete reaction for the higher generations (Chapter 2) .

In an effort to increase the efficiency of the polymerization reaction we next synthesized a monomer with aryl fluoride terminal units, keeping constant the other conditions. The reaction was improved but NMR and SEC characterization again suggested incomplete reaction for the higher generations (Chapter 3).

In the third stage we studied the effect of using a masked phenol and different condensation agents to increase the efficiency of the polymerization reactions. NMR suggested complete reaction through the fourth generation. Some of the properties of these materials were determined (Chapter 4).

In the latter stages of this research we obtained access to matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF-MS) and we used this instrument for the mass characterization of the dendrimers (Chapter 2, 3, and 4). MALDI-TOF-MS is a very valuable characterization technique since it allowed us to identify impurities, termination reactions, and intermediates in the polymerization. The information obtained with the MALDI-TOF instrument was invaluable for the characterization of the products. The methodology employed in the early stages of this research might have been different if this technique had been available from the beginning.

Simultaneously with this work, we synthesized several A_2B monomers for preparation of hyperbranched poly(aryl ether sulfone)s. Phenol-terminated, aryl chloride-terminated, and fluoride-terminated hyperbranched polymers were synthesized. NMR, SEC, and MALDI-TOF were used for their characterization and some of their properties were determined (Chapter 5).

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Chapter 2

Chloro poly(aryl ether sulfone) dendrimers from a pre-formed sodium phenolate, using the divergent approach.

2.1 Introduction.

The divergent initiator core method has been successfully used in the synthesis of many dendrimers, such as poly(amido amine), (1) poly(ethyleneimine), (2) iptycenes, (3) poly(alkyl ether)s, (4) poly(amido alcohol)s, (5) poly(amido ether)s, (6) poly(aryl amine)s, (7) polyphosphoniums. (8) polysiloxanes, (9) polycarbosilanes. (10) Dendrimers are produced directly by proliferating divergently from a core *in situ*; however, very high yields in the synthesis as well as efficient workup procedures for purification of the dendrimers are required. An advantage offered by this approach is that the steric bulk of the monomer is usually much lower than that of the dendron. This allows the advancement to higher generations by iterative reaction sequences before the cascade dense-packing occurs (11). Michael addition/amidation, (1) Diels-Alder adduct formation, (3) alkylation or benzylation reactions on polymethyl hydrocarbons ligands complexed with cationic organo-transition metal-fragments, (12) protection/deprotection methods using partially protected pentaerythritol, (4) alkylation/amidation, (5) etc., have been used as iterative sequences.

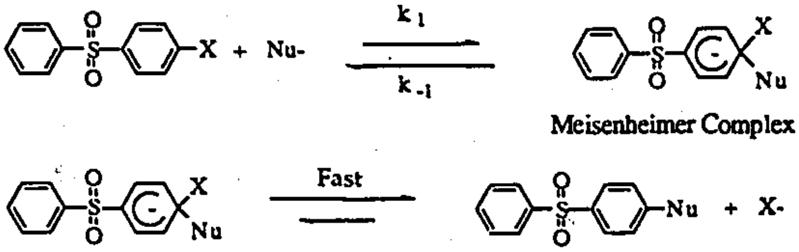
2.1.1 Nucleophilic aromatic substitution reactions in the synthesis of poly(aryl ether sulfone)s.

Poly(aryl ether sulfone)s are engineering plastics, which have been the subject of research and commercial enterprise since the 1960's. (13) They have been developed using two major methods. One method involves the base mediated nucleophilic displacement of aromatic bisphenols with activated aromatic dihalides. The second major method has involved the Friedel-Crafts type polysulfonylation of aromatic substrates with aromatic bissulfonyl chlorides. Recently, Fukawa (14) reported a novel etherification reaction. Aromatic halides activated by electron-withdrawing groups such as nitro, cyano, sulfone, and carbonyl react with sodium carbonate in the presence of silica/Cu salt catalyst.

In 1967, Johnson (15) described the synthesis of a large number of high molecular weight poly(aryl ether sulfone)s via condensation of bisphenols with activated aromatic dihalides. Additional papers by Rose, (16) and Robeson (17) are also important. The ether bonds are formed via the displacement of the halide by the phenolate.

It is generally accepted that this reaction proceeds via the S_NAr (aromatic nucleophilic substitution) mechanism, as shown in Scheme 2.1.(18)

Scheme 2.1



In S_NAr reactions, in which the aryl halide is activated toward nucleophilic attack by an electron-withdrawing group, the rate limiting step is typically the formation of the Meisenheimer complex. The rate constant, k_1, decreases in the order $F > Cl > Br > I$ for oxygen-based nucleophiles. This is attributed to the electronegativity of the halogen. As the electronegativity increases, the electropositive character of the aromatic carbon bonded to the halogen increases, and the rate of the nucleophilic attack increases.

It has been demonstrated that some polyetherifications of bis(aryl chloride)s were terminated at low molecular weights by the reductive elimination of chloride, which resulted in a polymer containing benzophenone chain ends. The occurrence of reductive elimination was found to be dependent on the structure of the aryl halide and bisphenolate, and the polymerization conditions, particularly the nature of the solvent and temperature. Polyetherifications and reductive dehalogenations conducted in N-methyl-2-pyrrolidinone, NMP, are quite sensitive to the dryness of the NMP and the polymerization temperature. In fact, unlike the behavior found in N,N-dimethylacetamide, DMAc, and dimethyl sulfoxide, DMSO, reductive dehalogenation of 4,4'-dichlorodiphenyl sulfone occurs in NMP with $KHCO_3$ at 180°C. The amount of reductive elimination of the halide relative to the amount of condensation between the aryl halide and the phenolate increased in the order $F < Cl < Br < I$.

2.1.1.1 Sodium and potassium phenolate.

Sodium bisphenolates can be formed by reacting a DMSO solution of a bisphenol with stoichiometric amounts of aqueous sodium hydroxide, followed by careful removal of the water as an azeotrope with chlorobenzene. Precise, stoichiometric addition of the dihalide results in the formation of the polymer. This method has some limitations. (19) It requires the exact stoichiometric amount of sodium hydroxide. Even a modest 1% deviation in the amount of the base drastically decreases the molecular weight obtained. A decrease in molecular weight in the presence of excess base has been attributed to a hydrolytic side reaction of the dihalide to the relatively inactive phenol. It has been reported that a deficiency of alkali not only disturbs the stoichiometric balance of the bisphenols but that unreacted phenol can hydrogen bond with an equivalent amount of sodium phenolate, thereby reducing the nucleophilicity of the phenolate. Although the ether bond is relatively stable to hydrolysis, the presence of excess base under the reaction conditions can cleave the activated ether linkage.

An alternate route uses anhydrous potassium carbonate as the condensation agent and a aprotic solvent such as DMAc. Viswanathant (19) reported the synthesis of poly(arylene ether sulfone)s via a potassium carbonate/DMAc process. DMAc has cation solvating power comparable to DMSO and is less sensitive to acidic or basic moieties. They observed from a kinetic study that the phenolate concentration in the reaction system increases with the temperature. The maximum concentration found was only a fraction of the total expected phenolate. This could be due to the incomplete formation of the phenolate caused by the poor solubility of the base under reaction conditions or the insolubility of the phenolate-terminal polymer. The addition of toluene, for removal of the water, would no doubt significantly reduce the solubility of base in DMAc. Compared to the DMSO/aqueous NaOH system, this process appears to be nearly 10 times slower. The slower reaction rates may be due to the hydrogen-bonding of the phenolate with unreacted phenol, the lower dielectric constant of the reaction medium due to the presence of significant amounts of toluene, or merely the initial heterogeneous nature of the K_2CO_3. A modest excess of anhydrous potassium carbonate did not reduced the intrinsic viscosity of the resultant polysulfones.

Recently, Miller (20) reported the synthesis of hyperbranched poly(aryl ether)s using a pre-formed sodium phenolate. He treated the monomer in THF with an excess of NaH. The solution was filtered to remove excess NaH. THF was removed in vacuum and DMAc or DMSO was added to the sodium salt, which was used directly. Heating the resulting solution for 0.5 - 2.0 hours effected polymerization.

2.1.2 Oxidation of aryl sulfide moieties .

Sulfides are readily oxidized to the corresponding sulfoxides or sulfones. Often, both products can be obtained on oxidation with the same oxidant, depending on whether one or two equivalents of the reagent are used. (21) Some of the oxidants, however, selectively oxidize sulfides to sulfoxides only or to sulfones only. The oxidation reagents used most frequently for the conversion of sulfides into sulfones are hydrogen peroxide and peroxy acids.

The oxidation of phenyl sulfides to phenyl sulfones has been carried out, using Oxone and wet alumina. (21, 22) Oxone is a stable mixture of potassium peroxymonosulfate, potassium hydrogen sulfate, and potassium sulfate, $KHSO_5$-$KHSO_4$-K_2SO_4. This mixture contains approximately two moles of $KHSO_5$ and one mole each of $KHSO_4$ and K_2SO_4. This mixture is a powerful oxidant with a wide range of applications. It can be stored without appreciable loss of active oxygen, and handled with negligible hazard to the user. The reactions are selective and high yields are obtained. The reagent is not expensive and can be used under simple operating conditions.

The oxidation potential of the peroxymonosulfate-bisulfate couple is 1.44 V. If the standard potential for the organic couple is known, it is possible to predict whether or not the oxidation reaction is thermodynamically feasible. Peroxymonosulfate ion can theoretically liberate a hydroxyl radical and a sulfate ion-radical.

Scheme 2.2

$$HOOSO_3^- \dashrightarrow HO^{\cdot} + {}^{\cdot}OSO_3^-$$

$$RCOOOH \dashrightarrow RCOO^{\cdot} + {}^{\cdot}OH$$

$$HOOH \dashrightarrow 2\,{}^{\cdot}OH$$

$$(O_3SOOSO_3)^{-2} \dashrightarrow 2\,{}^{\cdot}OSO_3^-$$

One or the other of these radicals can be obtained from an organic peroxy acid, hydrogen peroxide, or peroxydisulfate ion (Scheme 2.2). Thus peroxymonosulfate ion might be expected to behave somewhat like all of these substances.

2.1.3 Strategy and goals.

The objective of this section was the synthesis of chloro poly(aryl ether) dendrimers using the *divergent initiator core method* based on a condensation/activation sequence.

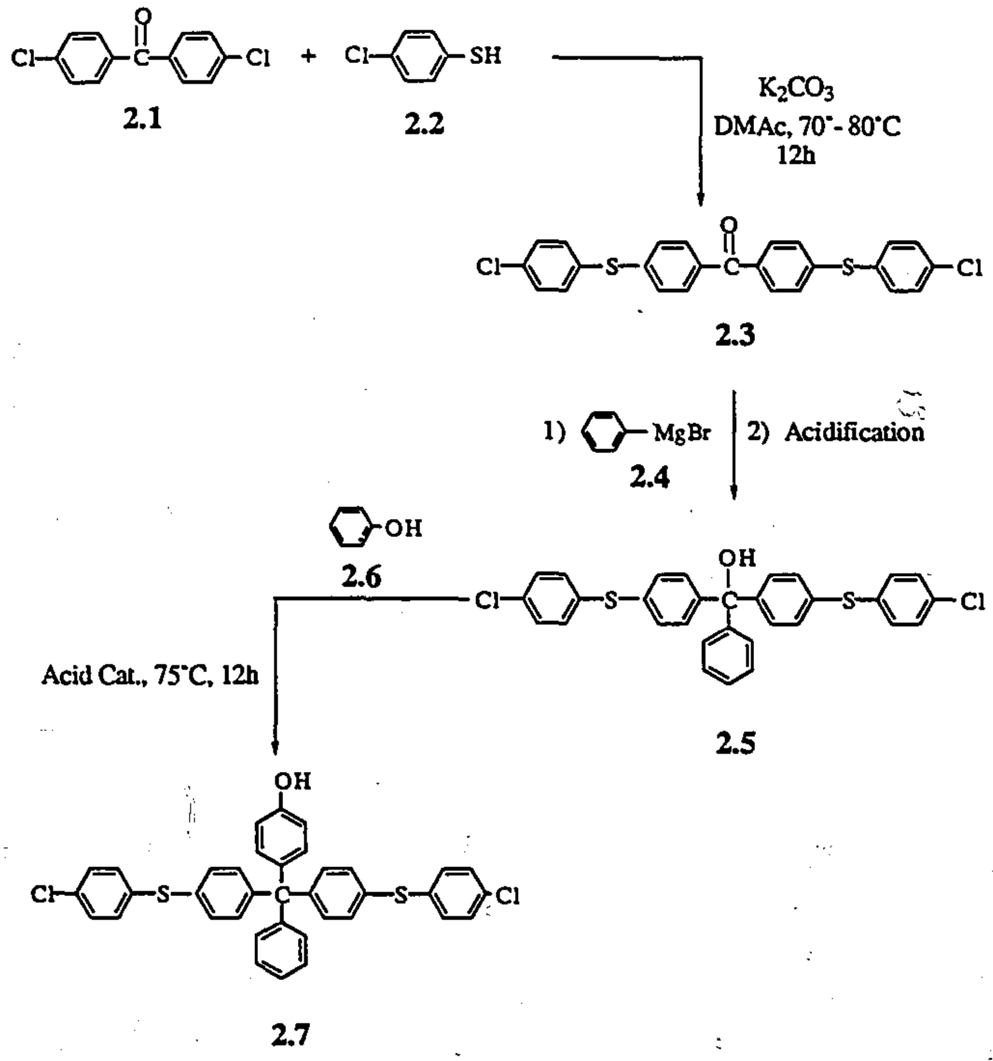
The condensation reaction we proposed to use is a displacement reaction of a chloride activated by a sulfone group using sodium phenolate. This type of reaction has been used extensively in Dr. Hay's Lab. (23) Sodium hydride was chosen to form the sodium salt of the phenol. The activation reaction used is the oxidation of an aryl sulfide moiety to produce an aryl sulfone group using Oxone and wet alumina. The general strategy for the synthesis is described in Chapter 1, Part 1.6.

In our dendrimer synthesis, 4,4'-difluorodiphenyl sulfone **2.8** was chosen as the core precursor and phenol **2.7** as the propagation unit. The relatively high molecular weight of phenol **2.7** allows the formation, in a few generations, of high molecular weight dendrimer. For example, our third generation chloro poly(aryl ether sulfone) dendrimer has a theoretical molecular weight of 9376 g/mol.

2.2 Preparation of the monomer.

The synthesis of phenol **2.7** is shown in Scheme 2.3. The reaction begins with displacement of the chloride groups of 4,4'-dichlorobenzophenone **2.1** by two molecules of 4-chlorothiophenol **2.2** using K_2CO_3 under mild conditions (24) to obtain the condensation product **2.3**. Then, product **2.3** is made to react with phenylmagnesium bromide **2.4** through a Grignard reaction (25) to produce the tertiary alcohol **2.5**. The alcohol **2.5** is condensed (26) with phenol **2.6** in the presence of an acid catalyst to generate the monomer **2.7**. The overall yield of **2.7** from 4,4'-dichlorobenzophenone **2.1** was 50 %. Nuclear magnetic resonance, NMR, and mass spectrometric characterization of each of those products confirmed the proposed structure (see Experimental Section). The purity of **2.7**, after purification on a chromatographic column and determined by high pressure liquid chromatography, HPLC, was 97%.

Scheme 2.3



2.3 Preparation of chloro poly (aryl ether) dendrimers.

The synthetic strategy that we used led to two dendrimer families which contained two different functionalities in the terminal units, aryl sulfide and aryl sulfone. Our nomenclature gives the dendrimer generation (1G, 2G, etc.) followed by letters denoting the nature of the terminal units (Cl = chloro, S = sulfide, SO_2 = sulfone).

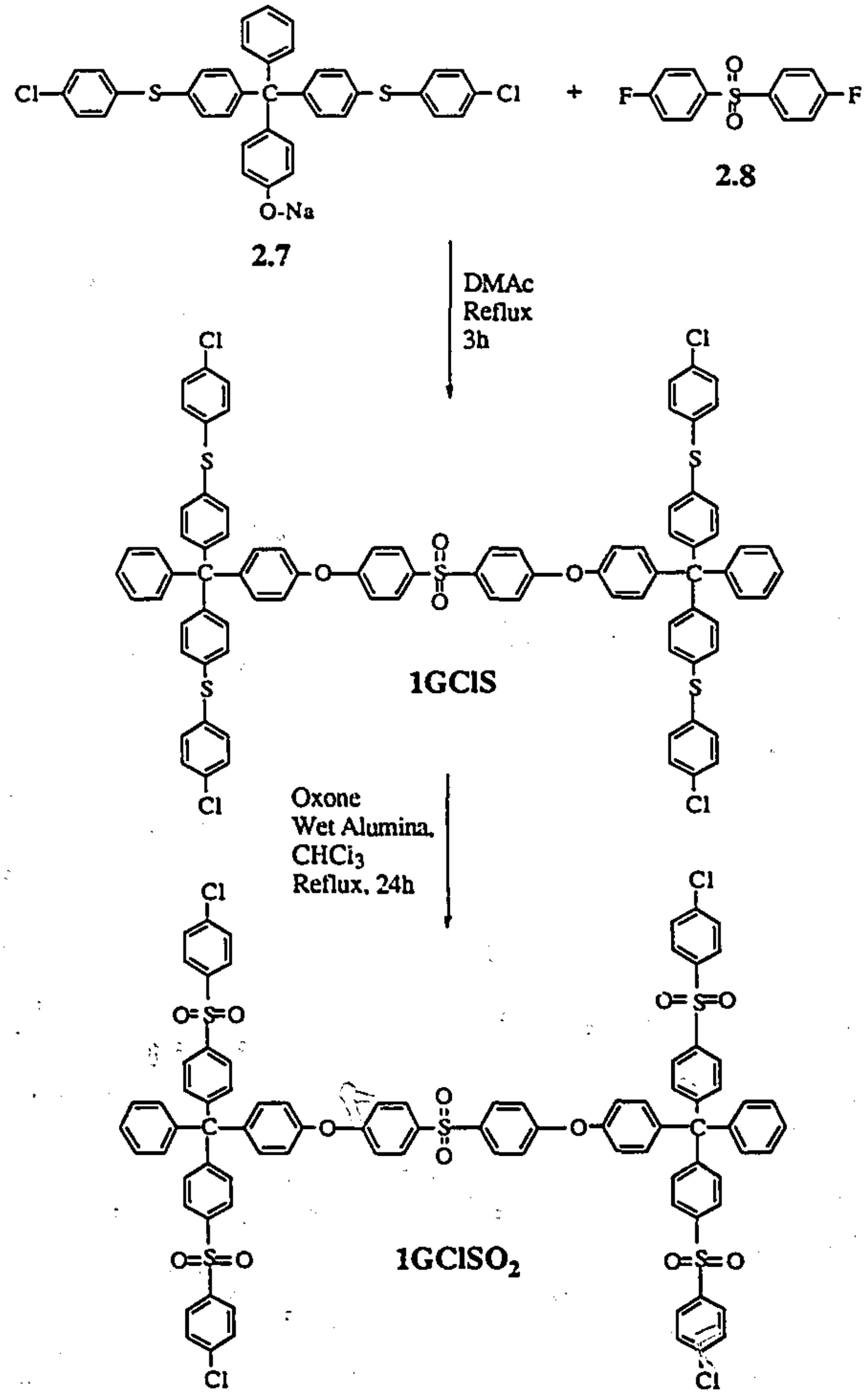
The synthesis of chloro poly(aryl ether sulfide) dendrimers up to five generations was carried out using N,N-dimethyl acetamide, DMAc, as the solvent for the reaction, reaction times from 3 to 8 hours, and temperatures from 130 °C to 164°C. Approximately stoichiometric amounts of the phenolate **2.7** and activated aryl chlorides were used, except in the synthesis of the first generation in which an excess of the phenolate was employed. The theoretical molecular weight of the dendrimers were used to calculate the quantities of reagents employed in the experiments and reaction yields. 4,4'-Difluorodiphenyl sulfone **2.8** was the core precursor. The phenolate was prepared by treating the purified phenol with NaH in ethyl ether. The dendrimers were purified by fractional precipitation and the reactions were followed by size exclusion chromatography, SEC. The syntheses of the first, second, and third generations are shown in Schemes 2.4, 2.5, and 2.6, respectively.

The activation reaction, in which the sulfide groups are oxidized to produce chloro poly(aryl ether sulfone) dendrimers, was performed under similar conditions for all four generations. Oxone and wet alumina were used as the oxidation reagent and chloroform was the solvent of the reaction under reflux conditions. (21, 22)

The products were characterized by SEC, NMR, and matrix-assisted laser desorption ionization time-of-flight mass spectrometry, MALDI-TOF-MS. Details of the characterization will be given later. The yields of the activation reactions were high (89% - 97%). Those of the condensation reactions, after the purification of the products, were around 60%.

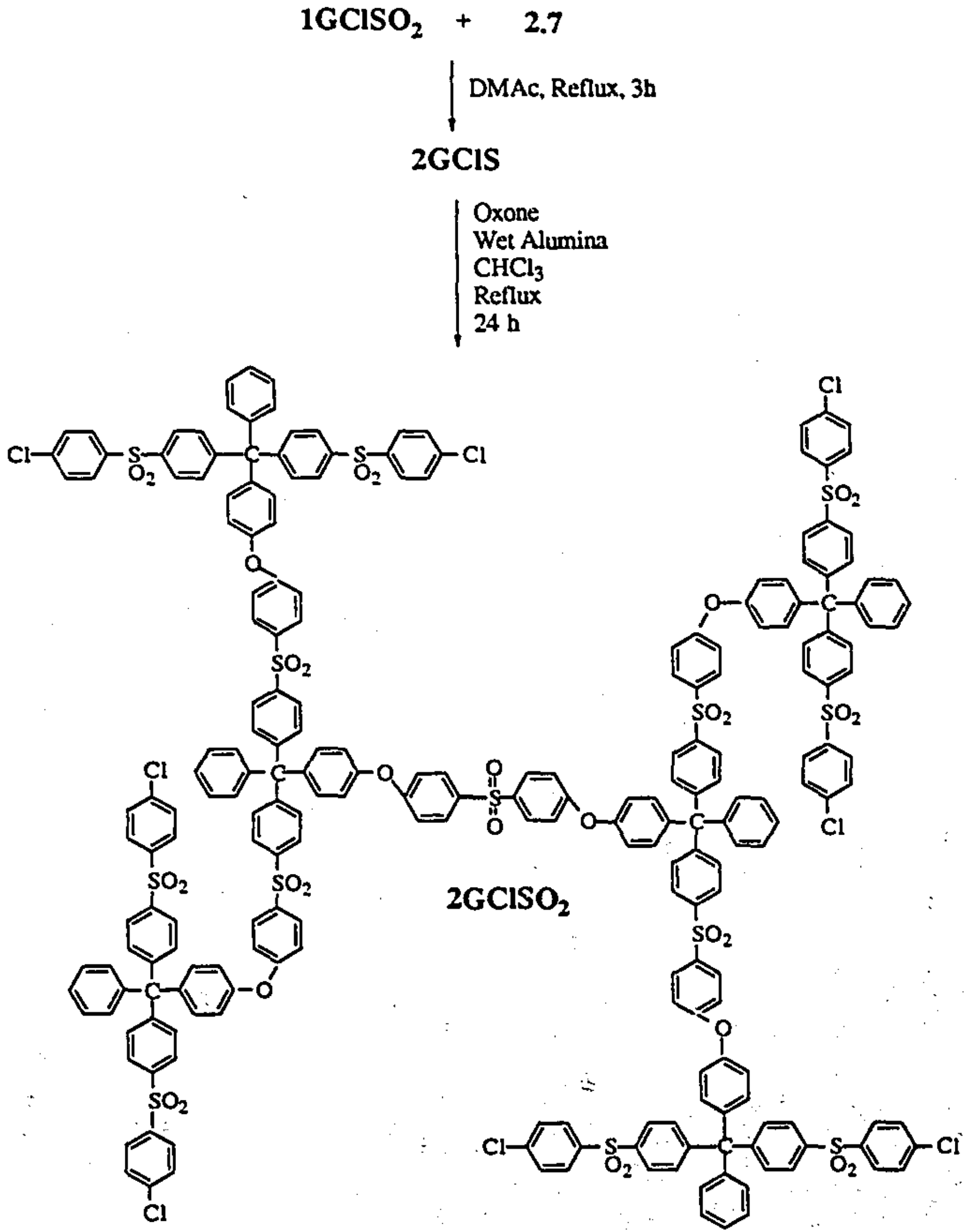
Scheme 2.4

Syntheses of first generation chloro poly(aryl ether)s.



Scheme 2.5

Syntheses of second generation chloro poly(aryl ether)s



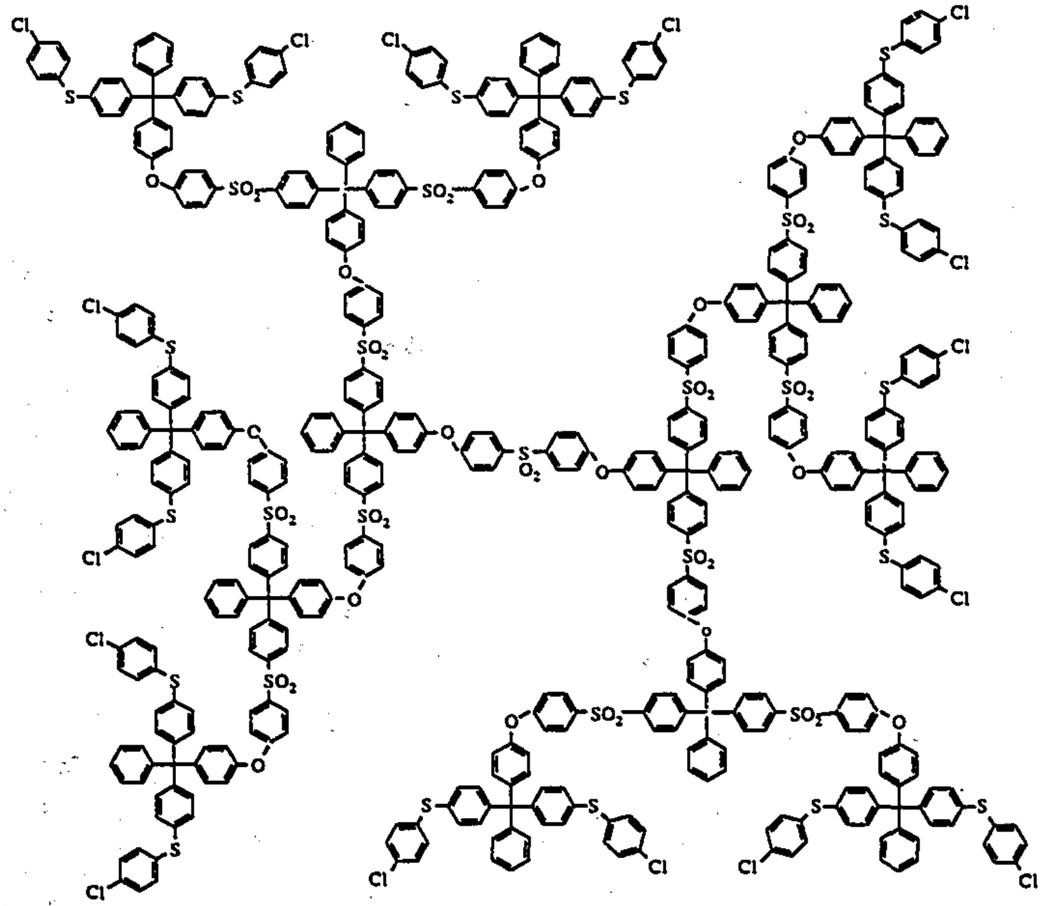
2GClSO$_2$

Scheme 2.6

Syntheses of third generation chloro poly(aryl ether)s

2GClSO2 + 2.7

$\downarrow$ DMAc, Reflux, 3h



3GClS

$\downarrow$ Oxone, Wet Alumina
$CHCl_3$, Reflux
24h

$3GClSO_2$

2.4 Effect of the temperature on the condensation reaction.

We explored the effect of the reaction temperature on the synthesis of two series of five generations of dendrimers. At this stage of our research, SEC and NMR were the only techniques available in our laboratory to study the homogeneity of the samples.

The synthesis of the first generation **1GClS** was performed under reflux condition (164°C). The elimination of the monosubstituted product became difficult when a lower temperature was used.

Table 2.1. Effect of the temperature of the reaction, T, on the syntheses of chloro poly(aryl ether sulfide) dendrimers

Dendrimer	Mw (g/mol) a)	PD a)	R (%) b)	t (h)	T (°C)
2GClS	2976	1.21	12	3	152
2GClS	2654	1.19	9	3	164
3GClS	6688	1.16	10	3.5	150
3GClS	6163	1.24	7	3	164
4GClS	10073	1.24	20	8	134
4GClS	10897	1.27	13	3.5	155
5GClS	14181	1.31	28	8	130
5GClS	15828	1.41	14	3	155

a) SEC, based on polystyrene standards, chloroform, 1mL/min, UV-detector; data was obtained from crude products. b) R = percent (%) of phenolate peak area with respect to the total area of peaks in the SEC chromatogram.

The amount of unreacted phenolate depends on the reaction temperature, as shown in Figure 2.1 and Table 2.1. In Figure 2.1 values of R versus reaction time are given for the second and third generations. R represents the % of phenolate peak area with respect to total area of peaks in the SEC chromatogram.

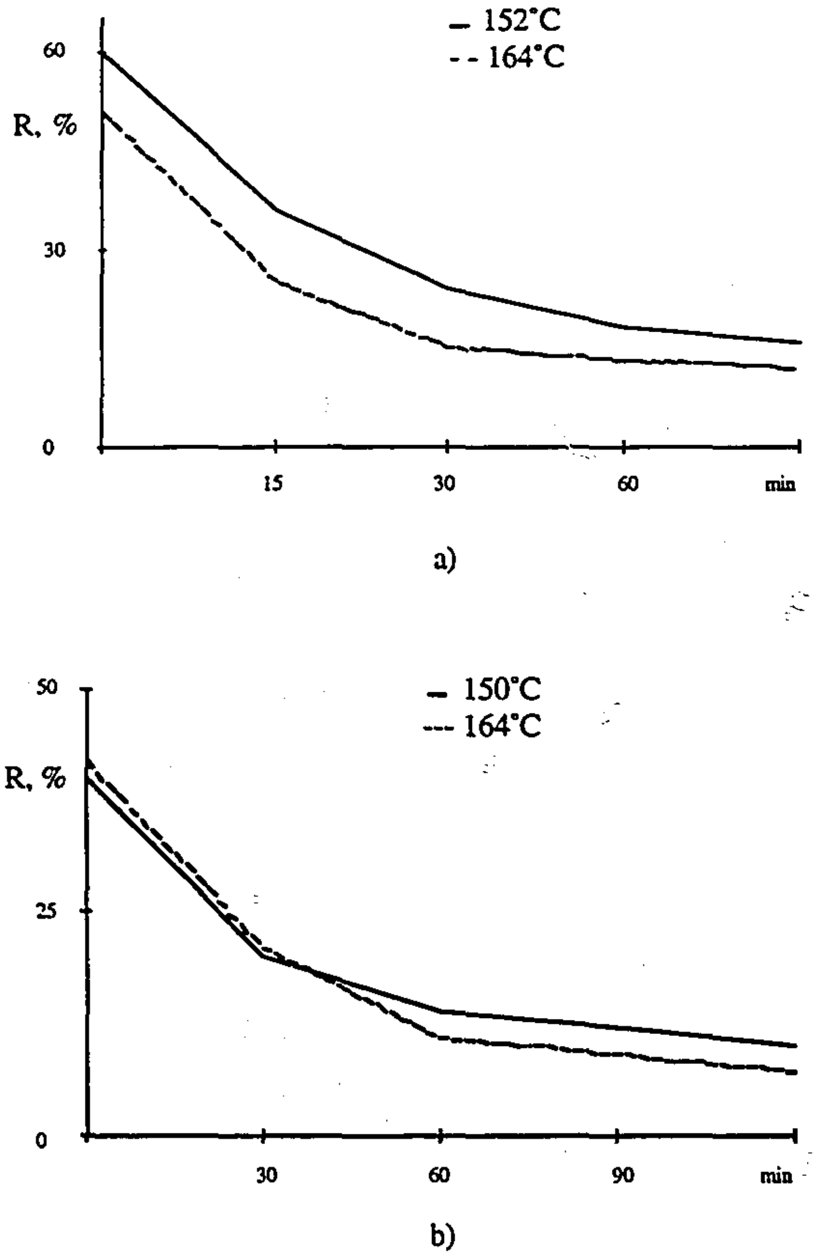


Figure 2.1. Effect of reaction temperature and reaction time on the unreacted phenolate. Chloro poly(aryl ether sulfide) dendrimers: a) **2GClS** and b) **3GClS**.

When temperatures around 150°C were used, R had values from 10 % to 14 %. Lower temperatures (130°C and 134°C) gave higher values of R (28% and 20%). Condensation reactions carry out under reflux conditions and reaction times of about three hours produced the lowest value of R (7%). Longer reaction times did not cause an appreciable improvement in the conversion of the reaction.

Molecular weights, Mw's, and polydispersities, PD's of the crude products, obtained by SEC at different temperatures are shown in Table 2.1. There was no special effect of the temperature on the molecular weights. However, the polydispersities tend to increase and the maximum of the chromatogram of the second generation moves to a higher molecular weight (Fig. 2.2) when a higher temperature was employed. These tendencies were reproducible.

This exploratory work indicated that a reaction temperature lower than the boiling point of the solvent is not practical under the conditions used in these syntheses.

2.5 Molecular characteristics.

2.5.1 Chromatography.

The SEC chromatograms, weight average molecular weights (Mw's), and polydispersities (PD's) of the different purified generations of dendrimers are given in Figure 2.3 and Table 2.2. Mw's increase with the number of generations from 706 to 14112. However, the polydispersity values, PD's, remain close to 1 as is expected for almost monodisperse materials. There is a significant difference between the weight average molecular weights and the formula weights (FW's) of the different generations of dendrimers. This can be explained if we assume that their structures are more compact than those of the polystyrene standards used in the calibration curve.

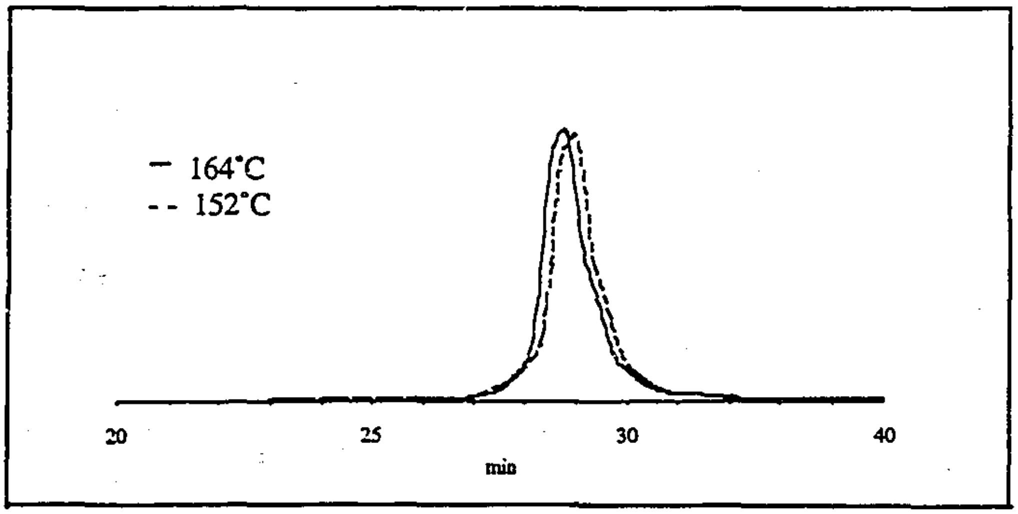


Figure 2.2. SEC chromatograms of second generation chloro poly(aryl ether sulfide) **2GClS**, obtained at 152°C and 164°C. Analysis conditions in **Table 2.1.**

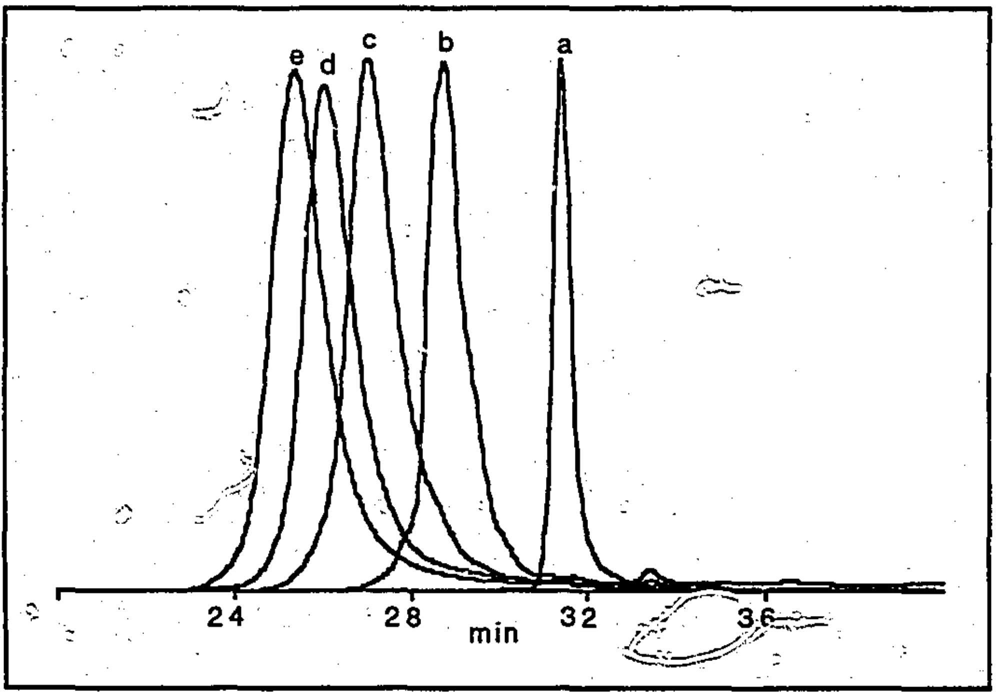


Figure 2.3. SEC chromatograms of chloro poly(aryl ether sulfide) dendrimers: a) **1GClS**, b) **2GClS**, c) **3GClS**, d) **4GClS**, and e) **5GClS**. Analysis conditions in **Table 2.2.**

The shape of the chromatograms of chloro poly(aryl ether sulfone) dendrimers was similar to those of the chloro poly(aryl ether sulfide) dendrimers of comparable molecular weight. This suggests that no important side reactions occurred during the oxidation of aryl sulfides to sulfones.

The crude chloro poly(aryl ether sulfide) dendrimers were purified by fractional precipitation since their chromatograms showed shoulders and/or tails of low molecular weight species. However, as shown in Figure 2.3, the complete purification of the dendrimers was not possible.

Table 2.2. Some characteristics and properties of chloro poly(aryl ether) dendrimers

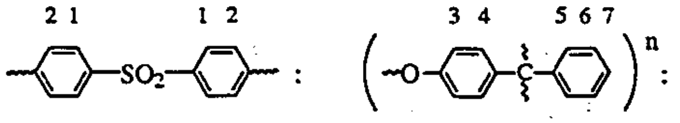
Dendrimer	1GClS	1GFClO$_2$	2GClS	2GClSO$_2$	3GClS	3GFSO$_2$	4GClS	4GClSO$_2$	5GClS
FW (g/mol)	1458	1586	3926	4182	8864	9376	18739	19763	38489
Mw (g/mol) a)	706	1042	2687	3286	6438	7287	10247	10785	14112
PD a)	1.06	1.09	1.14	1.16	1.17	1.17	1.21	1.20	1.27
η_{inh} (dL/g) b)	0.06	0.06	0.07	0.10	0.10	0.09	0.10	0.11	0.11
Tg (°C) c)	102	168	156	206	177	223	198	231	201
Yield$_1$ (%) d)	82	97	85	94	88	93	75	89	94
Yield$_2$ (%) e)	56	-	62	-	65	-	57	-	57

a) Analysis conditions in Table 2.1; data obtained from purified samples. b) NMP, 0.5 g/dL, 25 °C. c) Nitrogen, 10 °C/min. d) Yield before purification. e) Yield after purification.

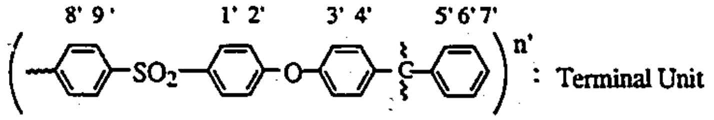
2.5.2 Nuclear magnetic resonance.

For the discussion of the NMR characterization of dendrimers it is useful to describe the building units that make up these polymers. The schematic representation of the different blocks that form chloro poly(aryl ether) dendrimers are shown in Scheme 2.7. Each of these blocks can be identified in the ideal structures of **1GClSO$_2$**, **2GClSO$_2$**, and **3GClS** given in Schemes 2.4, 2.5 and 2.6, respectively (see Chapter 1: Part 1.1 for more details). (27)

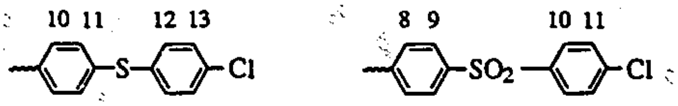
Scheme 2.7



Core **Repeat unit A**



Repeat unit B



Terminal Unit C **Terminal Unit D**

Dendrimers are formed from one core, internal layers, and one terminal layer. The layers are formed by internal (A, B) and terminal (C or D) units, where n and n' represent the number of layers in each molecule. The core and the first layer (n = 1) are common for all dendrimers. For example, the structure of **3GClS** contains one core, one first internal layer formed by two repeat units A, two subsequent layers formed by repeat units B, and one terminal layer formed by 16 terminal units C. The structure of **3GClSO$_2$**

differs only in the nature of the terminal unit. It contains 16 terminal units D. The first generation does not contain repeat units B (n' = 0). The numbers in Scheme 2.7 represent the different hydrogens in the dendrimer which were arbitrarily chosen.

The ^{1}H NMR spectra (500MHz) of these polymers are given in Figures 2.4 - 2.7. COSY experiments were carried out for the identification of the protons. The differences between the ^{1}H NMR spectra of chloro poly(aryl ether sulfide) and those of chloro poly(aryl ether sulfone) dendrimers confirm that structural changes occurred during the oxidation or displacement reactions. Before the oxidation reaction protons H_{12} and H_{13} at the terminal units C absorb at δ = 7.34 ppm and 7.42 ppm (Fig. 2.4a). After the oxidation reaction these protons, now close to the new sulfone group (terminal unit D : H_{10} and H_{11}), show resonances at about δ = 7.94 ppm and 7.66 ppm (Fig. 2.4b). The same behavior is observed with the higher generations.

The structure of **1GClS** contains only an internal layer formed by two repeat units A. However, some layers of the higher generations of chloro poly(aryl ether sulfide)s are formed by repeat units B. This explains the resonance observed at about δ = 7.80 ppm - 7.83 ppm which can be attributed to protons H_9 (Figs. 2.5a and 2.6). The similarities observe in the spectra of the dendrimers are a consequence of common protons present in their structures (Scheme 2.7).

The very low intensity peak (about 7.6 ppm) detected in the spectra of **2GClS**, **3GClS**, **4GClS**, and **5GClS** might be due to an incomplete reaction. Protons H_{11} in the starting material (terminal unit D) show resonances in the same area. In general, the peaks become broader as the generation number increases. Similar protons in different layers could absorb slightly different amounts of energy that can affect the width of the peaks.

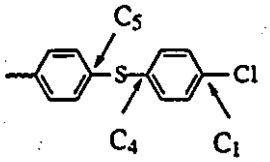
Some ^{1}NMR integrals are given in Table 2.3. The differences between the theoretical (Cal) and experimental values (Fnd) for the higher generations of chloro poly(aryl ether sulfide)s are higher than 10%, but those of the chloro poly(aryl ether sulfone)s were around 10%. The reproducibility of these measurements was also about 10%.

Table 2.3. ${}^1H$ NMR integrations of chloro poly(aryl ether) dendrimers

Dendrimer	n' a)	Z b)	$H_1+H_{1'}+H_9$		$H_1+H_1+H_9+H_9+H_{10}$	
			Cal.	Fnd.	Cal.	Fnd.
1GFS	0	4	4	4	-	
2GFS	1	8	20	22	-	
3GFS	2	16	52	59	-	
4GFS	3	32	116	157	-	
5GFS	4	64	244	306	-	
$1GFSO_2$	0	4	-		20	22
$2GFSO_2$	1	8	-		52	49
$3GFSO_2$	2	16	-		116	112
$4GFSO_2$	3	32	-		244	237

a) n' = number of layers with internal unit B. b) Z = number of terminal units.

The ${}^{13}C$ NMR spectra (50 MHz) are given in Figures 2.8 - 2.11 . The results were similar to those found previously. For example, before the oxidation reaction atoms C_1, C_4, and C_5 at the terminal unit C absorb at about $\delta = 134$ ppm. After the oxidation reaction these carbons, now close to the new sulfone group (terminal unit D), show resonances at about $\delta = 140$ ppm.



Since the number of peaks in each spectrum depends on the fact that similar carbons in different layers can absorb slightly different amounts of energy, it is possible to see more than one peak for similar C's.

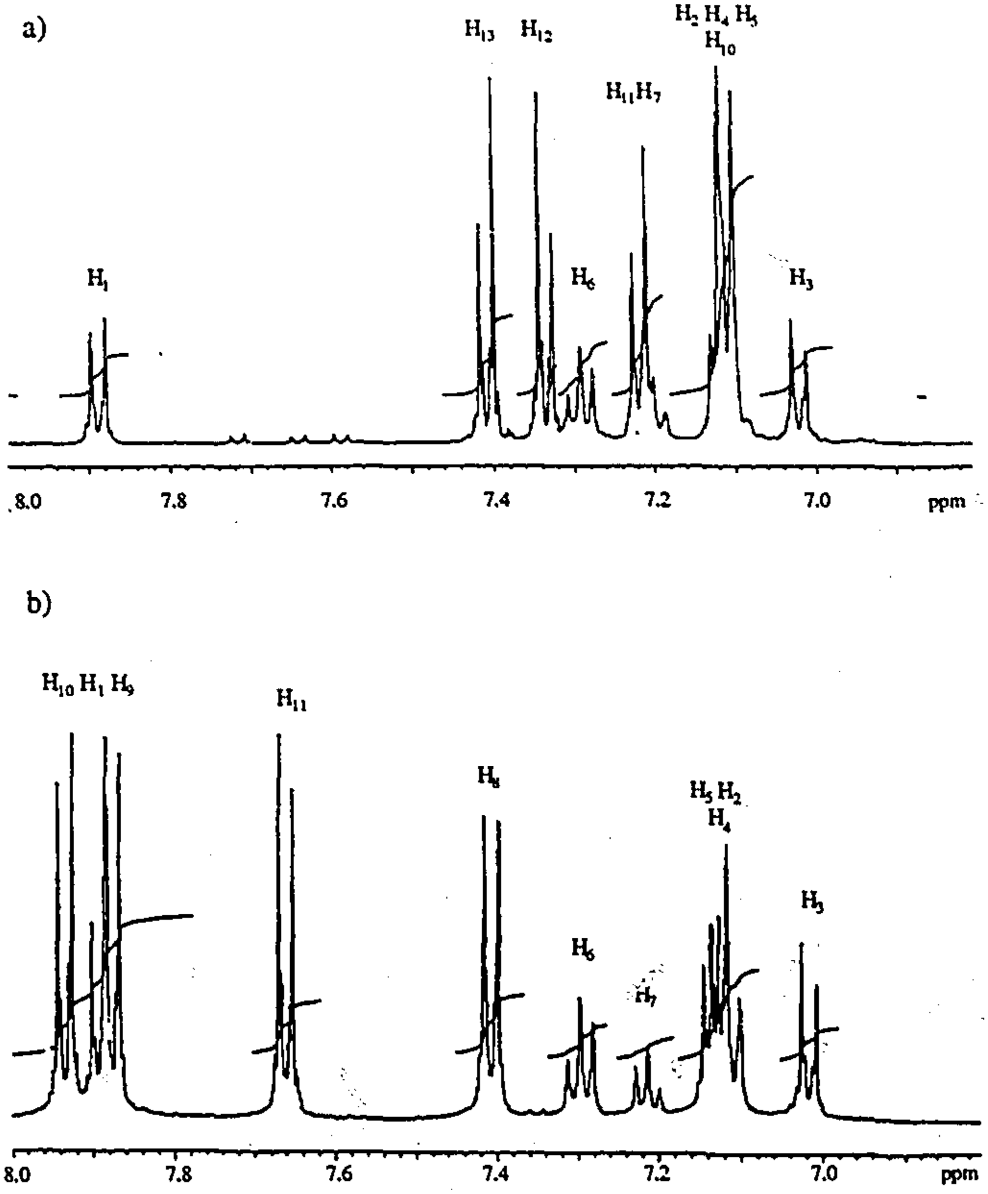


Figure 2.4. ^{1}H NMR spectra of first generation chloro poly(aryl ether)s: a) **1GClS** and b) **1GClSO$_2$**.

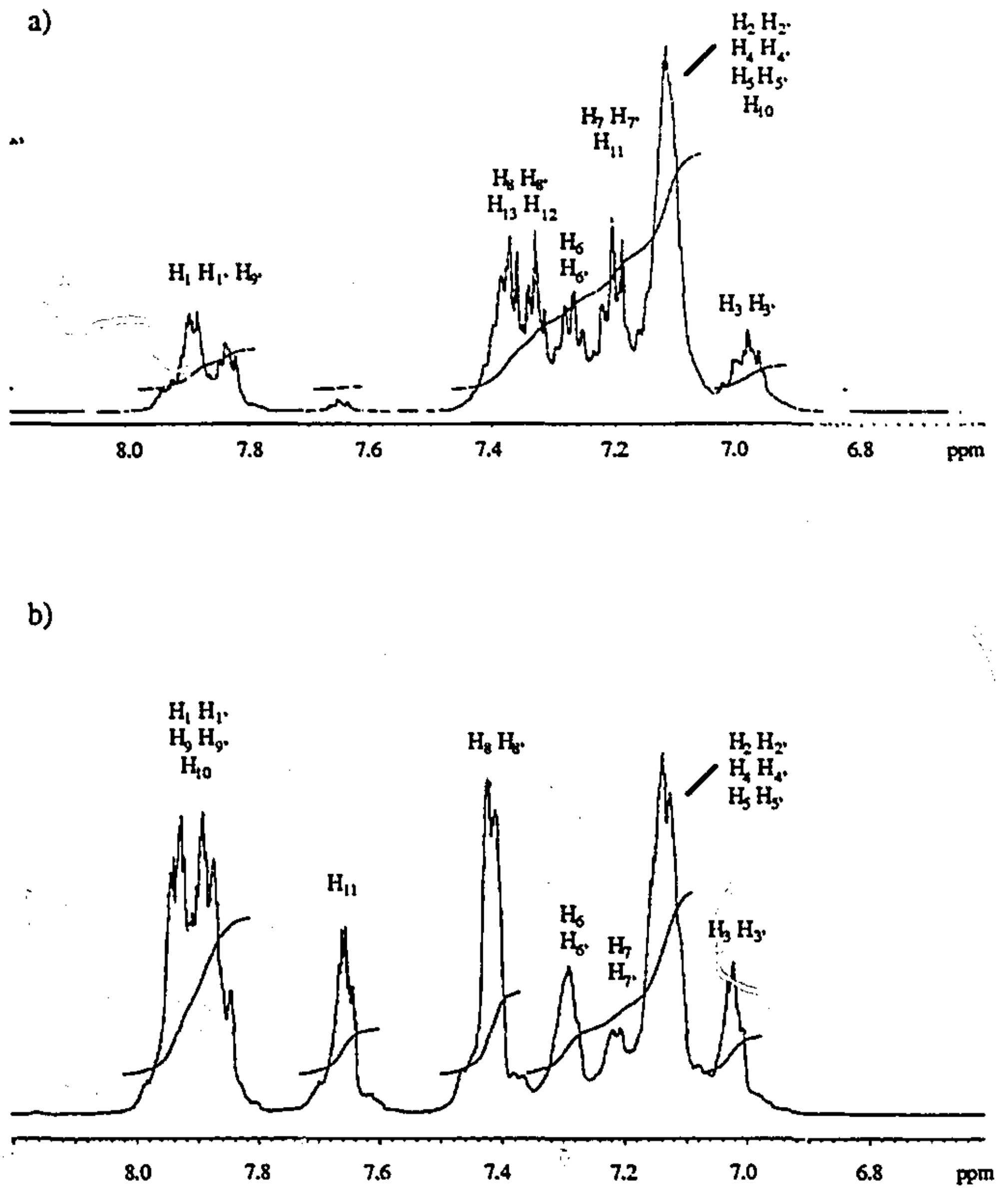


Figure 2.5. ^{1}H NMR spectra of the second generation chloro poly(aryl ether)s: a) **2GClS** and b) **2GClSO$_2$**.

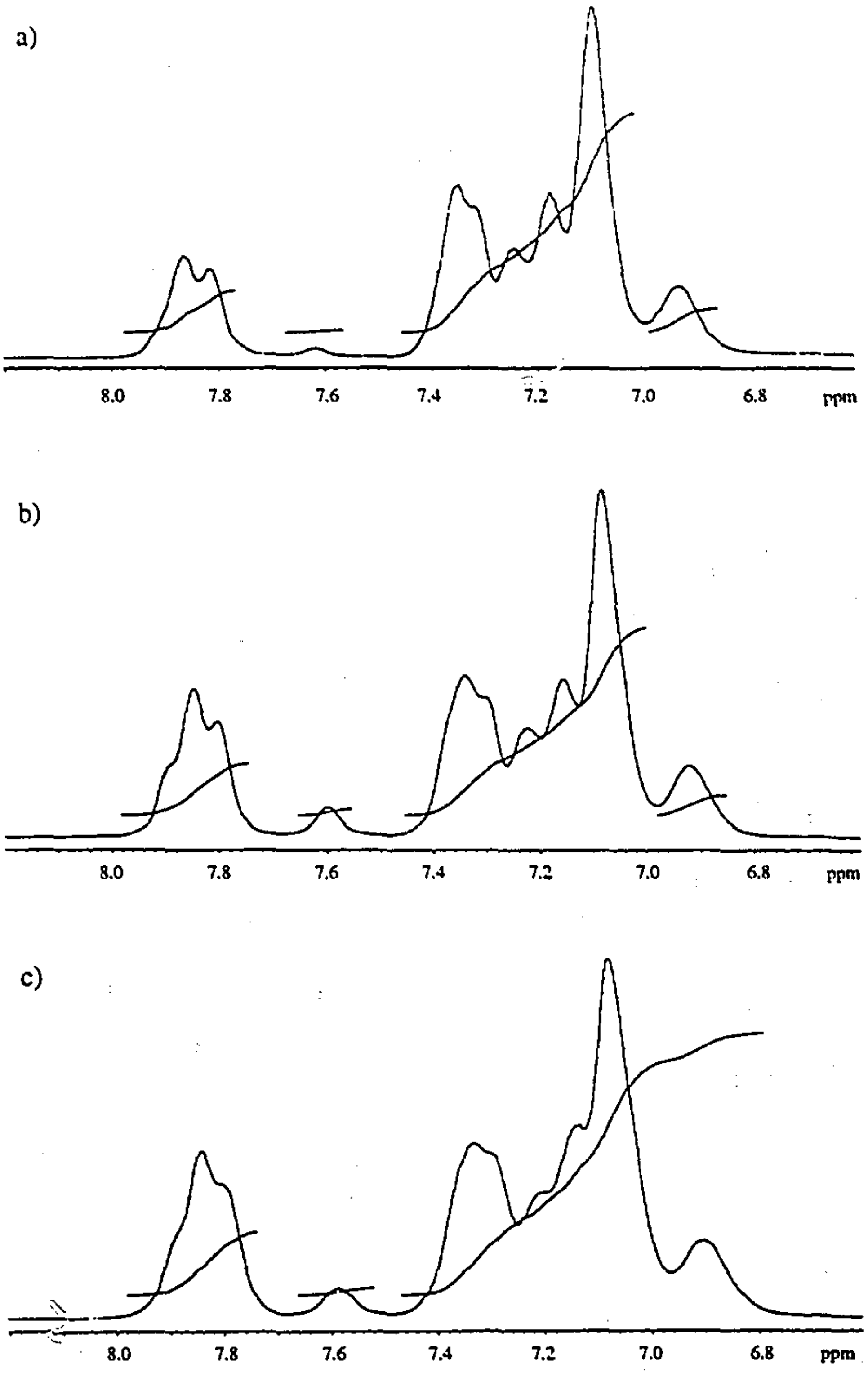


Figure 2.6. ^{1}H NMR spectra of chloro poly(aryl ether sulfide) dendrimers: a) **3GClS**, b) **4GClS**, and c) **5GClS**.

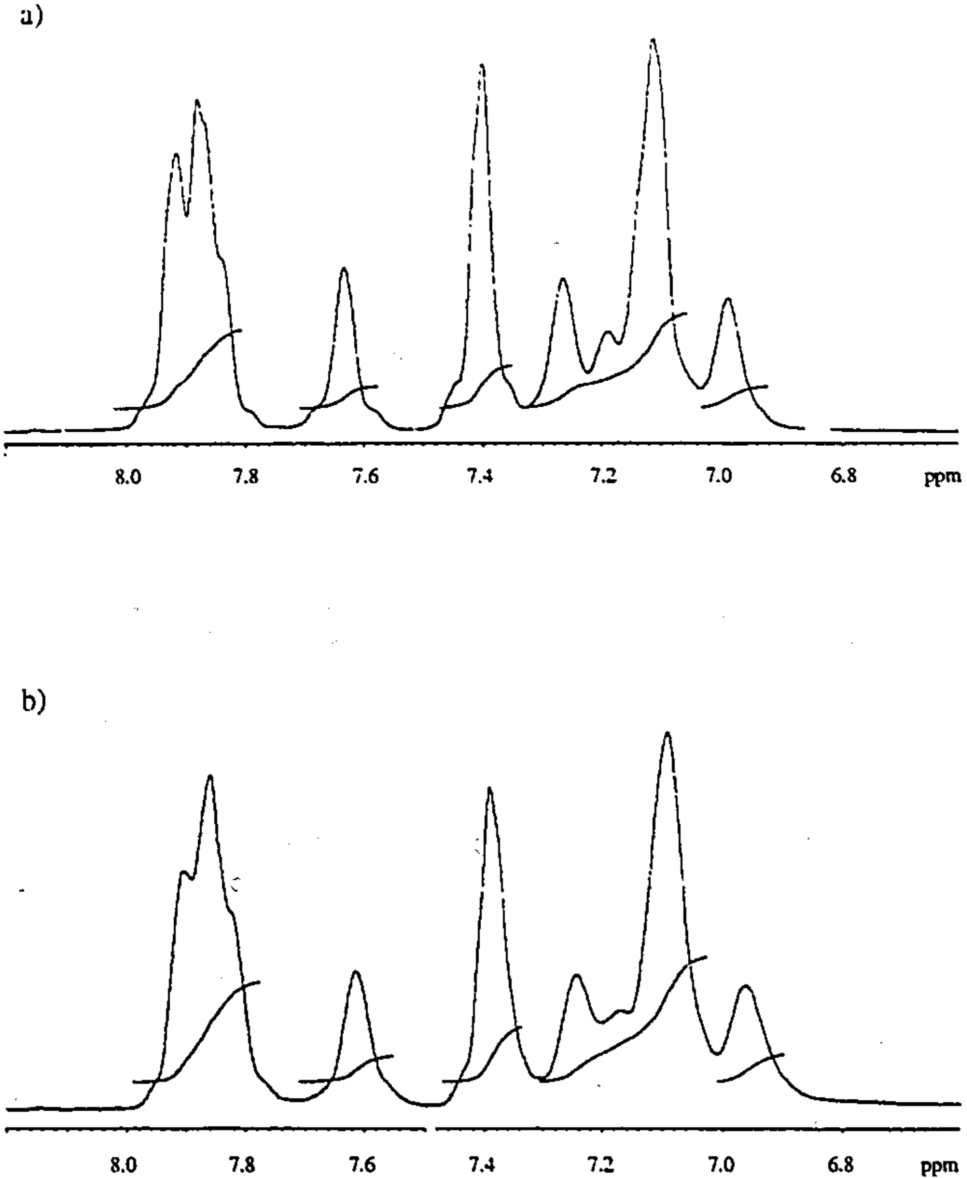


Figure 2.7. ^{1}H NMR spectra of chloro poly(aryl ether sulfone) dendrimers: a) **3GClSO$_2$** and b) **4GClSO$_2$**.

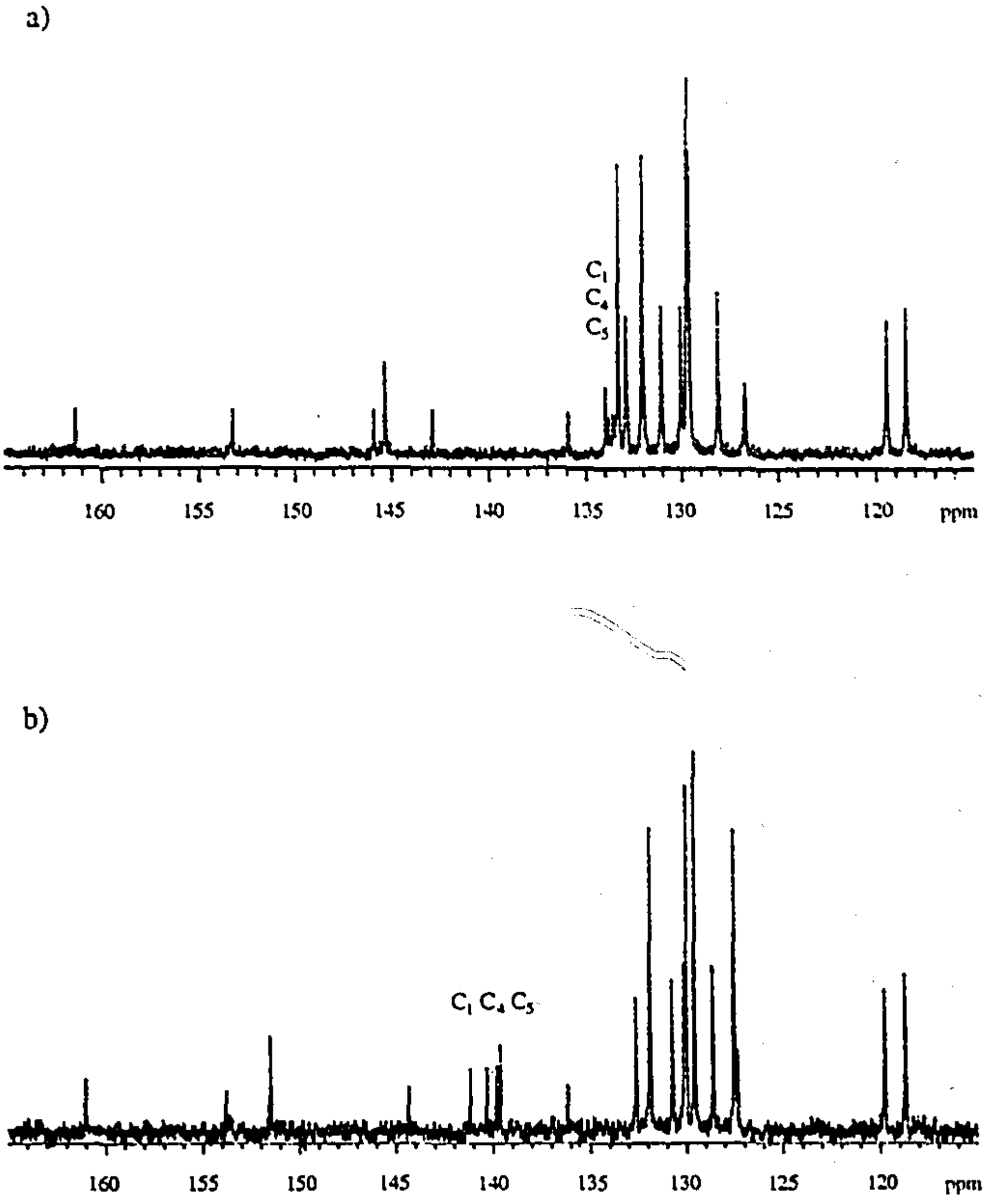


Figure 2.8. ^{13}C NMR spectra of first generation chloro poly(aryl ether)s: a) **1GClS** and b) **1GClSO$_2$**.

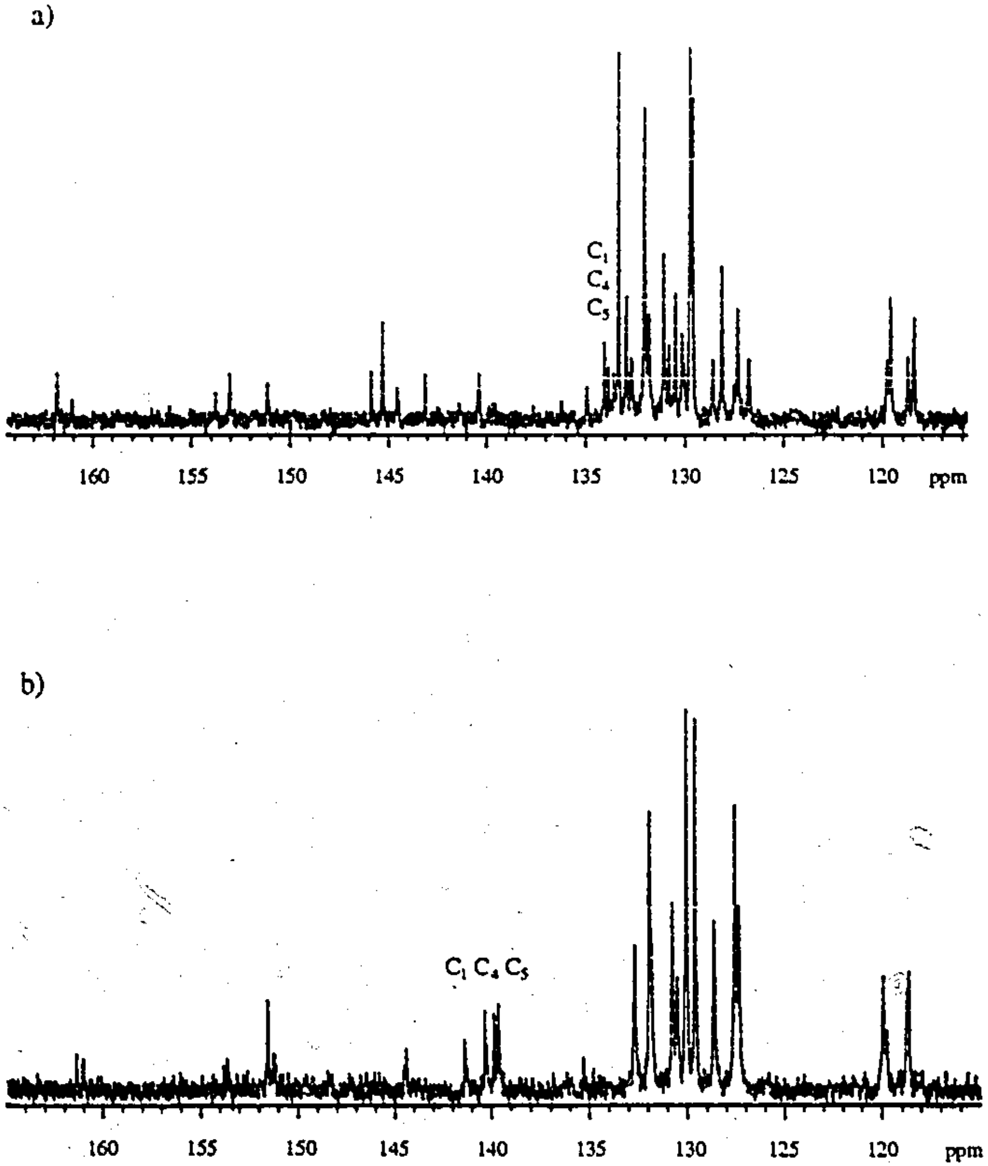


Figure 2.9. ^{13}C NMR spectra of second generation chloro poly(aryl ether)s: a) **2GClS** and b) **2GClSO$_2$**.

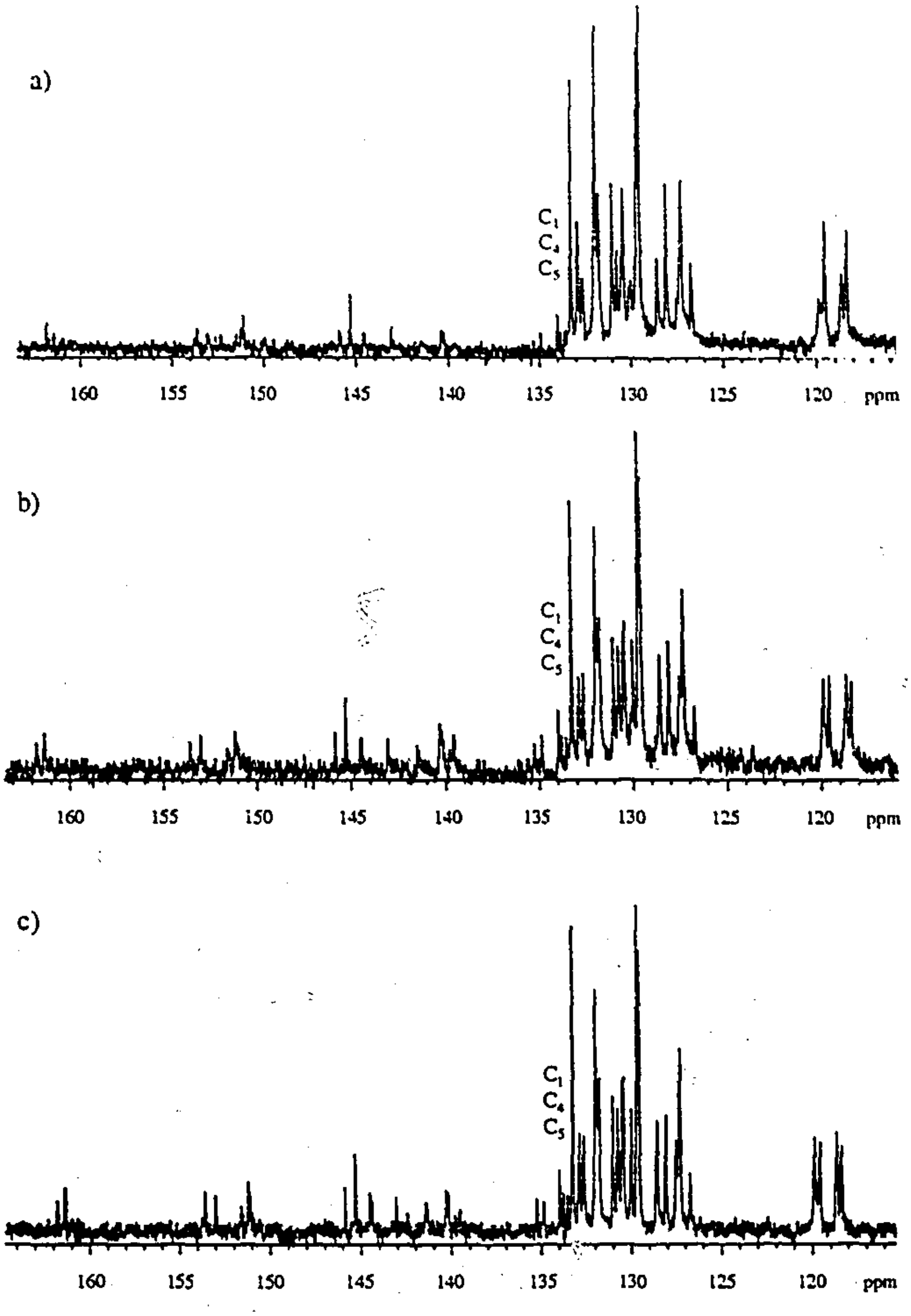


Figure 2.10. ^{13}C NMR spectra of chloro poly(aryl ether sulfide) dendrimers: a) **3GClS**, b) **4GClS**, and c) **5GClS**.

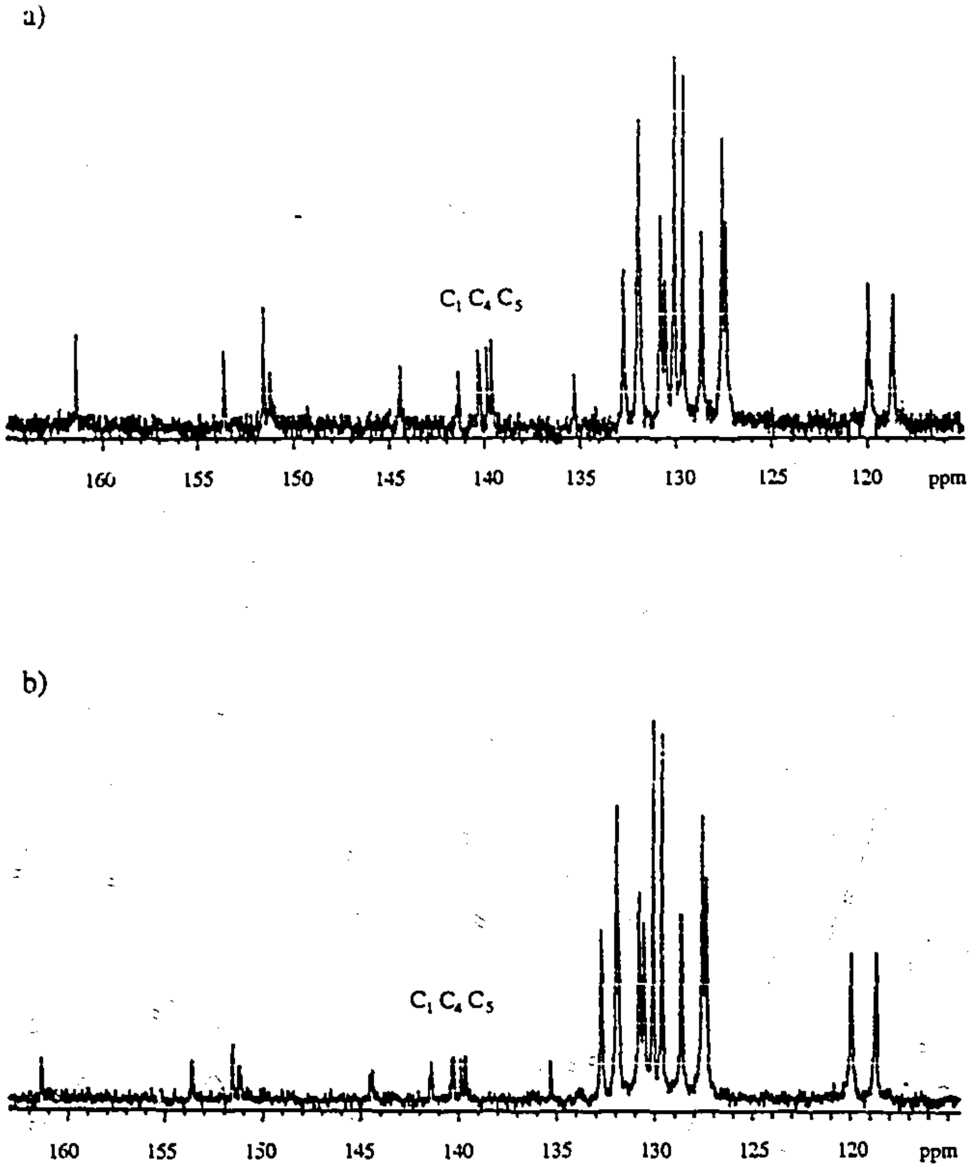


Figure 2.11. ^{13}C NMR spectra of chloro poly(aryl ether sulfone) dendrimers: a) **$3GClSO_2$** and b) **$4GClSO_2$**.

2.5.3 MALDI-TOF mass spectrometry.

Matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF-MS), a technique which is becoming of increasing importance for synthetic polymer chemistry, (28) was used for the mass determination of poly(aryl ether) dendrimers.

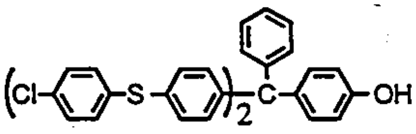
The analysis was carried out on a Kratos Compact MALDI III instrument in the reflectron mode using dithranol as the matrix. Silver trifluoroacetate was added to stabilize the system. The Figures 2.12, and 2.13 show the quality of the spectra achieved with excellent signal-to-noise ratio.

The molecular ion mass, MI, of the chloro poly(aryl ether sulfide) and chloro poly(aryl ether sulfone) dendrimers, were calculated using the following general equations, respectively:

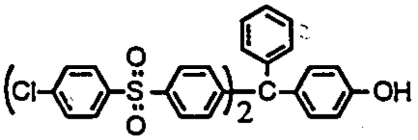
$$MI(iGClS) = A + (B - D)(2^{i} - 2) + (C - D)\,2^{i}$$

$$MI(iGClSO_2) = A + (B - D)(2^{i+1} - 2)$$

In these equations, i represents the generation number (1, 2, 3, ...), A the molecular mass of the core precursor **2.8** (287.17 Da), B the molecular mass of phenol **2.9** (685.65 Da), C the molecular mass of phenol **2.7** (621.65 Da), and D the molecular mass of HCl (36.46 Da):



2.7



2.9

HCl is the small molecule eliminated during the condensation reaction. The values obtained for the first and second generations of dendrimers are given in Table 2.4. For example, the molecular ion mass of **2GClS** was obtained using i = 2, A = 287.17 Da, B = 685.65 Da, C = 621.65 Da, and D = 36.46 Da. The true core precursor was 4,4'-

difluorodiphenyl sulfone, but to utilize the previous equations, 4,4'-dichlorodiphenyl sulfone was chosen as a theoretical core precursor.

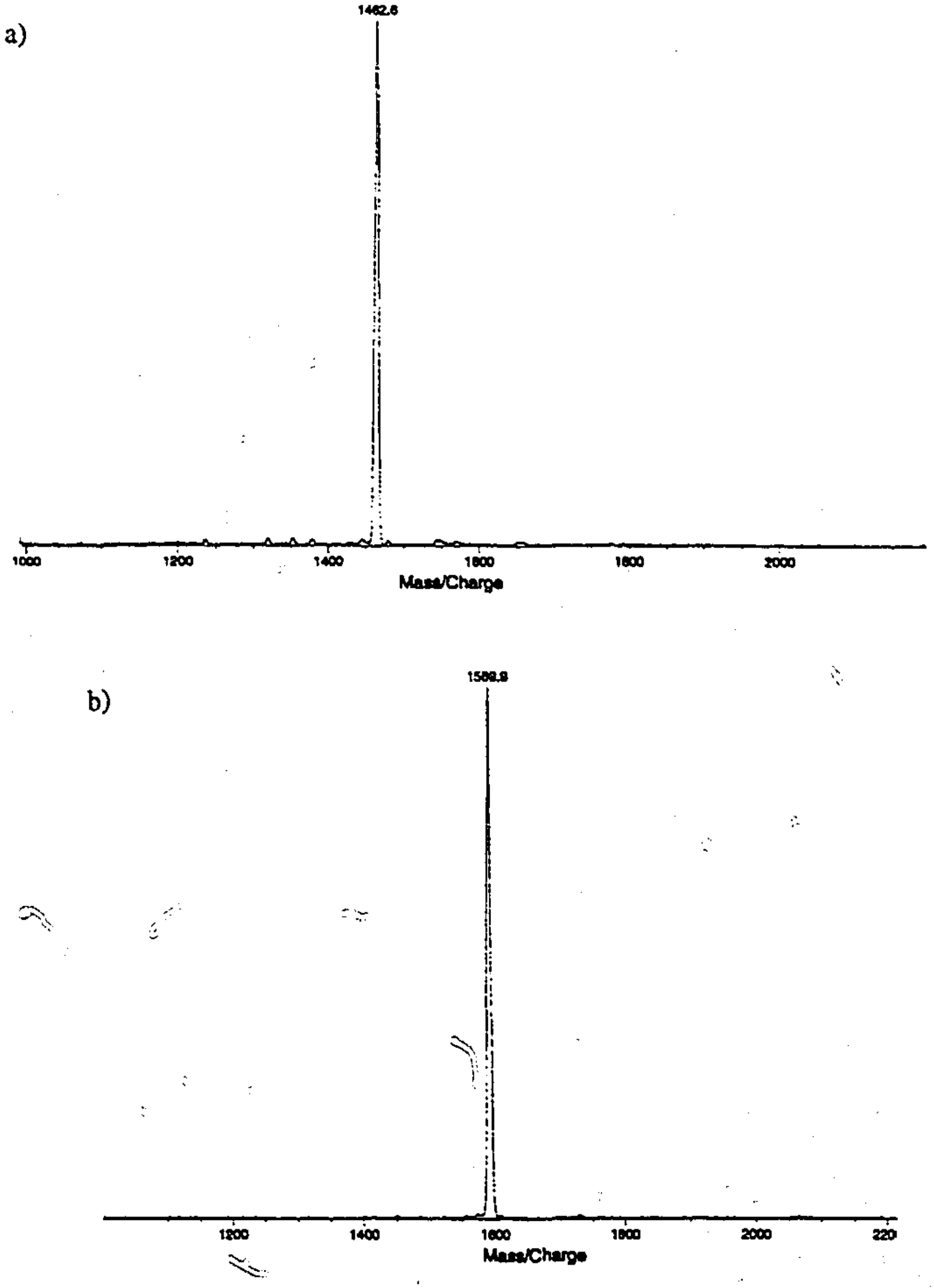


Figure 2.12. MALDI mass spectra of first generation chloro poly(aryl ether)s: a) **1GClS** and b) **1GClSO$_2$**.

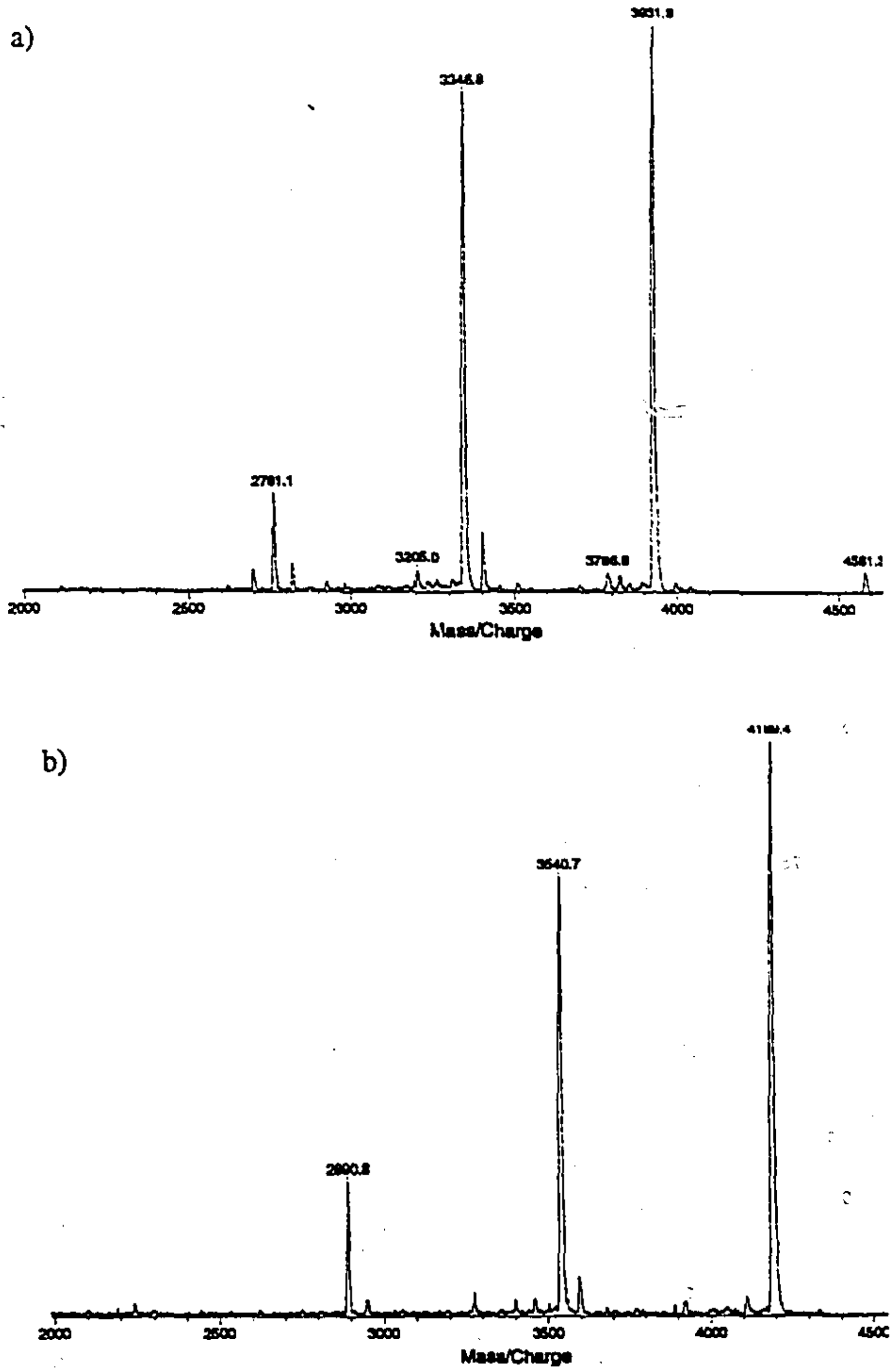


Figure 2.13. MALDI mass spectra of second generation chloro poly(aryl ether)s: a) **2GClS** and b) **2GClSO$_2$**.

The mass spectra of the first generation dendrimers show only one signal (peak 1) which corresponds to the molecular ion. However, the spectra of the second generation dendrimers show three signals corresponding to the molecular ion (peak 1) and intermediates of the reaction (peaks 2 and 3).

Table 2.4. MALDI mass spectrometry analyses of first and second generation chloro poly(aryl ether)s [a]

Dendrimer	MI [b] Da	MI_1 [c] Da	MI_2 [c] Da	Mass/Charge Peak 1	 Peak 2	 Peak 3
1GClS	1457.6	872.4	-	1462.6	-	-
$1GClSO_2$	1585.6	936.4	-	1589.9	-	-
2GClS	3926.3	3341.1	2755.9	3931.8	3346.8	2761.1
$2GClSO_2$	4182.3	3533.1	2883.9	4189.4	3540.7	2890.8

a) Dithranol:Sample:CF_3CO_2Ag = 40:4:1. b) MI = molecular ion mass. c) MI_1, MI_2: molecular ion masses of reaction intermediates.

The difference between the calculated and found values are between 4.2 and 7.7 Da. The error of these measurements is higher than 0.1% and lower than 0.35%. The reported error for the MALDI measurements is 0.1%. These deviations can be explained assuming that a lithium cation (7 Da) is complexed with the sample. Lithium cations can come from the metallic sample holder used for the analysis. Silver cations were not detected, probably due to the low concentration of CF_3CO_2Ag employed. However, it is absolutely necessary to use this reagent to avoid the fragmentation of the sample. Taking into account this fact, the mass differences between the calculated values and the experimental values are around 0.1%. The presence of reaction intermediates was also detected for the third generation dendrimers, as we describe below.

The following general equations were used to calculate the molecular ion mass of the intermediates, MI_n:

$$MI_n(iGClS) = MI(iGClS) - n\,(C - D)$$

$$MI_n(iGClSO_2) = MI(iGClSO_2) - n(B - D)$$

In these equations, MI(iGClS) and MI($iGClSO_2$) are the molecular ion masses of **iGClS** and **iGClSO$_2$**, respectively, and n represents the necessary number of monomer units required to obtain a perfectly globular dendrimer structure. For example, the mass spectrum of **3GClSO$_2$** (Fig. 2.14), shows signals which can correspond to the molecular ions of reaction intermediates. A lithium cation can also be complexed with each of the intermediate molecular ions.

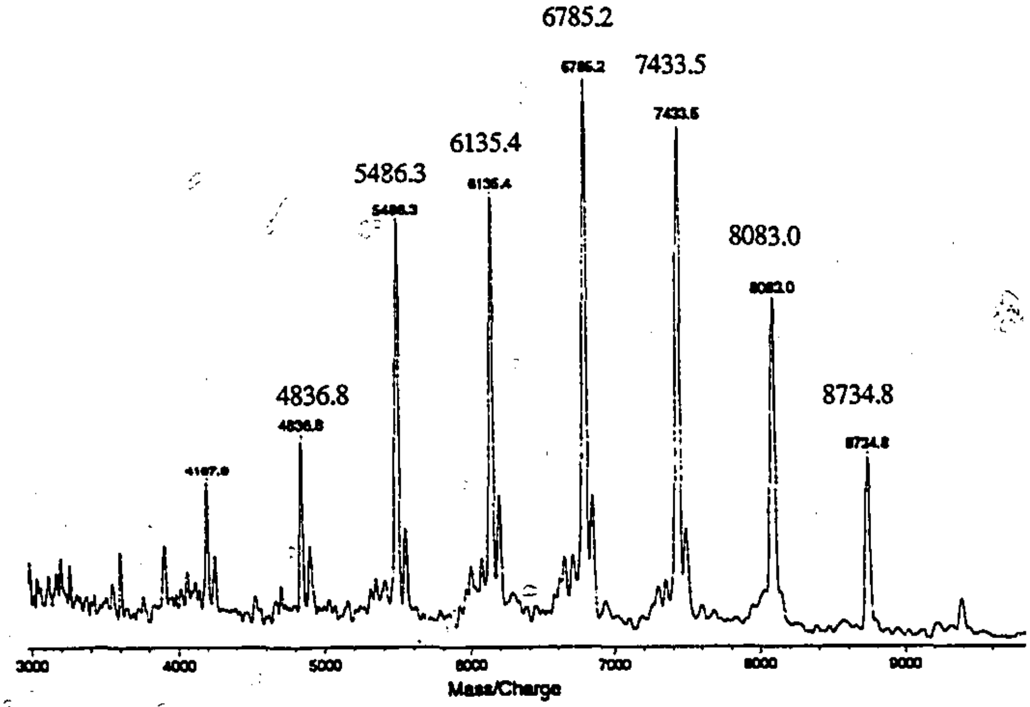


Figure 2.14. MALDI mass spectrum of third generation chloro poly(aryl ether sulfone) **3GClSO$_2$**.

Table 2.5. MALDI mass spectrometry analysis of third generation chloro poly(aryl ether sulfone) 3GClSO$_2$

Mass	MI	MI$_1$	MI$_2$	MI$_3$	MI$_4$	MI$_5$	MI$_6$	MI$_7$
Calc'd	9375.8	8726.6	8077.4	7428.2	6779.0	6129.9	5480.7	4831.5
Found	-	8734.8	8083.0	7433.5	6785.2	6135.4	5486.3	4836.8
Differ.	-	8.2	5.6	5.3	6.2	5.5	5.6	5.3

Details in **Table 2.4.**

The values of MI$_n$(3GClSO$_2$) calculated using MI(3GClSO$_2$) = 9375.8 Da; B = 685.65 Da; D = 36.46 Da, with n taking values from 1 to 7 are given in Table 2.5. In this case only traces of the expected product were observed. A small amount of the starting material **2GClSO$_2$** was also detected.

The data accumulated indicates that the condensation agent and conditions employed in the reactions were efficient in the synthesis of the first generation since no signal was detected for the reaction intermediate; only the molecular ion was observed. But this data also indicated that the synthesis of the second generation was not quantitative and suggests that the perfectly globular third generation dendrimer was not formed in an appreciable amount.

Elimination of Cl$^-$ by reductive elimination was not detected for these systems. Unfortunately, it was not possible to characterize the fourth and fifth generations and quantify the purity of our samples using this technique. Variations in the peak intensities for a single sample analyzed several times were detected. It is known that the way the sample, matrix, and stabilizer interact and coprecipitate affects the characteristics of the mass spectra, as well as other conditions such as beam power, shot number, area analyzed, and nature of the sample.

2.6 Physical properties.

The physical properties of these materials are given in Table 2.2. The glass transition temperature, Tg, of chloro poly(aryl ether) dendrimers increase with the generation number and molecular weight from 102°C - 231°C. After Tg (and until 450°C), no other thermal transition was detected by DSC. Since a chloro poly(aryl ether sulfone) dendrimer has a more polar structure, its Tg is higher than that of a chloro poly(aryl ether sulfide) dendrimer of comparable molecular weight. For example, Tg's for **1GClS** and **1GClSO$_2$** are 102°C and 1[illegible]8°C, respectively. The inherent viscosity, n_{inh}, also tends to increase with the generation number (0.06 dL/g - 0.11 dL/g). All these samples showed a high solubility in common organic solvents such as tetrahydrofuran, chloroform, toluene, DMAc, and DMSO.

2.7 Conclusions

We have been carried out the syntheses of five generations of chloro poly(aryl ether) dendrimers with activated aryl chloride terminal functionality from 4,4'-difluorodiphenyl sulfone and a relatively high molecular weight bis(chloroaryl) phenolate. An iterative procedure was employed that involved oxidation of the aryl sulfide moieties followed by the displacement of the chlorides activated by sulfone groups. The results obtained confirm that the size and molecular weight of these molecules increase with the generation number. The polydispersities of all these samples are close to one. NMR characterization confirms that structural changes occurred during the condensation and oxidation reactions but suggests that the reaction of the higher generations are not complete. SEC characterization indicates that temperatures lower than the boiling point of the solvent are not practical for the conversion of the condensation reactions.

MALDI-TOF mass spectrometry was a very useful characterization technique which was only available in the last stages of this research. It confirms that the synthesis of the first generation occurs in high yield and that the perfect globular second generation dendrimer is also synthesized. However, intermediates of the last reaction are also detected. This data suggests that the perfect globular third generation dendrimer is not formed in any appreciable amount, but only intermediates are formed in high proportion. Unfortunately, the fourth and fifth generations could not be characterized using this technique.

It has been demonstrated that the method used is successful in the high yield syntheses of readily accessible, first generation chloro poly(aryl ether sulfide) and chloro poly(aryl ether sulfone) dendrimers. The synthesis of the second generation, however could not be accomplished in quantitative fashion. The sodium phenolate and/or the aryl chloride are not active enough to force the condensation reactions to be quantitative. Improvements have been made in this area which will be discussed in the next Chapters.

2.8 Experimental.

Materials. In experiments requiring dry solvent, N,N-dimethyl acetamide, DMAc (Aldrich), was dried over calcium hydride and distilled under vacuum; diethyl ether, DEE (BDH), and tetrahydrofuran, THF (BDH), were dried over sodium and distilled under nitrogen. 4,4'-Difluorodiphenyl sulfone (Lancaster) was recrystallized from toluene. Acetone (BDH), alumina (Aldrich), anhydrous potassium carbonate (Omega), anhydrous magnesium sulfate (Omega), chloroform (BDH), hydrochloric acid (Caledon), 4-chlorothiophenol (Aldrich), 4,4'-dichlorobenzophenone (Aldrich), ethyl acetate (BDH), hexane (BDH), methanol (BDH), N-methylpyrrolidinone, NMP (Aldrich), Oxone (Aldrich), phenol (A&C), phenyl magnesium bromide (Aldrich), sodium hydride

(Aldrich), sodium hydroxide (ACS), silica gel 60 (EM), sulfuric acid (BDH) and toluene (BDH) were used as obtained.

General methods. ^{1}H and ^{13}C NMR spectra were recorded as a $CDCl_3$ or a DMSO solution on Varian XL - 200 and on Varian 500 MHz instruments, and chemical shifts are given in parts per billion downfield from tetramethyl silane as internal standard.

Conventional mass spectra were recorded on KRATOS MS 25 RFA and DuPont 21-492B spectrometers with the ion sources operating at 200°C and 250°C respectively, and with an impact energy of 70 eV, direct inlet: m/z (assignment).

MALDI mass spectrometric analyses were performed on a Kratos Kompact MALDI III in Reflectron High Power mode at a wavelength of 337 nm. Dithranol was the matrix and trifluoroacetic acid the stabilizer for the system. The solutions of sample, A (5 mg/mL), and matrix, B (10 mg/mL), were in chloroform. The solution of the stabilizer, C, was in THF (2.5 mg/mL). The sample was prepared using 40 µL A, 200 µL B, and 20 µL C.

Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected.

HPLC analyses was carried out with a Milton Roy CM4000 instrument with auto injector using methanol as the mobile phase, a Lichrosphere 5 RP18e column (250mm x 4mm), and UV detector (Milton Roy Spectro Monitor 3100) at a wavelength of 254 nm.

Elemental analyses were performed by Galbraith Laboratories Inc..

Dendrimer characterization. Inherent viscosities were measured in a calibrated number one Ubbelohde viscometer at a concentration of 0.5 g/dL in NMP at 25°C. Efflux time of the solvent was about 145 sec and the repeatabily of the measurements about 5%.

Polymer molecular weights were determined relative to polystyrene by size exclusion chromatography, SEC, in chloroform as the solvent on a Waters 510 HPLC with a set of four 5 µ columns (300 mm x 8 mm) arranged in series: one linear column (50 Å - 10^6 Å) and three Phenogel columns (500 Å); UV detector was used at wavelength of 254 nm. The repeatability was lower than 10%.

Differential scanning calorimetry, DSC, and thermogravimetric analyses, TG, were performed with Seiko 220 instruments under nitrogen at a heating rate of 10°C/min with gas flows of 160 mL/min and 200 mL/min, respectively. The values of Tg were recorded from the second scan and taken from the midpoint of the change in slope of the baseline. The repeatability was about 2°C.

Monomer synthesis.

Synthesis of 4,4'-Bis(4-chlorophenylthio)diphenyl ketone 2.3. A mixture of 4-chlorothiophenol **2.2** (36.16 g, 0.25 mol), 4,4'-dichlorobenzophenone **2.1** (25.11 g, 0.1 mol), anhydrous potassium carbonate (20.73 g, 0.15 mol), and DMAc (500 mL) was mechanically stirred under nitrogen for 0.5 h at room temperature. Then, the temperature was increased to 70°C (no higher since by-products make the purification of the product difficult) and the reaction was allowed to go for 12 h (the reaction was followed by HPLC). When the reaction finished, it was poured into 1500 mL of water and filtered. The solid obtained was washed with water, poured into 1000 mL of acetone and boiled for 0.5 h. The mixture was filtered and the solid obtained dried overnight under vacuum at 80°C. After the workup 44.88 g of **2.3** was obtained (yield = 96%, purity of the isolated product by HPLC = 97%): m.p. 202-203°; ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.71-7.63 (d, 4.9H), 7.55-7.51 (s, 6.7H), 7.35-7.28 (d, 4.4H); IR ($CDCl_3$) 962.8, 1013.2, 1087.6, 1180.8, 1286.3, 1311.6, 1396.2, 1475.7, 1552.3, 1589.0, 1652.5 cm-1; MS (EI) m/e calc'd for $C_{25}H_{16}S_2Cl_2O$: 466.00196, found 466.00196; 466, 323, 247, 184, 152, 108, 76; Analysis calc'd for $C_{25}H_{16}S_2Cl_2O$: C, 64.24%; H, 3.45%; S, 13.72%; found: C, 64.04%; H, 3.47%; S, 13.84%.

Synthesis of 4,4'-Bis(4-chlorophenylthio)triphenylcarbinol 2.5. Product **2.3** (23.37 g, 50 mmol) previously dried, and sodium-dried ether (600 mL) were placed into a 1000 mL flask, fitted with a magnetical stirrer, a Claisen adapter with a rubber stopper and an efficient double surface condenser with an inlet of nitrogen. The apparatus was arranged so that the flask could be heated with a heating plate. All parts of the apparatus were thoroughly dried. The ethyl ether could be collected during its distillation in the 1000 mL flask previously charged with the dried product **2.3**.

The reaction mixture was placed under nitrogen for 0.5 h; after that, the phenyl magnesium bromide **2.4** (3M solution in diethyl ether, 20 mL, 60 mmol) was introduced, in two fractions separated by 0.5 h, through the rubber stopper with a syringe. When the reaction finished, approximately 2 h later (the reaction was followed by HPLC), it was cooled and poured into 30% aqueous sulfuric acid (600 mL) to dissolve the magnesium hydroxide. The ethereal phase was separated and dried with anhydrous magnesium sulfate. The solution was filtered and the ether evaporated under vacuum. A green-yellow viscous liquid was recovered and used in this form in the synthesis of **2.7**. After the workup, 22.91 g of **2.5** was obtained (yield = 84%, purity of the isolated product by HPLC = 85%). Product **2.5** can be purified by chromatographic column using hexane: ethyl acetate (8.5:1.5 in volume) and silica gel 60 (0.040 mm-0.063 mm): ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.45-7.10 (m, 21H), 6.64 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 146.3, 145.6, 135.2, 133.8 (d), 133.1, 130.2, 129.8, 129.1, 128.5, 128.1, 128.0, 82.4; MS (EI) m/e calc'd for $C_{31} H_{22} S_2 Cl_2 O$: 544.04891, found 544.04891; 544, 528, 467, 385, 325, 296, 247, 241, 220, 184, 165, 152, 144, 108, 105, 77.

Synthesis of p-[4,4'-Bis(4-chlorophenylthio)]triphenylmethyl phenol 2.7. A mixture of phenol **2.6** (94.11 g, 1.00 mol), **2.5** (21.82 g, 0.04 mol) and a catalytic amount of sulfuric acid was placed in a 1000 mL flask with a condenser at 75°C for 12 h (the reaction was followed by HPLC). When the reaction finished, water (500 mL) was added and the reaction mixture was stirred for one half hour. The water phase was separated and the organic phase (a viscous liquid) was diluted with diethyl ether and extracted with 20% aqueous sodium hydroxide until the color faded in the aqueous phase. The ethereal phase was washed several times with water, dried with anhydrous magnesium sulfate, filtered, and the ether evaporated under vacuum. The brown viscous liquid (purity by HPLC = 84%) separated was purified using flash chromatography, 5 g of sample, a column of 12 cm x 5 cm, hexane:ethyl acetate (8.5:1.5 in volume) and silica gel 60 (0.040 mm-0.063 mm). After the purification of all the row material, 16.67 g of **2.7** (purity of the isolated product by HPLC = 97%) was obtained. The yield of the reaction after purification was 62%: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.33-7.06 (m, 21H), 7.06-6.97 (d, J = 8.8 Hz, 2H), 6.75-6.65 (d, J = 8.8 Hz, 2H), 5.50 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 154.3, 146.8, 146.4, 138.8, 134.1, 133.9, 133.7, 133.3, 132.7, 132.4, 131.4, 129.9, 128.2, 126.7, 115.0, 64.2; MS (EI) m/e calc'd for $C_{37}H_{26}S_2Cl_2O$: 620.08021, found 620.08021; 620, 543, 527, 477, 401, 257, 238, 228, 215, 181, 165, 152, 144, 108, 77; MS (MALDI(Ag)) m/e 731.9 (MI).

Dendrimer syntheses.

First generation chloro poly(aryl ether sulfide) 1GClS. The sodium salt of **2.7** was prepared by treating **2.7** (24.87 g, 0.04 mol) in ethyl ether (1000 mL) with excess of NaH (1.92 g, 0.08 mol). The solution was filtered to removed excess NaH. The ether was removed in vacuum to obtain 24.97 g of the sodium salt of **2.7** (yield = 97%, purity of the isolated product by HPLC = 96%).

To a 250 mL round bottomed flask, fitted with a condenser and a nitrogen inlet, there was added 4,4'-difluorodiphenyl sulfone **2.8** (1.271g, 5.00 mmol), the sodium salt (7.08 g, 11.0 mmol) and DMAc (110 mL). The mixture was stirred vigorously and maintained under reflux for 3 h. The reaction was followed by SEC. When the reaction was finished, it was cooled, poured into methanol (440 mL) and filtered. The solid recovered was dissolved in DMAc (110 mL), coagulated in aqueous HCl (440 mL), filtered and dried overnight at 70°C under vacuum. In general the volumes of methanol and acid solution were 4 times the volume of DMAc used in the reaction and the volume of DMAc for the separation procedure was the same as that used in the reaction. The crude product (5.99 g, isolated yield = 82%) was purified by fractional precipitation by dissolving the sample in chloroform (15 -20 mL/g) and using methanol as the nonsolvent. After the workup 4.08 g of **1GClS** was obtained (isolated yield after purification = 56%): ^{1}H NMR (500 MHz, DMSO-d_6/25°C) δ 7.91-7.87 (d, calc'd 4, found 3.6), 7.43-7.39 (d, calc'd 8, found 7.4), 7.36-7.32 (d, calc'd 8, found 7.9), 7.32-7.27 (t, calc'd 4, found 4.6), 7.24-7.18 (m, calc'd 10, found 10.0), 7.14-7.08 (m, calc'd 20, found 20.3), 7.04-7.01 (d, calc'd 4, found 4.1); ^{13}C NMR (50 MHz, $CDCl_3$) δ 161.4, 153.3, 145.9, 145.4, 142.9, 136.0, 134.0, 133.9, 133.6, 133.3, 132.9, 132.1, 131.1, 130.1, 129.8, 129.7, 128.1, 126.8, 119.5, 118.5, 65.1; MS (MALD(Li)) m/e 1462.6 (MI); TG: 102°C (10°C/min, N_2); η_{inh} = 0.06 dL/g (NMP, 0.5 g/dL, 25°C).

First generation chloro poly(aryl ether sulfone) 1GClSO$_2$. Wet alumina was prepared by adding water (10 mL) to the alumina (50 g; Brockman grade I, 200 mesh) and shaking until a free flowing homogeneous powder was obtained.

The first generation chloro cascade poly(aryl ether sulfide) **1GClS**, (4.37 g, 3.00 mmol) was added to a vigorously stirred suspension of wet alumina (12.00 g) and Oxone (22.20 g, 36.00 mmol) in chloroform (150 mL). The mixture was heated at reflux for 24 h. When the reaction finished, it was cooled, filtered, and the solid washed thoroughly with chloroform. The solution was concentrated, coagulated in methanol (300 mL), and the solid separated was dried overnight at 100°C under vacuum. After the workup, 4.61 g of **1GClSO$_2$** was obtained (isolated yield = 97%): ^{1}H NMR (500 MHz, DMSO-d_6/25°C) δ 7.96-7.92 (d, calc'd 8, found 7.6), 7.92-7.86 (m, calc'd 12, found 11.5), 7.68-7.64 (d, calc'd 8, found 7.4), 7.43-7.39 (d, calc'd 8, found 8.3), 7.32-7.28 (t, calc'd 4, found 4.5), 7.24-7.19 (t, calc'd 2, found 2.4), 7.16-7.09 (m, calc'd 12, found 12.2), 7.04-7.00 (d, calc'd 4, found 4.2); ^{13}C NMR (50 MHz, $CDCl_3$) δ 161.0, 153.8, 151.5, 144.4, 141.2, 140.3, 139.9, 139.6, 136.2, 132.6, 131.9, 130.8, 130.1, 130.0, 129.6, 128.6, 127.5, 127.4, 119.8, 118.7, 65.8; MS (MALDI(Li)) m/e 1589.9 (MI); Tg = 168°C (10°C/min, N_2); n_{inh} = 0.06 dL/g (NMP, 0.5 g/dL, 25°C).

Second generation chloro poly(aryl ether sulfide) 2GClS. The reaction was carried out using a procedure similar to that employed to synthesize **1GClS** using **1GClSO$_2$** (2.38 g, 1.50 mmol), sodium salt of **2.7** (3.86 g, 6.00 mmol), DMAc (60 mL), a reaction time of 3 h, and temperatures of 152°C and 164°C. The separated solid (5.01 g, isolated yield = 85%) was purified by fractional precipitation and dried overnight at 100°C under vacuum. After the workup 3.65 g of **2GClS** was obtained (isolated yield after purification = 62%): ^{1}H NMR (500 MHz, DMSO-d_6/80°C) δ 7.96-7.80 (m, calc'd 20, found 22), 7.44-7.04 (m, calc'd 126, found 122), 7.04-6.94 (m, calc'd 12, found 14); ^{13}C NMR (50 MHz, $CDCl_3$) δ 161.8, 161.1, 153.8, 153.1, 151.2, 145.9, 145.3, 144.6, 143.1, 140.4, 134.9, 134.1, 133.9, 133.6, 133.3, 133.0, 132.7, 132.0, 131.8, 131.7, 131.1, 131.0, 130.8, 130.5, 130.2, 130.0, 129.8, 129.6, 128.6, 128.1, 127.3, 126.8, 119.8, 119.6, 118.7, 118.4, 65.1; MS (MALDI(Li)) m/e 3931.8 (MI), 3346.8, 2761.1; Tg = 156°C (10°C/min, N_2); n_{inh} = 0.07 dL/g (NMP, 0.5 g/dL, 25°C).

Second generation chloro poly(aryl ether sulfone) 2GClSO$_2$. A procedure similar to that used to synthesize **1GClSO$_2$** was employed using **2GClS** (2.95 g, 0.75 mmol), wet alumina (6.00 g) and Oxone (11.10 g, 18.00 mmol) in chloroform (37.5 mL). The solution was concentrated and coagulated in methanol (75 mL) to afford 2.95 g of **2GClSO$_2$** (isolated yield = 94%): ^{1}H NMR (500 MHz, DMSO-d_6/60°C) δ 8.00-7.80 (m, calc'd 52, found 49), 7.72-7.60 (m, calc'd 16, found 15), 7.48-7.36 (m, calc'd 24, found

25), 7.36-7.08 (m, calc'd 54, found 55), 7.08-6.96 (m, calc'd 12, found 14); ^{13}C NMR (50 MHz, $CDCl_3$) δ 161.4, 161.1, 153.6, 151.5, 151.2, 144.4, 141.4, 140.3, 139.8, 139.6, 135.3, 132.7, 131.9, 130.8, 130.5, 130.0, 129.6, 128.7, 127.6, 127.4, 120.0, 119.8, 118.7, 65.9, 65.8; MS (MALDI(Li)) m/e 4189.4 (MI), 3540.7, 2890.8; Tg = 206°C (10°C/min, N_2); n_{inh} = 0.10 dL/g (NMP, 0.5 g/dL, 25°C).

Third generation chloro poly(aryl ether sulfide) 3GClS. The reaction was carried out using a procedure similar to that employed to synthesize **1GClS** using **2GClSO$_2$** (2.09 g, 0.50 mmol), sodium salt of **2.7** (2.58 g, 4.00 mmol), DMAc (40 mL), and temperatures of 150°C (reaction time = 3.5 h) and 164°C (reaction time = 3.0 h). The separated solid (3.90 g, isolated yield = 88%) was purified by fractional precipitation and dried overnight at 100°C under vacuum. After the workup 2.88 g of **3GClS** was obtained (isolated yield after purification = 65%): ^1H NMR (500 MHz, DMSO-d_6/80°C) δ 7.96-7.76 (m, calc'd 52, found 59), 7.44-7.00 (m, calc'd 278, found 271), 7.00-6.86 (m, calc'd 28, found 28); ^{13}C NMR (50 MHz, $CDCl_3$) δ 161.8, 161.4, 153.0, 152.0, 151.1, 145.9, 145.3, 144.5, 143.1, 140.4, 134.9, 134.0, 133.8, 133.6, 133.3, 133.0, 132.7, 132.0, 131.8, 131.1, 130.8, 130.5, 130.1, 130.0, 129.8, 129.6, 128.6, 128.1, 127.4, 126.8, 119.9, 119.6, 118.7, 118.4, 65.1; Tg = 177°C (10°C/min, N_2); n_{inh} = 0.10 dL/g (NMP, 0.5 g/dL, 25°C).

Third generation chloro poly(aryl ether sulfone) 3GClSO$_2$. A procedure similar to that used to synthesize **1GClSO$_2$** was employed, using **3GClS**, (2.22 g, 0.25 mmol), wet alumina (4.00 g) and Oxone (7.40 g, 12.00 mmol) in chloroform (25 mL). The solution was concentrated, coagulated in methanol (50 mL) to afford 2.18 g of **3GClSO$_2$** (isolated yield = 93%): ^1H NMR (500 MHz, DMSO-d_6/80°C) δ 8.00-7.78 (m, calc'd 116, found 112), 7.70-7.56 (m, calc'd 32, found 30), 7.48-7.34 (m, calc'd 56, found 57), 7.34-7.04 (m, calc'd 126, found 130), 7.04-6.92 (m, calc'd 28, found 29); ^{13}C NMR (50 MHz, $CDCl_3$) δ 161.4, 153.6, 151.6, 151.2, 144.4, 141.4, 140.3, 140.2, 139.8, 139.6, 135.3, 132.7, 131.9, 130.8, 130.5, 130.0, 129.6, 128.7, 127.6, 127.4, 120.0, 118.7, 65.9; Tg = 223°C (10°C/min, N_2); n_{inh} = 0.09 dL/g (NMP, 0.5 g/dL, 25°C).

Fourth generation chloro poly(aryl ether sulfide) 4GClS. The reaction was carried out using a procedure similar to that employed to synthesize **1ClGS** using **3GClSO₂** (1.88 g, 0.20 mmol), sodium salt of **2.7** (2.06 g, 3.2 mmol), DMAc (64 mL), and temperatures of 134°C (reaction time = 8 h) and 155°C (reaction time = 3.5 h). The separated solid (2.81 g, isolated yield = 75%) was purified by fractional precipitation and dried overnight at 100°C under vacuum. After the workup 2.14 g of **4GClS** was obtained (isolated yield after purification = 57%): ^{1}H NMR (500 MHz, DMSO-d_6/80°C) δ 7.94-7.75 (m, calc'd 116, found 157), 7.44-7.00 (m, calc'd 582, found 537), 7.00-6.84 (m, calc'd 60, found 64); ^{13}C NMR (50 MHz, $CDCl_3$) δ 161.8, 161.4, 153.6, 153.0, 151.2, 145.9, 145.3, 144.5, 143.1, 141.5, 140.3, 139.6, 135.4, 134.9, 134.0, 133.8, 133.6, 133.3, 132.9, 132.7, 132.0, 131.9, 131.8, 131.1, 130.8, 130.5, 130.0, 129.7, 129.6, 128.6, 128.1, 127.5, 127.4, 126.8, 119.9, 119.6, 118.7, 118.4, 65.8, 65.1; Tg = 198°C (10°C/min, N_2); n_{inh} = 0.10 dL/g (NMP, 0.5 g/dL, 25°C).

Fourth generation chloro poly(aryl ether sulfone) 4GClSO₂. A procedure similar to that used to synthesize **1GClSO₂** was employed, using **4GClS** (1.87 g, 0.10 mmol), wet alumina (3.20 g) and Oxone (5.92 g, 9.60 mmol) in chloroform (20 mL). The solution was concentrated and coagulated in methanol (40 mL) to afford 1.76 g of **4GClSO₂** (isolated yield = 89%): ^{1}H NMR (500 MHz, DMSO-d_6/80°C) δ 7.98-7.76 (m, calc'd 244, found 237), 7.68-7.54 (m, calc'd 64, found 59), 7.46-7.32 (m, calc'd 120, found 126), 7.32-7.02 (m, calc'd 270, found 277), 7.02-6.88 (m, calc'd 60, found 59); ^{13}C NMR (50 MHz, $CDCl_3$) δ 161.4, 153.6, 151.5, 151.2, 144.5, 144.4, 141.5, 141.4, 140.3, 140.2, 139.8, 139.6, 135.3, 132.7, 131.9, 131.8, 130.8, 130.5, 130.0, 129.6, 128.6, 127.6, 127.4, 120.0, 118.7, 65.9; Tg = 231°C (10°C/min, N_2); n_{inh} = 0.11 dL/g (NMP, 0.5 g/dL, 25°C).

Fifth generation chloro poly(aryl ether sulfide) 5GClS. The reaction was carried out using a procedure similar to that employed to synthesize **1GClS** using **4GClSO$_2$** (0.99 g, 0.05 mmol), sodium salt of **2.7** (1.03 g, 1.60 mmol by HPLC), DMAc (15 mL), and temperatures of 130°C (reaction time = 8 h) and 155°C (reaction time = 3 h). The separated solid (1.81 g, isolated yield = 94%) was purified by fractional precipitation and dried overnight at 100°C under vacuum. After the workup 1.10 g of **5GClS** was obtained (isolated yield after purification = 57%): ^{1}H NMR (500 MHz, DMSO-d_6/60°C) δ 7.96-7.72 (m, calc'd 244, found 306), 7.44-6.80 (m, calc'd 1314, found 1252); ^{13}C NMR (50 MHz, $CDCl_3$) δ 161.8, 161.4, 153.6, 153.0, 151.2, 145.9, 145.3, 144.6, 143.1, 145.5, 140.4, 139.6, 135.3, 134.9, 134.0, 133.8, 133.6, 133.3, 133.0, 132.7, 132.0, 131.9, 131.8, 131.1, 130.8, 130.5, 130.0, 129.7, 129.6, 128.6, 128.1, 127.6, 127.4, 126.8, 119.9, 119.6, 118.7, 118.4, 65.8, 65.1; Tg = 201°C (10°C/min, N_2); n_{inh} = 0.11 dL/g (NMP, 0.5 g/dL, 25°C).

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Chapter 3

Fluoro poly(aryl ether sulfone) dendrimers from a pre-formed sodium phenolate, using the divergent approach.

3.1 Introduction.

As we described in Chapter 1, the divergent initiator core method has been successfully used in the synthesis of many dendrimers. For example, Tomalia (1, 2) have used this strategy to synthesize poly(alkyl ether) dendrimers. We also used the divergent initiator core method with a novel condensation/activation sequence (Chapter 2), to produce in high yield, readily accessible first generation chloro poly(aryl ether) dendrimers with aryl sulfide and aryl sufone terminal functionality. The second generation dendrimers were also synthesized but not in quantitative fashion. A probable explanation for this result is the low rate of the aryl chloride displacement.

It is known that the halide displacement by a phenolate proceeds via the S_NAr (aromatic nucleophilic substitution) mechanism. (3) The rate limiting step is typically the formation of the Meisenheimer complex, and the rate constant decreases in the order F > Cl > Br >I for oxygen-based nucleophiles. This is attributed to the electronegativity of the halogen. As the electronegativity increases, the electropositive character of the aromatic carbon bonded to the halogen increases, and the rate of the nucleophilic attack increases.

Poly(aryl ether)s have been the subject of research and commercial enterprise since the 1960's. (4) The linear polymers are characterized by their high thermal stability and hydrolytic resistance, in addition of their excellent mechanical properties for some applications. They have been referred to as high performance polymers.

3.1.1 Strategy and goals

The objective of the research described in this section was the synthesis of fluoro poly(aryl ether) dendrimers using the *divergent initiator core method* based on a condensation/activation sequence.

Taking into account the above described mechanism for the condensation reaction and our previous results, the displacement of fluorides activated by sulfone groups becomes an attractive option to produce, in high yield, poly(aryl ether) dendrimers and to overcome the previous limitations found in the synthesis of the higher generations.

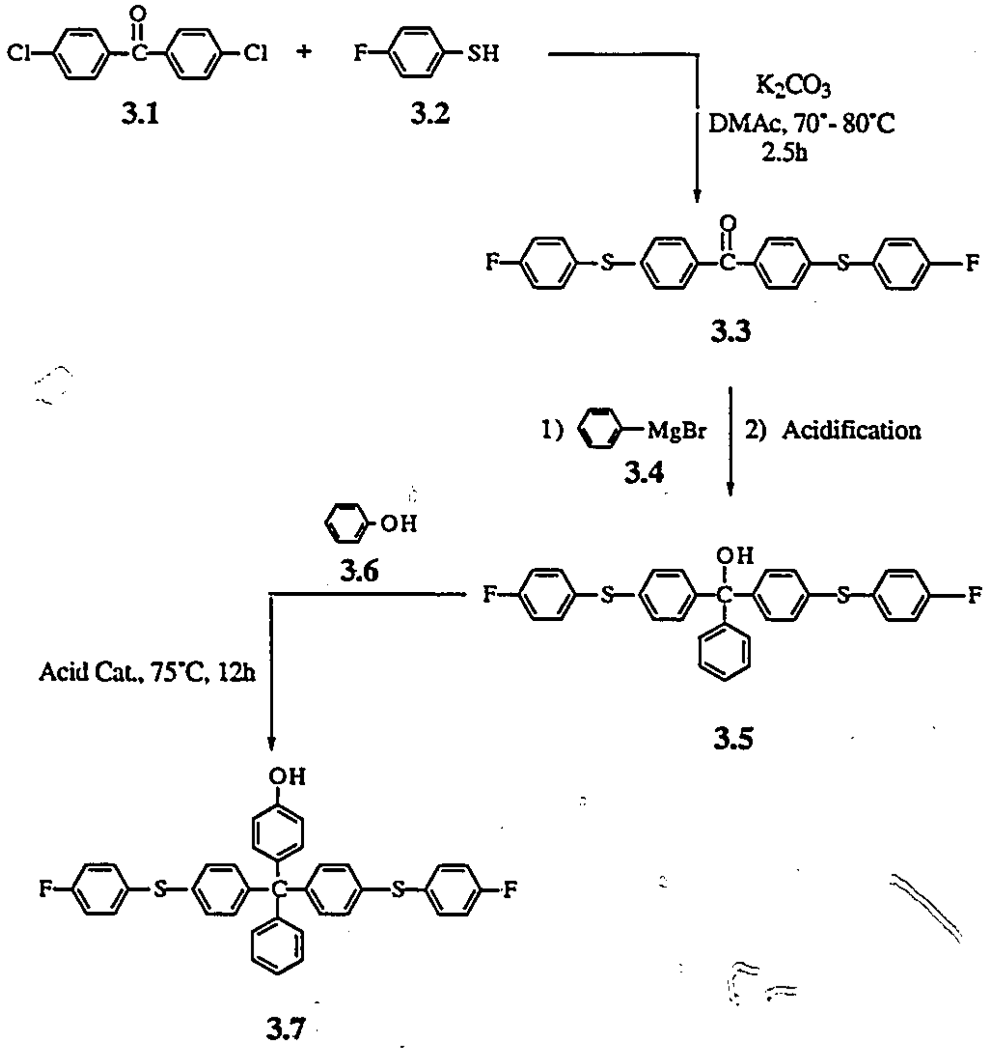
We proposed to use the same method employed in the synthesis of chloro poly(aryl ether) dendrimers but employing a higher rate condensation reaction in which a fluoride, activated by a sulfone group, is displaced by a pre-formed sodium phenolate. The aryl sulfone moieties are produced by oxidation of an aryl sulfone group using Oxone and wet alumina. The general strategy for the synthesis is described in Chapter 1, Part 1.6.

In our dendrimer syntheses, 4,4'-difluorodiphenyl sulfone **3.8** was chosen as the core precursor and phenol **3.7** as the propagation unit. Phenol **3.7** contains very active aryl fluoride end groups in its structure and has a relatively high molecular weight. The last characteristic allows the formation, in a few generations, of high molecular weight dendrimer.

3.2 Preparation of the monomer.

The synthesis of phenol **3.7** is similar to that of phenol **2.7** (Scheme 3.1). The reaction begins with displacement of the chloride groups of 4,4'-dichlorobenzophenone **3.1**, by two molecules of 4-fluorothiophenol **3.2**, using K_2CO_3 under mild conditions (5) to obtain the condensation product **3.3**. Then, product **3.3** is made to react with phenyl magnesium bromide **3.4** through a Grignard reaction (6) to produce the tertiary alcohol **3.5**. The alcohol **3.5** is condensed (7) with phenol **3.6** in the presence of an acid catalyst to generate the monomer **3.7**.

Scheme 3.1



The overall yield of **3.7** from 4,4'-dichlorobenzophenone **3.1**, was 36 %. Nuclear magnetic resonance, NMR, and mass spectrometric characterization of each of those products confirmed the proposed structure (see Experimental Section). However, high pressure liquid chromatography, HPLC, indicated the presence of an impurity which could not be completely separated on a chromatographic column (purity of **3.7** = 92%).

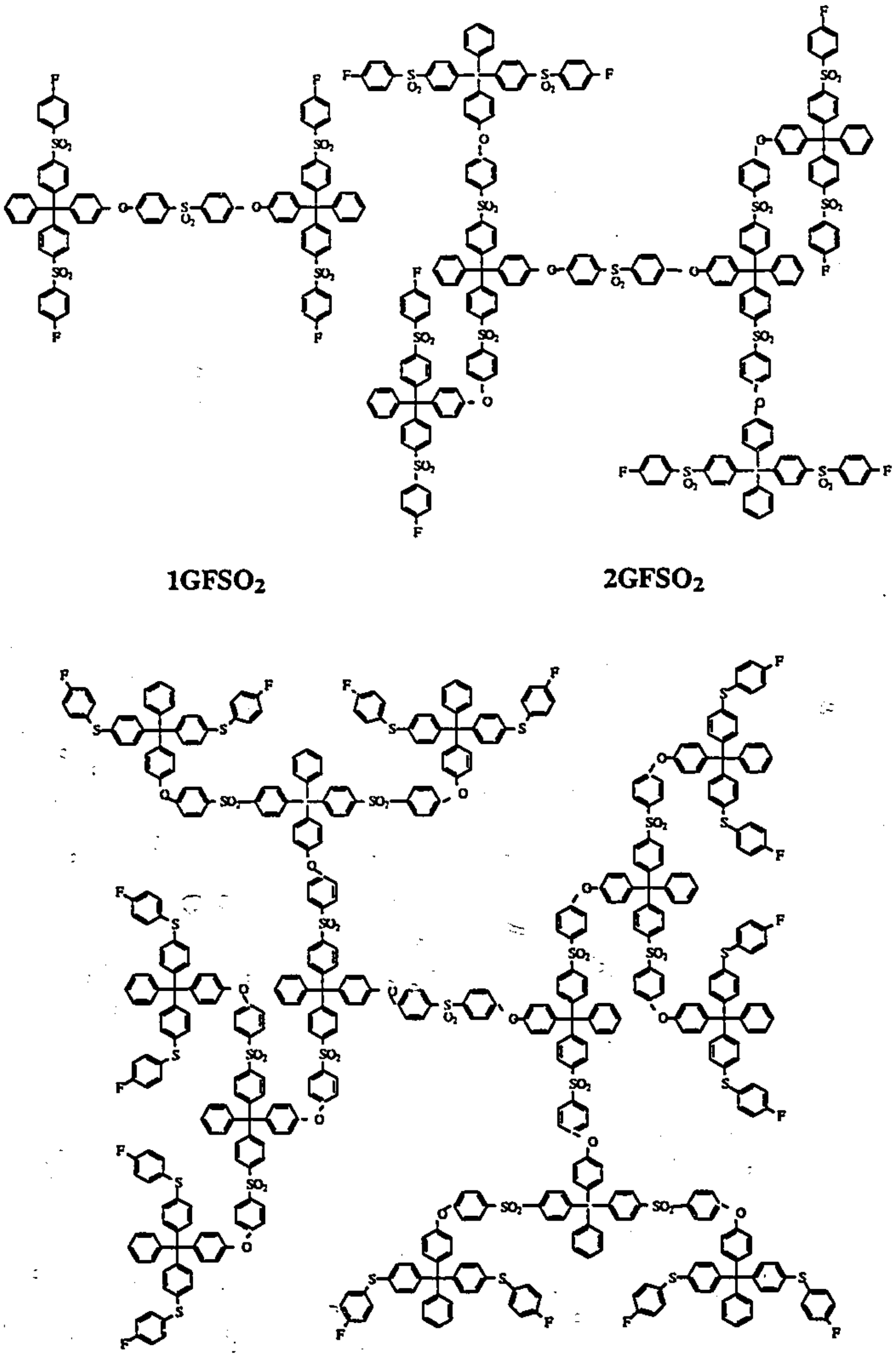
3.3 Preparation of fluoro poly(aryl ether) dendrimers.

The synthetic strategy that we used led to two dendrimer families which contained two different functionalities in the terminal units, aryl sulfide and aryl sulfone. Our nomenclature gives the dendrimer generation (1G, 2G, etc.) followed by letters denoting the nature of the terminal units (F = fluoro, S = sulfide, SO_2 = sulfone).

We work in the syntheses of five generations of fluoro poly(aryl ether sulfide) dendrimers using DMAc as the solvent for the reaction, reaction times from 1 to 3 hours, and temperatures of the reaction from 75°C to 164°C. Approximately stoichiometric amounts of the phenolate **3.7** and activated aryl fluorides were used, except in the synthesis of the first generation in which an excess of the phenolate was employed. The theoretical molecular weights of the dendrimers were used for the calculations of the quantities of reagents of the experiments and reaction yields. 4,4'-Difluorodiphenyl sulfone **3.8** was the core precursor. The phenolate was prepared by treating the purified phenol with NaH in ethyl ether. The reactions were followed by size exclusion chromatography, SEC.

The structures of fluoro poly(aryl ether) dendrimers (Scheme 3.2) differ from those of chloro poly(aryl ether) dendrimers (Schemes 2.4, 2.5, and 2.6) only in the aryl halide end groups, the fluoro poly(aryl ether) dendrimers contains aryl fluoride end groups.

Scheme 3.2



1GFSO$_2$

2GFSO$_2$

3GFS

The activation reaction, in which the sulfide groups are oxidized to produce fluoro poly(aryl ether sulfone) dendrimers, was carried out under similar conditions for all four generations. Oxone and wet alumina (8) was used as the oxidation reagent and chloroform was the solvent for the reaction under reflux conditions.

The products were characterized by SEC, NMR, and MALDI-TOF-MS. Details of the characterization will be given later. The yields of the activation reactions were high (88% - 98%). Those of the condensation reactions, after the purification of the products, were around 65%.

3.4 Effect of the temperature on the condensation reaction.

We explored the effect of the reaction temperature on the synthesis of two series of five generations of fluoro poly(aryl ether sulfide) dendrimers. At this stage of our research, SEC and NMR were the only techniques available in our laboratory to study the homogeneity of the samples.

The synthesis of the first generation **1GFS** was carried out under reflux condition (164°C). The elimination of the monosubstituted product became difficult when a lower temperature was used.

As shown in Table 3.1, the amount of unreacted phenolate depends on the reaction temperature. For example, a lower value of R was found when temperatures of 155°C, 128°C, and 126°C were employed in the synthesis of **2GFS**, **4GFS**, and **5GFS**, respectively. R is a rough measurement of unreacted phenolate percent (%) with respect to its initial concentration. The values of R were calculated from: a) ratio of phenolate peak area to peak total area in the SEC chromatogram of the reaction mixture, and b) ratio of grams of unreacted phenolate to grams of formed fluoro poly(aryl ether sulfide) dendrimers. The last ratio was obtained from a calibration curve.

These results indicate that the reaction conversion increases with the temperature. The lowest value of R (17%) was obtained at 155°C for the synthesis of **2GFS**.

Table 3.1. Effect of the temperature of the reaction, T, on the syntheses of fluoro poly(aryl ether sulfide) dendrimers

Dendrimer	Mw (g/mol) a)	PD a)	R (%) b)	t (h)	T (°C)
2GFS	2654	1.11	34	3	96
2GFS	2921	1.12	17	2	155
3GFS	7042	1.14	27	1	94
			23	3	
3GFS	6149	1.16	29	1	115
4GFS	12427	1.22	39	1	75
			25	3	
4GFS	11946	1.16	19	1	128
5GFS	19453	1.29	33	1	93
5GFS	20053	1.34	26	1	126

a) SEC, based on polystyrene standards, chloroform, 1mL/min, UV-detector. b) R = 100 x moles of phenolate at the end of the reaction / moles of phenolate at the beginning of the reaction.

Incomplete reactions are suggested from these results. A 17% R value is relatively high, assuming that approximately stoichiometic amounts of the starting materials were used.

Molecular weights, Mw's, and polydispersities, PD's, of the crude products, obtained by SEC at different temperatures, are shown in Table 3.1. There was no special effect of the temperature on Mw's and PD's. The chromatograms of higher generations **3GFS**, **4GFS**, and **5GFS** were apparently not affected by the temperature of the reaction, but the maximum of the chromatogram of the second generation **2GFS** moved to a lower molecular weight when the reaction temperature was decreased from 155°C to 96°C (Fig. 3.1).

The effect of the temperature on these systems is similar to that found previously for chloro poly(aryl ether sulfide) dendrimers. However, the displacement of fluorides instead of chlorides made the reaction cleaner. The polydispersities of the crude fluoro poly(aryl ether sulfide)s tends to be lower than those of the crude chloro poly(aryl ether sulfide)s.

3.5 Molecular characteristics.

3.5.1 Chromatography.

The SEC chromatograms, weight average molecular weights (Mw's), and polydispersities (PD's) of the different generations of purified dendrimers are given in Figure 3.2 and Table 3.2. Mw's increase with the number of generations from 786 to 19643. However, the polydispersity values, PD's, remain close to 1 as is expected for almost monodisperse materials. The difference between the weight average molecular weights and the formula weights (FW's) can be explained if we assume that dendrimer structures are more compact than those of the polystyrene standards used in the calibration curve.

The shape of SEC chromatograms of fluoro poly(aryl ether sulfone) dendrimers were similar to those of the fluoro poly(aryl ether sulfide) dendrimers of comparable molecular weight. This suggests that no important side reactions occur during the oxidation of aryl sulfides to sulfones. A low concentration, lower retention time by-product was detected in **1GFS**. By-products with similar characteristics were also present in the higher generations of fluoro poly(aryl ether sulfide)s. The complete purification by fractional precipitation was not possible.

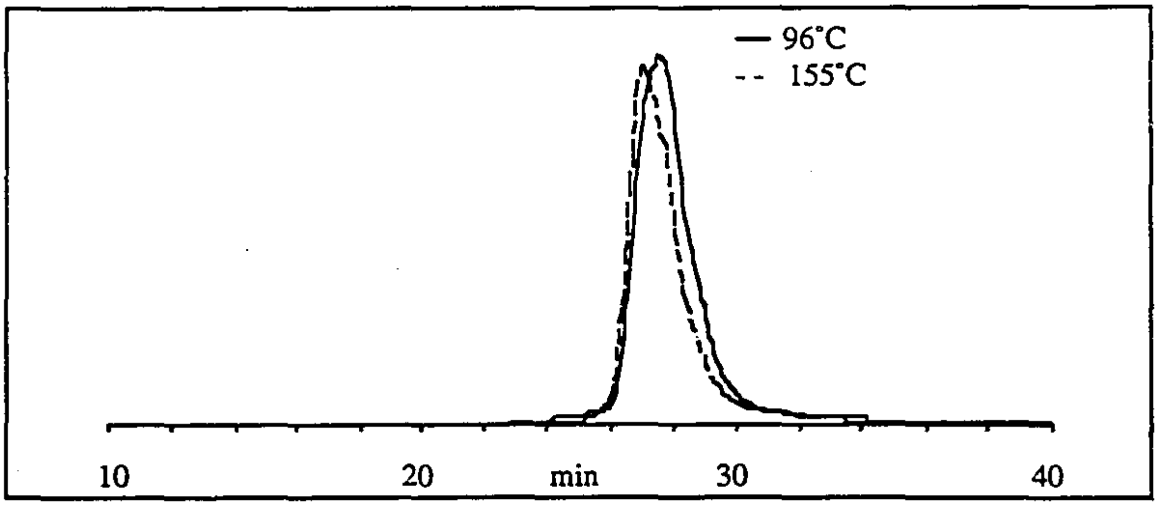


Figure 3.1. SEC chromatograms of first generation fluoro poly(aryl ether sulfide)s **1GFS** obtained at 96°C and 155°C. Analysis conditions in **Table 3.1.**

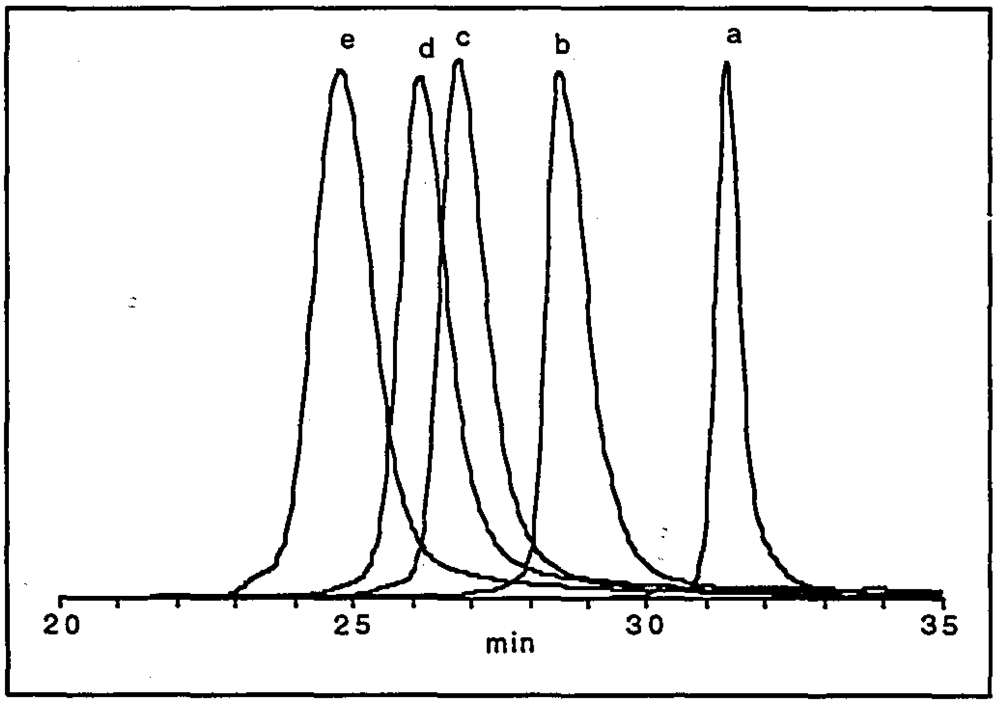


Figure 3.2. SEC chromatograms of fluoro poly(aryl ether sulfide) dendrimers: a) **1GFS**, b) **2GFS**, c) **3GFS**, d) **4GFS**, and e) **5GFS**. Analysis conditions in **Table 3.2.**

Table 3.2. Some characteristics and properties of fluoro poly(aryl ether) dendrimers

Dendrimer	1GFS	$1GFSO_2$	2GFS	$2GFSO_2$	3GFS	$3GFSO_2$	4GFS	$4GFSO_2$	5GFS
FW (g/mol)	1392	1520	3795	4051	8601	9113	18212	19236	37434
Mw (g/mol) a)	786	1061	2743	3120	6544	6751	11946	12109	19643
PD a)	1.05	1.05	1.10	1.11	1.09	1.14	1.16	1.20	1.25
η_{inh} (dL/g) b)	0.05	0.05	0.07	0.07	0.08	0.08	0.10	0.10	0.11
Tg (°C) c)	91	165	148	205	177	221	186	228	200
Td (°C) d)	487	501	490	510	475	497	491	507	497
Yield_1 (%) e)	97	92	95	98	88	88	84	95	85
Yield_2 (%) f)	75	-	57	-	65	-	-	-	70

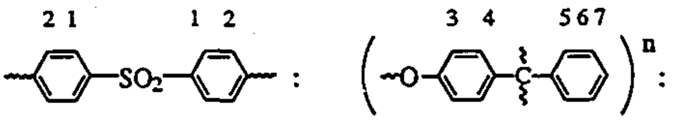
a) SEC, based on polystyrene standards, chloroform, 1mL/min, UV-detector. b) NMP, 0.5 g/dL, 25 °C. c) Nitrogen, 10 °C/min. d) 5% weight loss, nitrogen, 10 °C/min. e) Yield before purification. f) Yield after purification.

3.5.2 Nuclear magnetic resonance.

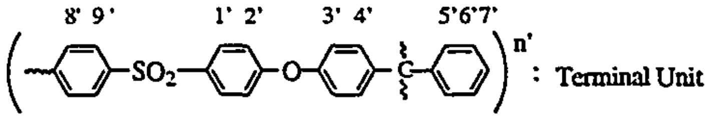
For the discussion of the NMR characterization of dendrimers it is useful to describe the building units that make up these polymers. The schematic representation of the different blocks that form fluoro poly(aryl ether) dendrimers are shown in Scheme 3.3. Each of these blocks can be identified in the ideal structures of **$1GFSO_2$**, **$2GFSO_2$**, and **3GFS** given in Scheme 3.2. For more details see Chapter 1: Part 1.1 and Chapter 2: Part 2.5.2. The number in Scheme 3.2 represent the different hydrogens in the dendrimer which were arbitrarily chosen.

The ^1H NMR spectra (500 MHz) of these polymers are given in Figures 3.3 - 3.6. Cosy experiments were carried out for the identification of the protons. The differences between the ^1H NMR spectra of fluoro poly(aryl ether sulfide) and those of fluoro poly(arylethersulfone) dendrimers confirm that structural changes occurred during the oxidation or displacement reactions. Before the oxidation reaction protons H_{12} at the terminal units C absorb at δ = 7.45 ppm (Fig. 3.3a). After the oxidation reaction these protons, now close to the new sulfone group (terminal unit D : H_{10}), show resonances at about δ = 8.02 ppm (Fig. 3.3b).

Scheme 3.3



Core　　**Repeat unit A**



Repeat unit B

Terminal Unit C　　**Terminal Unit D**

The structure of **1GFS** possesses only an internal layer formed by two repeat units A. However, some layers of the higher generations of fluoro poly(aryl ether sulfide)s are formed by repeat units B. This explains the resonance observed at about δ = 7.8 ppm which can be attributed to protons $H_{9'}$ (Figs. 3.4 and 3.5). The similarities observed in the spectra of fluoro poly(aryl ether)s are a consequence of common protons present in their structures (Scheme 3.3).

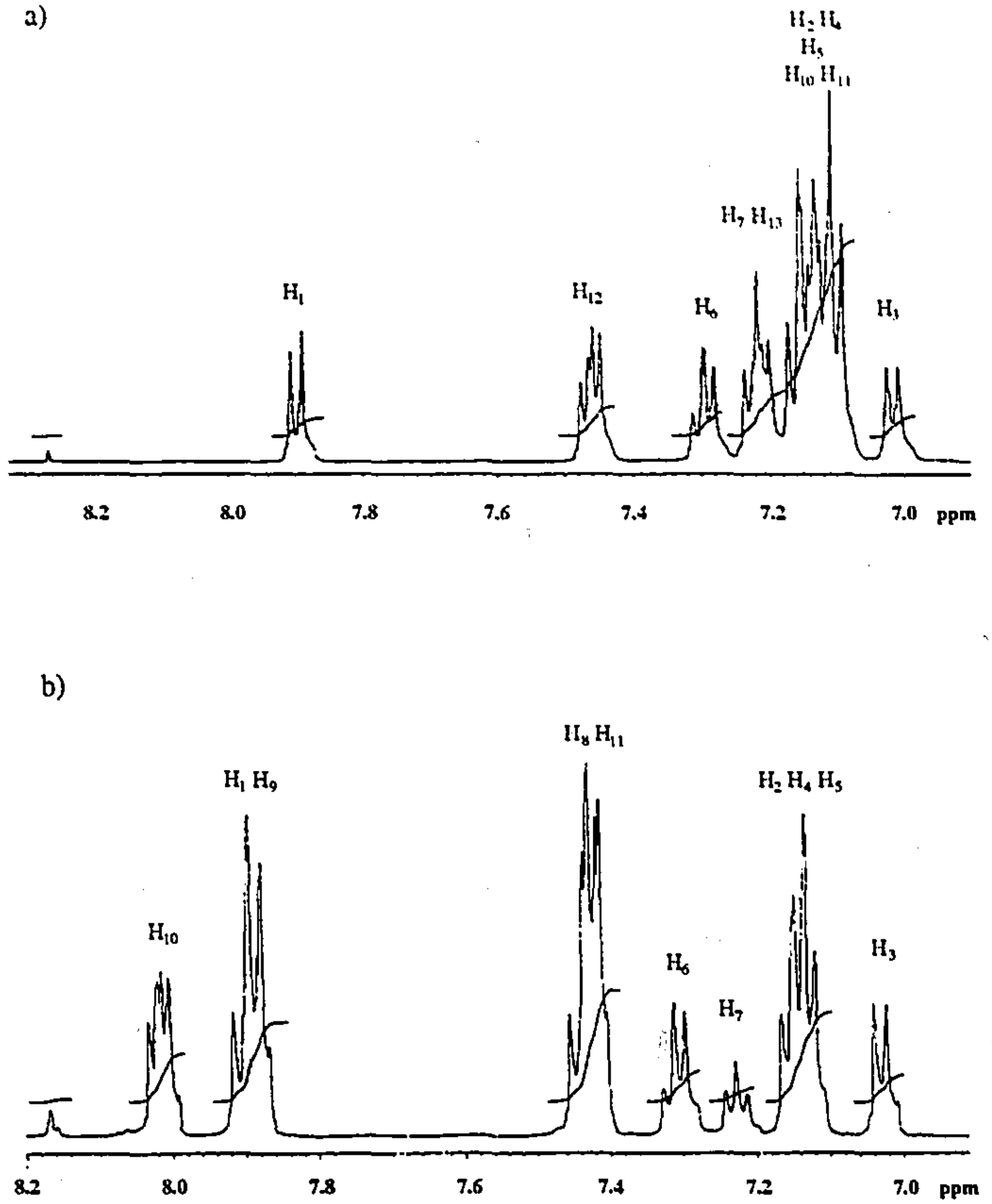


Figure 3.3. ^{1}H NMR spectra of the first generation fluoro poly(aryl ether)s: a) **1GFS** and b) **1GFSO$_2$**.

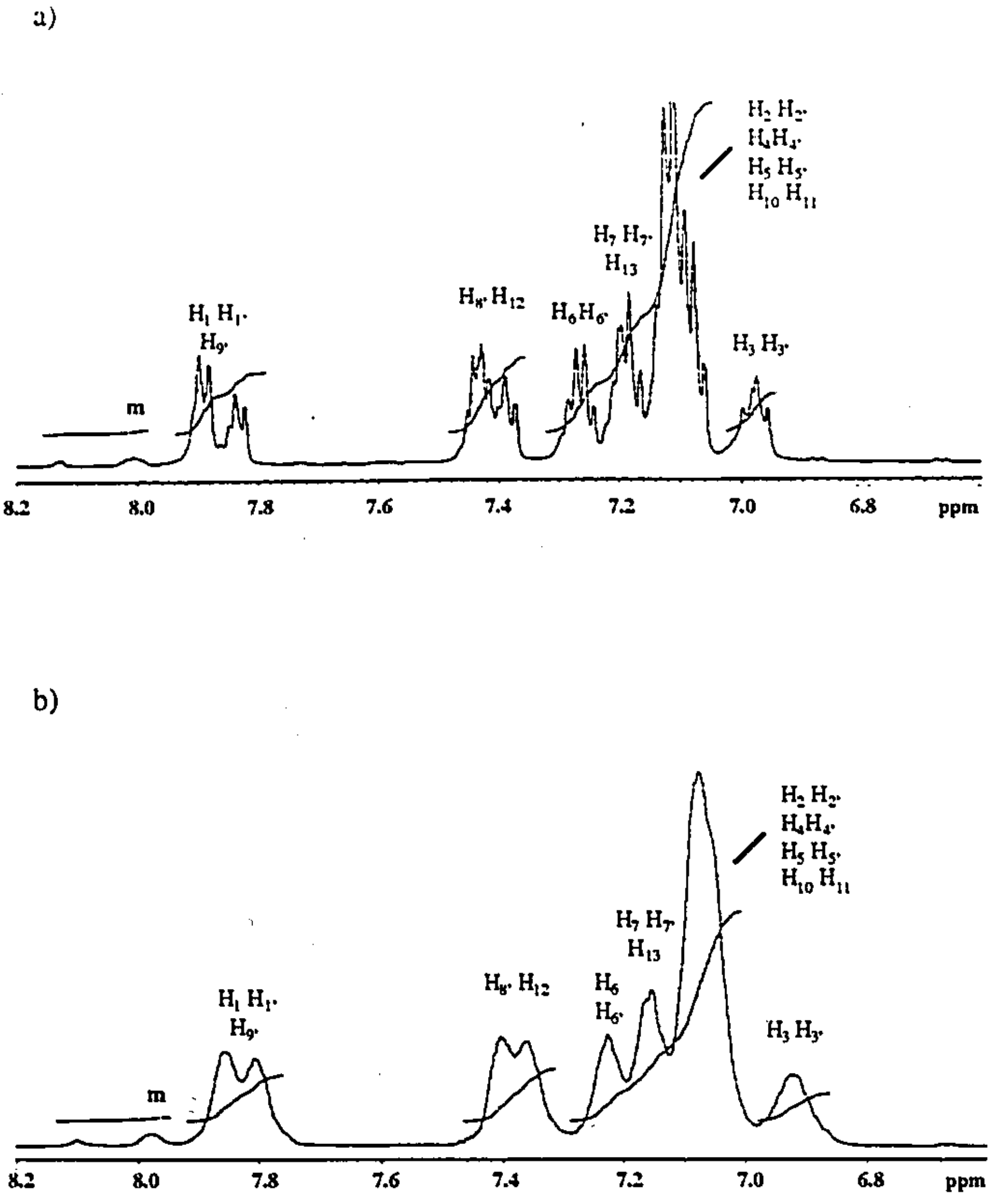
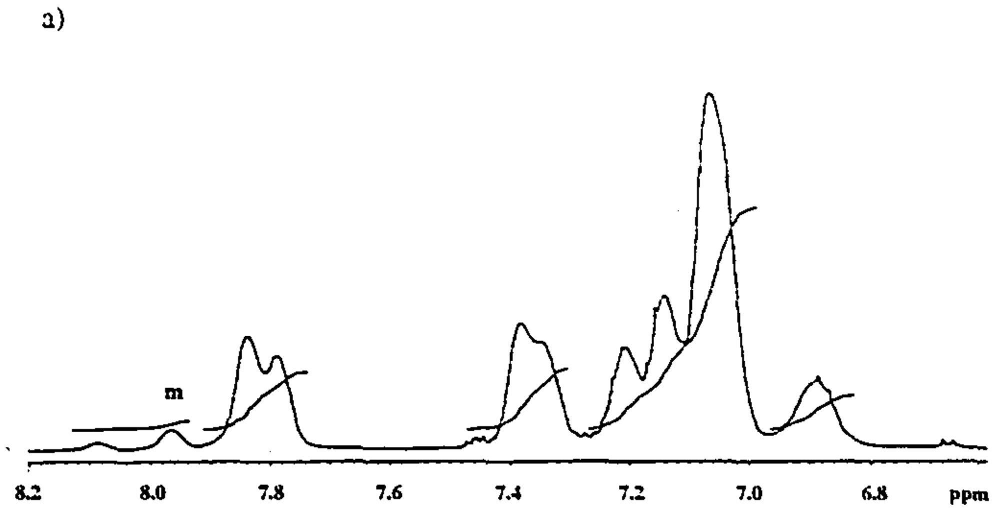


Figure 3.4. ^{1}H NMR spectra of fluoro poly(aryl ether sulfide) dendrimers: a) **2GFS** and b) **3GFS** .



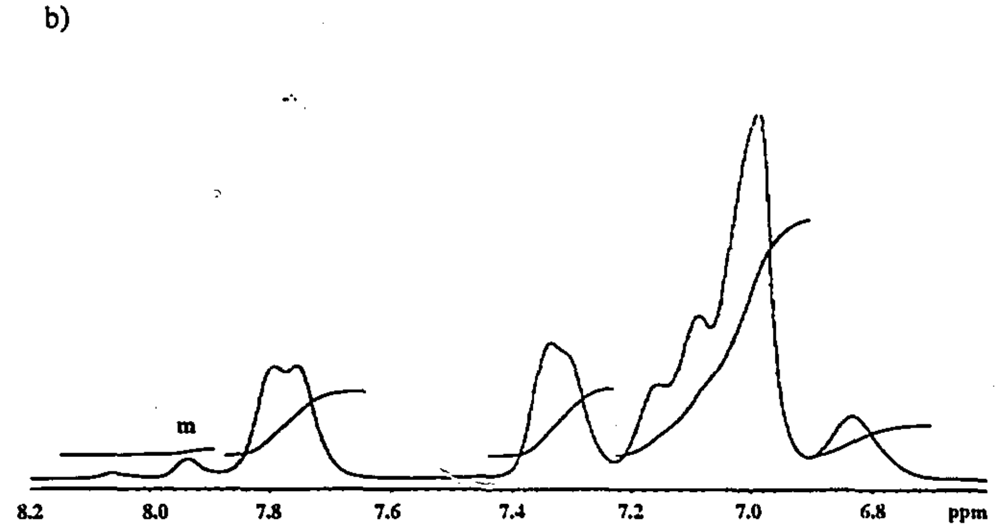


Figure 3.5. ^{1}H NMR spectra of fluoro poly(aryl ether sufide) dendrimers: a) **4GFS** and b) **5GFS**.

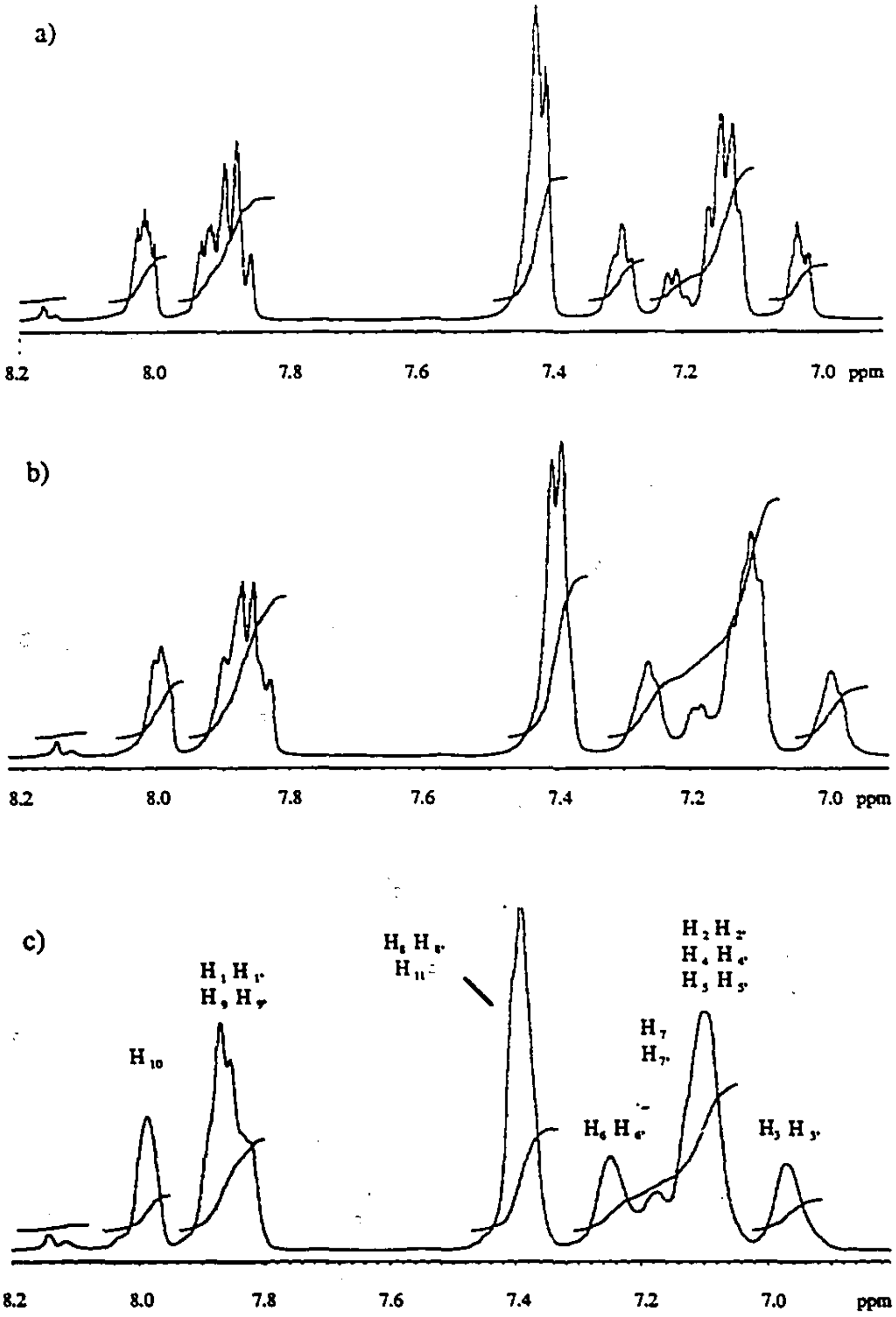


Figure 3.6. ^{1}H NMR spectra of fluoro poly(aryl ether sulfone) dendrimers: a) **$2GFSO_2$**, b) **$3GFSO_2$**, and c) **$4GFSO_2$**.

The very low intensity peak (m) detected in the spectra of fluoro poly(aryl ether sulfide) dendrimers might be a consequence of an incomplete reaction since protons H_{10} in the starting materials (terminal unit D) showed resonances around the same area. In general, the peaks become broader as the generation number increases. Similar protons in different layers could absorb slightly different amounts of energy that can affect the width of the peaks.

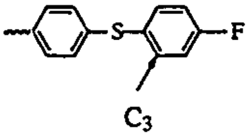
Some ^1H NMR integrals of these dendrimers are given in Table 3.3. The theoretical values (Cal) and the experimental values (Fnd) of the integrals of the spectra for all generations are in good agreement (differences ≤ 5 %).

Table 3.3. ^1H NMR integrations of fluoro poly(aryl ether) dendrimers

Dendrimer	n' [a]	Z [b]	Resonances					
			$H_1+H_{1'}+H_{9'}$		H_{10}		$H_8+H_{8'}+H_{11}$	
			Cal.	Fnd.	Cal.	Fnd.	Cal.	Fnd.
1GFS	0	4	4	4	-		-	
2GFS	1	8	20	19	-		-	
3GFS	2	16	52	49	-		-	
4GFS	3	32	116	115	-		-	
5GFS	4	64	244	246	-		-	
1GFSO$_2$	0	4	-		8	7	16	16
2GFSO$_2$	1	8	-		16	15	40	41
3GFSO$_2$	2	16	-		32	30	88	89
4GFSO$_2$	3	32	-		64	65	184	188

a) n' = number of layers with internal unit B; b) Z = number of terminal units.

The ^{13}C NMR spectra (50 MHz) are given in Figures 3.7 - 3.9. The results were similar to those found previously. For example, before the oxidation reaction atoms C_3 at the terminal unit C absorb at $\delta = 135.25$ ppm. But after the oxidation reaction these carbons, now close to the new sulfone group (terminal unit D), show resonances at $\delta = 130.65$ ppm (Fig. 3.7).



Since the number of peaks in each spectrum depends on the fact that similar carbons in different layers can absorb slightly different amounts of energy, it is possible to see more than one peak for similar C's.

3.5.3 MALDI-TOF mass spectrometry.

Matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF-MS), a technique which is becoming of increasing importance for synthetic polymer chemistry, (9) was used for the mass determination of the poly(aryl ether) dendrimers. We have to point out that this technique was only available in the last stages of our research. The analysis was carried out on a Kratos Compact MALDI III instrument in the reflectron mode using dithranol as the matrix. Silver trifluoroacetate was added to stabilize the system. The Figures 3.10, 3.11, and 3.12 show the quality of the spectra achieved with excellent signal-to-noise ratio.

The molecular ion mass, MI, of the fluoro poly(aryl ether sulfide) and fluoro poly(aryl ether sulfone) dendrimers, were calculated using the following general equations, respectively:

$$MI(iGFS) = A + (B - D)(2^i - 2) + (C - D)\,2^i$$

$$MI(iGFSO_2) = A + (B - D)(2^{i+1} - 2)$$

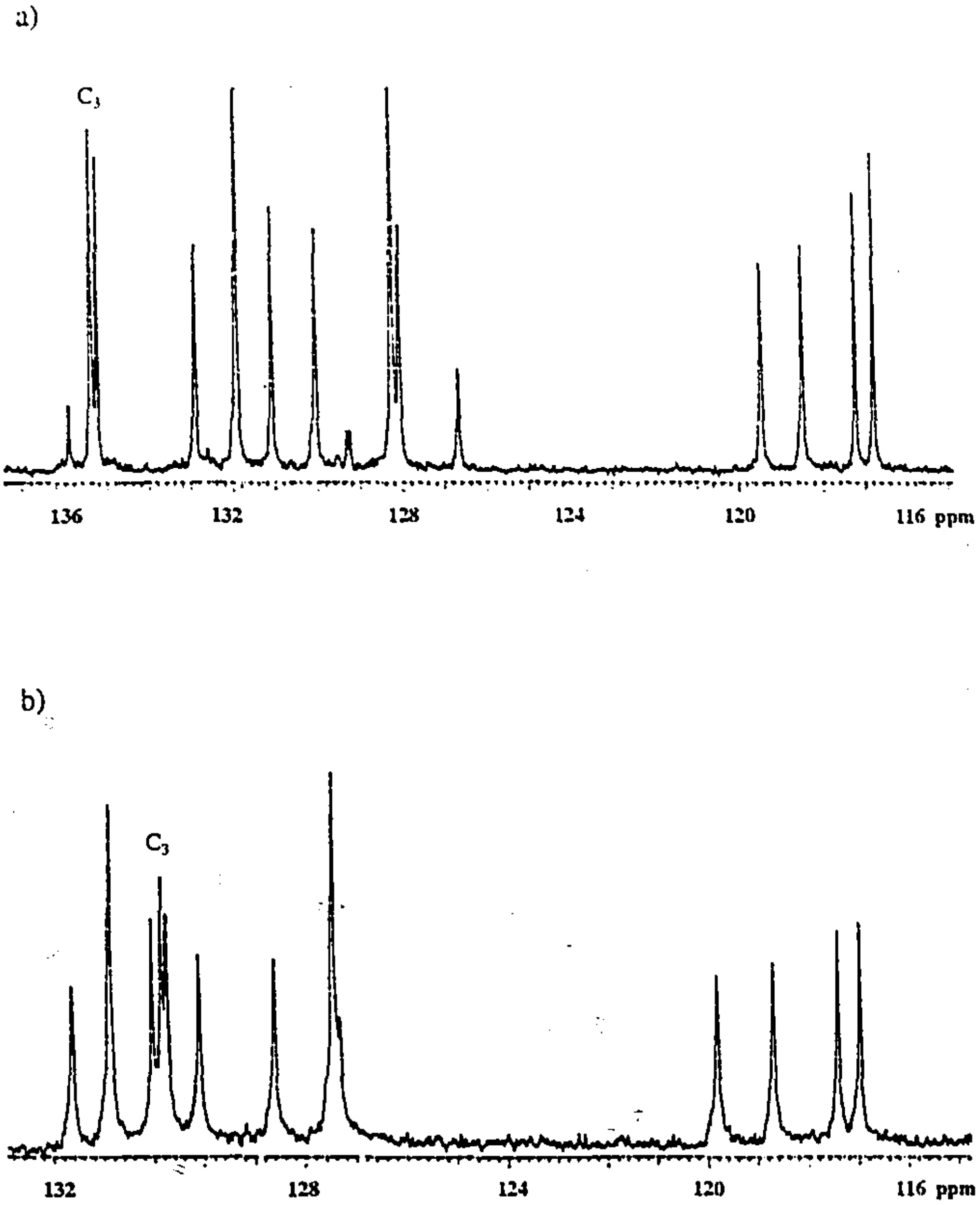


Figure 3.7. ^{13}C NMR spectra of first generation fluoro poly(aryl ether)s: a) 1GFS and b) **1GFSO$_2$.**

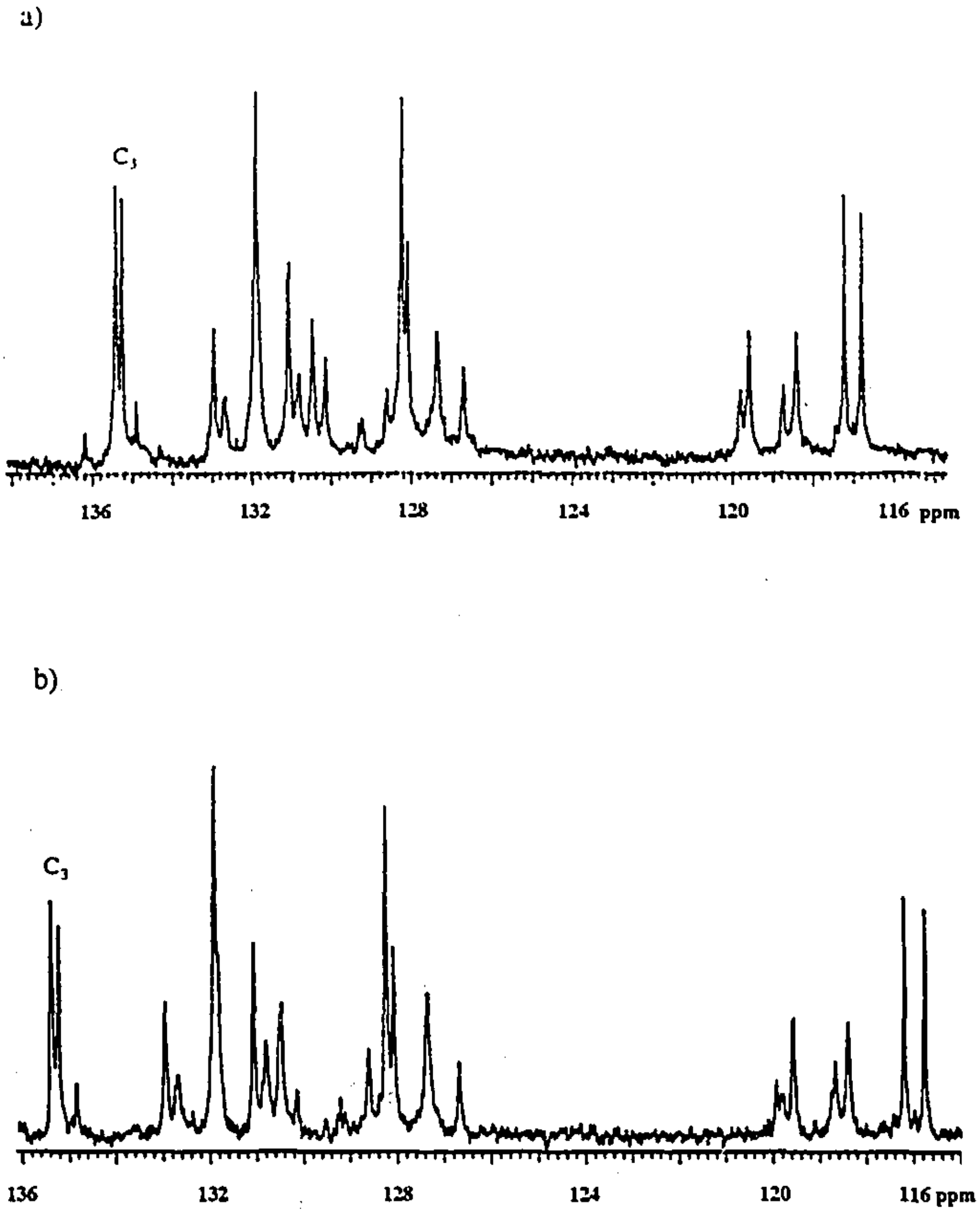


Figure 3.8. ^{13}C NMR spectra of fluoro poly(aryl ether sulfide) dendrimers: a) **2GFS** and b) **3GFS.**

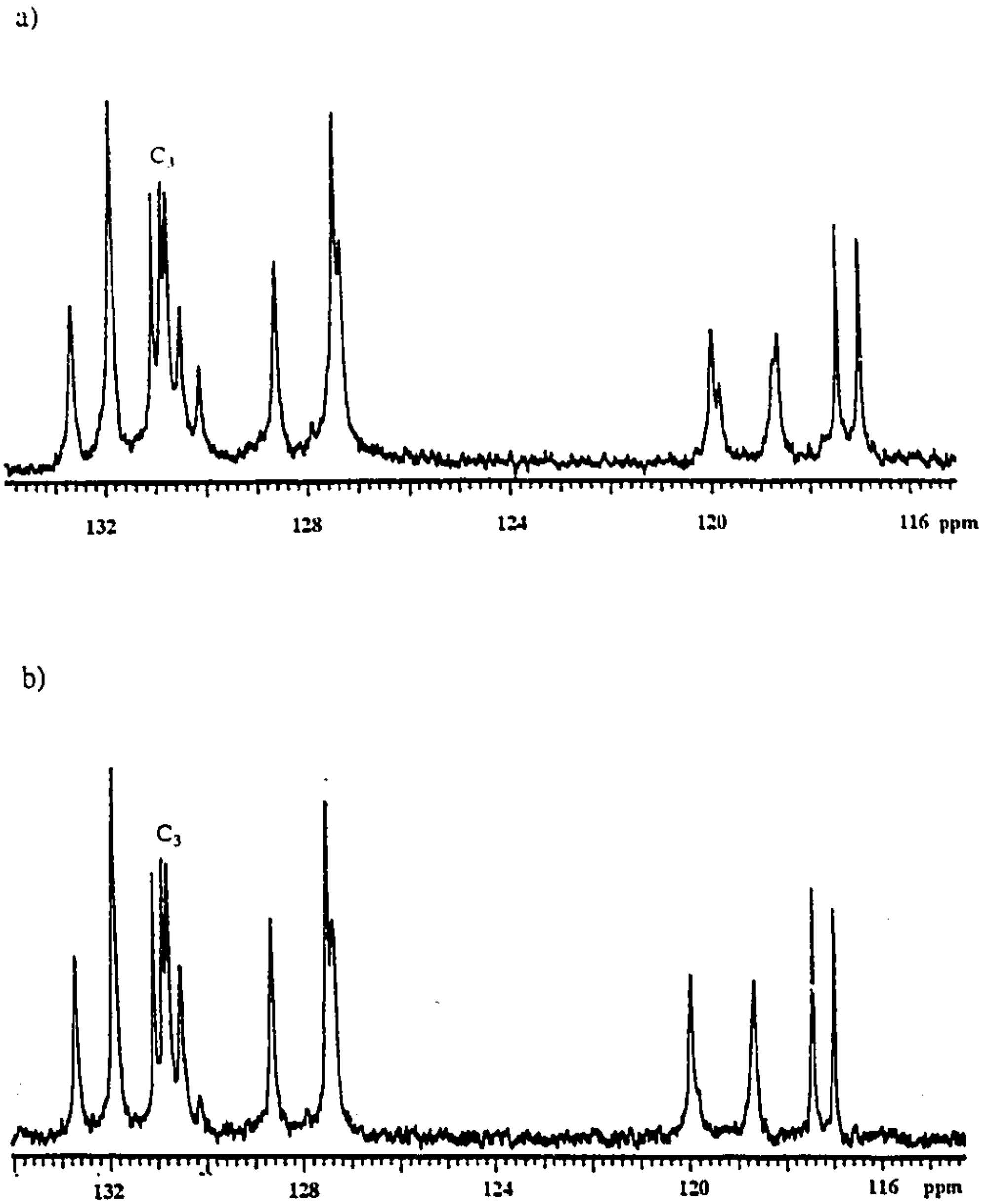
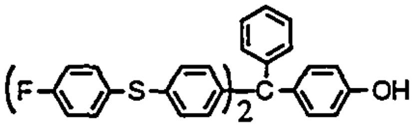
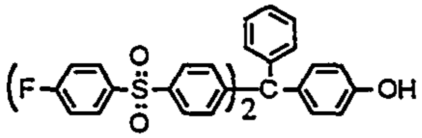


Figure 3.9. ^{13}C NMR spectra of fluoro poly(aryl ether sulfone) dendrimers: a) **2GFSO$_2$** and b) **3GFSO$_2$**.

Where i represents the generation number (i = 1, 2, 3, ...), A the molecular mass of the core precursor **3.8** (254.25 Da), B the molecular mass of phenol **3.9** (652.73 Da), C the molecular mass of phenol **3.7** (588.73 Da), and D the molecular mass of HF (20.01Da):



3.7



3.9

HF is the small molecule eliminated during the condensation reaction: The values obtained for the first and second generations of dendrimers are given in Table 3.4. For example, the molecular ion mass of 2GFS was obtained using i = 2, A = 254.25 Da, B = 652.73 Da, C = 588.73 Da, and D = 20.01 Da.

Table 3.4. MALDI mass spectrometry analyses of first and second generation fluoro poly(aryl ether)s [a)]

Dendrimer	MI (Da) [b)]	MI_1 (Da) [b)]	MI_2 (Da) [b)]	Mass/Charge		
				Peak 1	Peak 2	Peak 3
1GFS	1391.7	-	-	1396.8	-	-
IGFSO$_2$	1519.7	-	-	1524.8	-	-
2GFS	3794.6	3225.9	2657.2	3804.1	3234.7	2665.7
2GFSO$_2$	4050.6	3417.9	2785.2	4056.6	3423.7	2790.8

a) Dithranol: sample:CF_3CO_2Ag = 40:4:1. b) MI = molecular ion mass; MI_1, MI_2: reaction intermediate molecular ion masses.

The mass spectra of the first and second generation (Figs. 3.10 - 3.12) show one intense signal (peak 1) corresponding to the molecular ion. However, the presence of reaction intermediates are also detected for the second (peaks 2 and 3) and third generation.

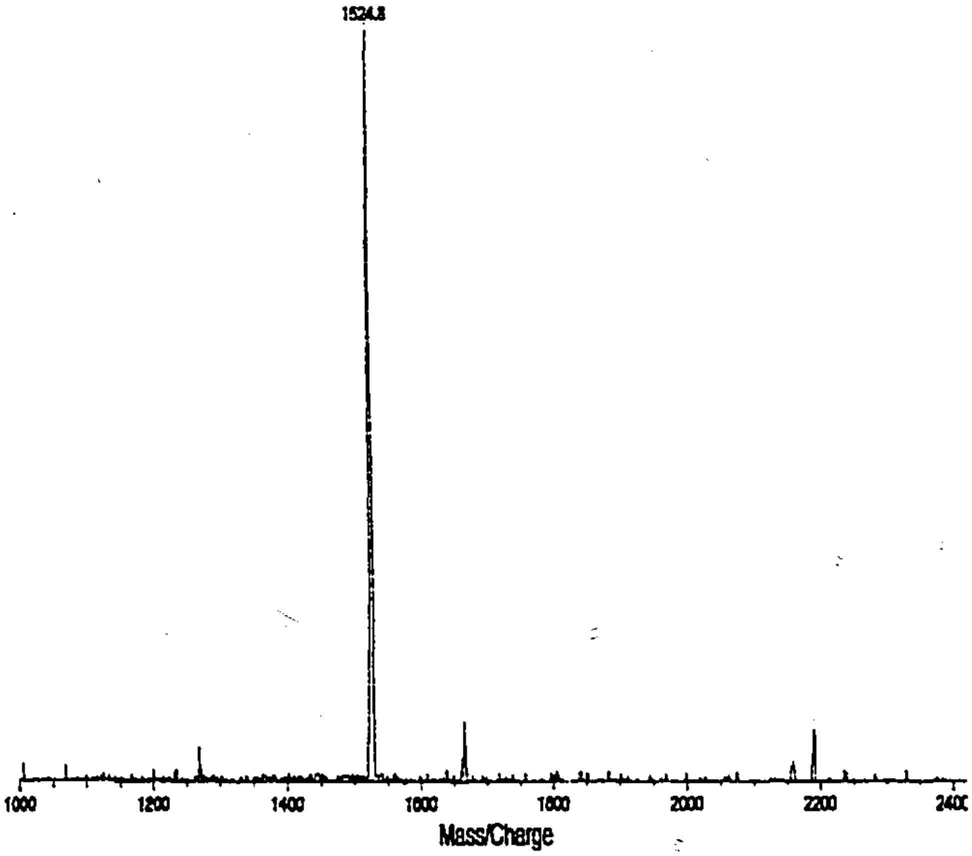


Figure 3.10 . MALDI mass spectra of first generation fluoro poly(aryl ether sulfone)s **1GFS$_2$**. Analysis conditions in **Table 3.4.**

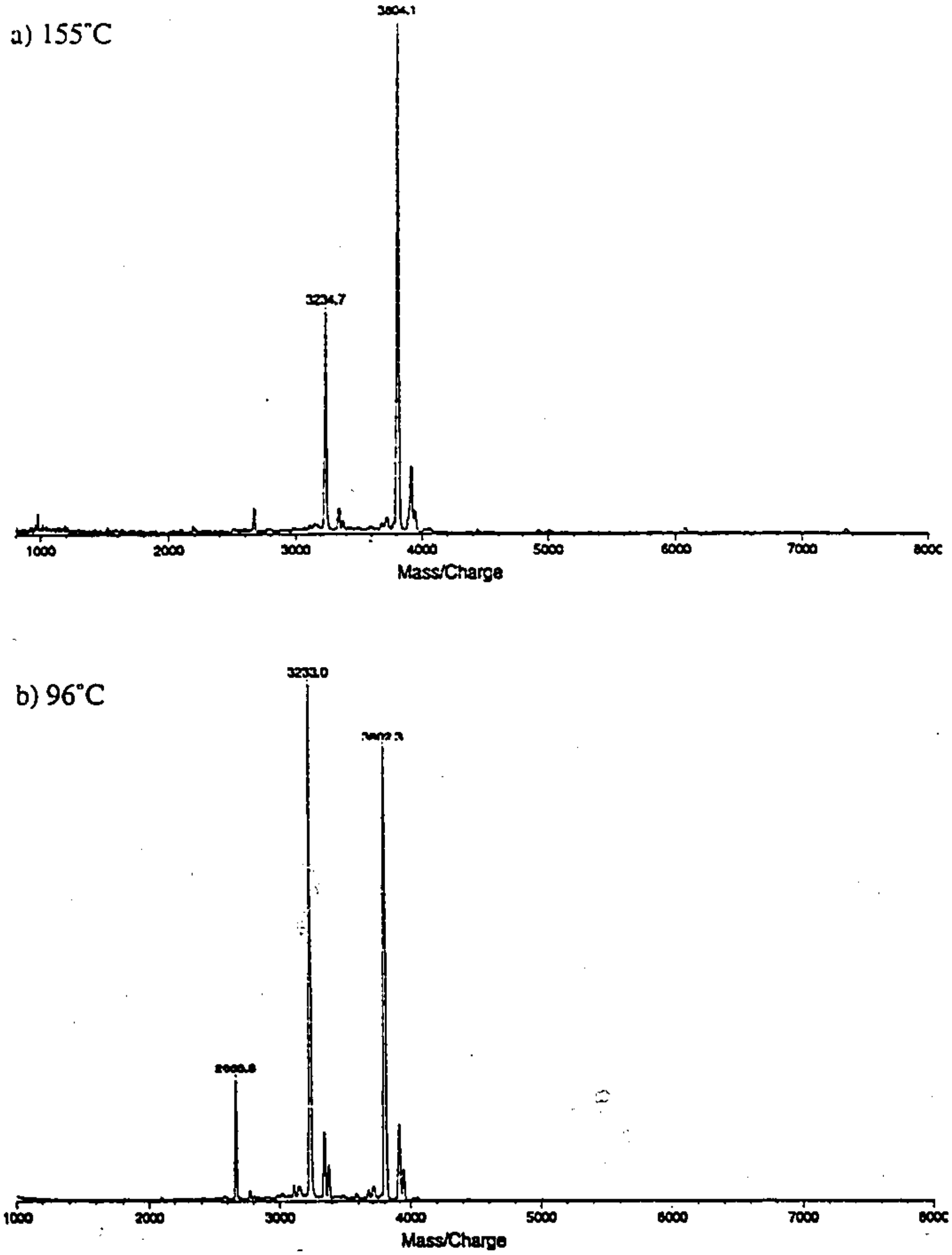


Figure 3.11 . MALDI mass spectra of second generation fluoro poly(aryl ether sulfide) 2GFS, synthesized at a) 155°C and b) 96°C. Analysis conditions in **Table 3.4.**

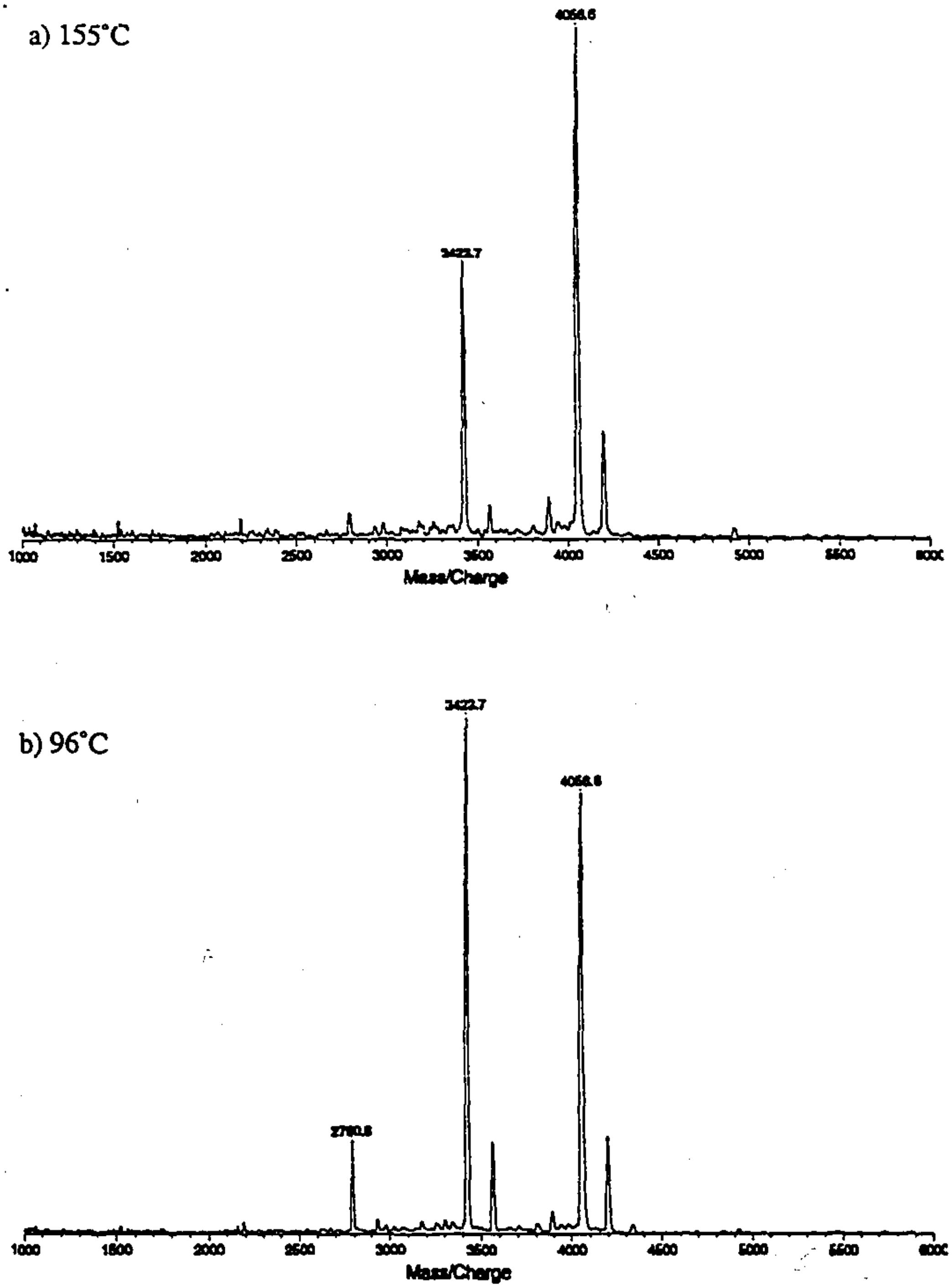


Figure 3.12 . MALDI mass spectra of second generation fluoro poly(aryl ether sulfone) **2GFSO$_2$**. Precursors were synthesized at: a) 155°C and b) 96°C. Analysis conditions in **Table 3.4.**

The difference between the calculated and found values are between 5.0 and 9.5 Da. The error of these measurements is higher than 0.14 % and lower than 0.38 %. The reported error for the MALDI measurements is 0.1 %. These deviations can be explained assuming that a lithium cation (7 Da) is complexed with the sample. Lithium cations can come from the metallic holder used for the analysis. Silver cations were not detected, probably due to the low concentration of CF_3CO_2Ag employed. But, it absolutely necessary to use this reagent to avoid the fragmentation of the sample. Taking into account this fact the mass differences between the calculated and the experimental values are around 0.1 %.

The following general equations were used to calculate the molecular ion masses of the intermediates, MI_n:

$$MI_n(iGFS) = MI(iGFS) - n\,(C - D)$$

$$MI_n(GFSO_2) = MI(iGFSO_2) - n(B - D)$$

Where MI(iGFS) and $MI(iGFSO_2)$ are the molecular ion masses of **iGFS** and **$iGFSO_2$**, respectively, and n represents the necessary number of monomer units required to obtain a perfectly globular dendrimer structure. For example, the mass spectrum of **$3GFSO_2$** (Fig. 3.13), shows signals which can correspond to the molecular ions of reaction intermediates. Since a higher concentration of silver trifluoroacetate was used, a silver cation is complexed with each of the intermediate molecules. The values of $MI_n(3GFSO_2)$ calculated using $MI(3GFSO_2) = 9{,}112.3$ Da; B = 652.73 Da; D = 20.01 Da, with n taking values from 1 to 7 are given in Table 3.5. In this case the expected product was not detected.

Each of those peaks was accompanied by a low intensity signal. The same low intensity signals were also detected in the mass spectra of the lower generations. The mass difference between them was about 108 Da for poly(aryl ether sulfide)s and 140 Da for poly(aryl ether sulfone)s. The origin of these signals might be related to the impurity found in the phenol **3.7**. Progress has been made in this area which will be discussed in the next Chapter.

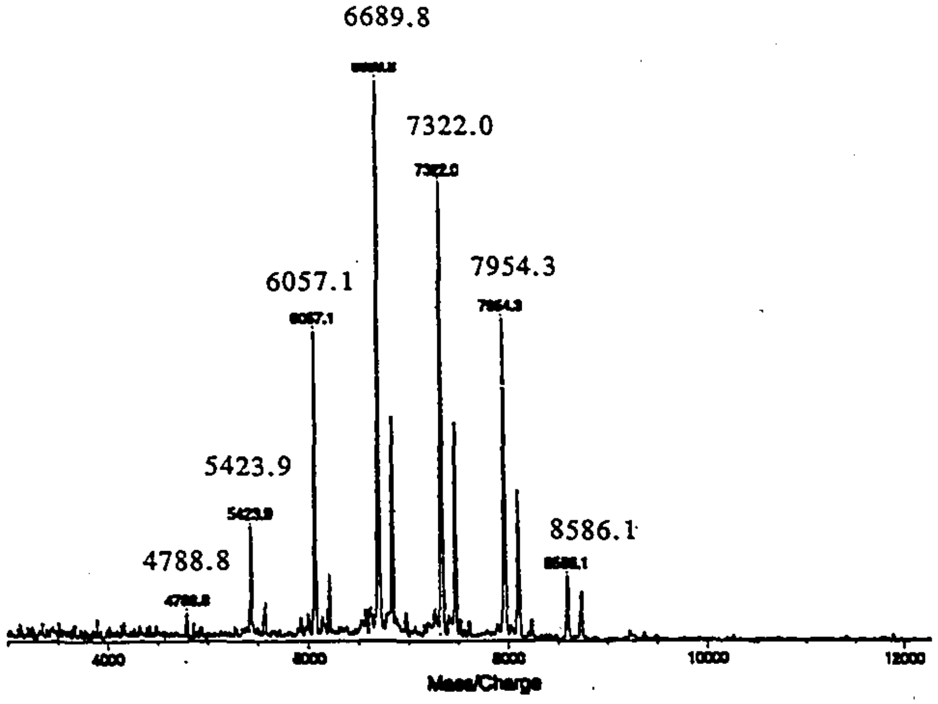


Figure 3.13 . MALDI mass spectrum of third generation fluoro poly(aryl ether sulfone) **3GFSO$_2$**. Analysis conditions in **Table 3.4.**

Table 3.5. MALDI mass spectrometry analysis of third generation fluoro poly(aryl ether sulfone) 3GFSO$_2$

Mass	MI	MI$_1$	MI$_2$	MI$_3$	MI$_4$	MI$_5$	MI$_6$	MI$_7$
Calc'd	9112.3	8479.6	7846.9	7214.2	6581.5	5948.8	5316.1	4683.4
Found	-	8586.1	7954.3	7322.0	6689.8	6057.1	5423.9	4788.8
Differ.	-	106.5	107.4	107.8	108.3	108.3	107.8	105.4

a) Dithranol:sample:CF_3CO_2Ag = 40:4:2; b) MI = molecular ion mass, Da ;MI$_1$, MI$_2$: reaction intermediate molecular ion masses, Da.

The date accumulated indicates that the condensation agent and conditions employed in the synthesis were efficient in the synthesis of the first generation since no signal was detected for the reaction intermediate and only the molecular ion was observed. However, this data also indicates that the synthesis of the second generation was not quantitative and suggests that the perfectly globular third generation dendrimer was not formed.

The MALDI spectra of the second generation poly(aryl ether sulfide) synthesized at a higher temperature showed a lower concentration of the reaction intermediates, as shown in Figure 3.11. The oxidation product gave the same result (Figs. 3.12). It confirms our previous considerations about the use of a temperature close to the boiling point of the solvent to increase the conversion of the reaction.

Unfortunately, it was not possible to characterize the fourth and fifth generations of dendrimers and quantify the purity of our samples using this technique. Variations in the peak intensities for a single sample analyzed several times were detected. It is known that the way the sample, matrix, and stabilizer interact and coprecipitate affects the characteristics of the mass spectra, as well as other conditions such as beam power, shot number, area analyzed, and nature of the sample.

These results of mass characterization are similar to those found previously for chloro poly(aryl ether) dendrimers, except for the fact that in this case an impurity was detected.

3.6 Physical properties.

The physical properties of these materials are given in Table 3.2. The glass transition temperature, Tg, of the fluoro poly(aryl ether) dendrimers increases with the generation number and molecular weight from 91°C - 228°C. Since a fluoro poly(aryl ether sulfone) dendrimer has a more polar structure, its Tg is higher than that of a poly(aryl ether sulfide) of comparable molecular weight. For example, for the first generation: Tg(1GFS)

= 91°C and Tg(1GFSO$_2$) = 165 °C. The inherent viscosity, η_{inh}, also increased with the generation number (0.05 dL/g - 0.11 dL/g).

All of these samples showed a high solubility in common organic solvents such as tetrahydrofuran, chloroform, DMAc, and DMSO. All of them showed a high thermal stability (5 % loss weight = 487°C - 507°C by TGA).

The physical properties of fluoro poly(aryl ether) dendrimers were similar to those of the chloro poly(aryl ether) dendrimers synthesized previously.

3.7 Conclusions

We have carried out the synthesis of five generations of fluoro poly(aryl ether)s with activated aryl fluoride terminal functionality from 4,4'-difluorodiphenyl sulfone and a relatively high molecular weight bis(fluoroaryl)phenolate. An iterative procedure was employed that involved oxidation of the aryl sulfide moieties followed by the displacement of the fluorides activated by sulfone groups.

The results obtained confirm that the size and molecular weight of these molecules increase with the generation number. The polydispersities of all these samples are close to one (measured by SEC). NMR characterization confirms that structural changes occurs during the condensation and activation reactions, but suggests that the reaction of the higher generations are not complete. SEC characterization indicates that temperatures lower than the boiling point of the solvent are no practical for the conversion in the condensation reactions.

MALDI mass spectrometry was a very useful characterization technique. It confirmed that the synthesis of the first generation occurs in high yield and that the perfect globular second generation dendrimer is also synthesized. However, intermediates in the last reaction were also detected. These data suggest that the perfect globular third generation dendrimer are not formed, but only intermediates in high proportion. Unfortunately, the fourth and fifth generations could no be characterized using this technique. MALDI mass spectrometry results confirmed our previous considerations about the use of a temperature close to the boiling point of the solvent to increase the conversion of the reaction.

It has been demonstrated that the iterative sequence employed is easy to carry out and produces in high yield the first generation fluoro poly(aryl ether sulfide) and fluoro poly(aryl ether sulfone) dendrimers. The synthesis of the second generation, however could not be accomplished in quantitative fashion.

The displacement of fluorides by sodium phenolate did not overcome the limitations found in the synthesis of chloro poly(aryl ether sulfide) dendrimers. However, the displacement of fluorides instead of chlorides allowed us to obtain crude products with lower polydispersities and made the reaction cleaner. These results indicate that sodium phenolate is the major limitation in the synthesis of the higher generations, since it is not active enough to force the condensation reactions to be quantitative. Improvements have been made in this area which will be discussed in the next Chapters.

3.8 Experimental.

Materials. 4-Fluorothiophenol was obtained from Aldrich Chemical Co. More details in Chapter 2: Part 2.8.

General methods, and dendrimer characterization. For details see Chapter 2: Part 2.8.

Monomer synthesis.

Synthesis of 4,4'-Bis(4-fluorophenylthio)diphenyl ketone 3.3. A mixture of 4-fluorothiophenol **3.2** (19.23 g, 0.15 mol), 4,4'-dichlorobenzophenone **3.1** (18.33 g, 0.073 mol) and DMAc (325 mL) was mechanically stirred under nitrogen for 0.5 h at 80°C. Anhydrous potassium carbonate (12.44 g, 0.09 mol) was added and the mixture was allowed to react under the same conditions for 2.5 h (the reaction was followed by HPLC). When the reaction finished, it was poured into 650 mL of water and filtered. The solid obtained was washed with water, recrystallized from acetone (3 g/50 mL), and dried overnight under vacuum at 80°C. After the workup 22.52 g of **3.3** was obtained (yield = 71%, purity of the isolated product by HPLC = 86%): ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.80-7.56 (m, 8H), 7.45-7.18 (m, 8H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 194.1, 165.6-160.7 (J = 247.3 Hz), 144.5, 136.8-136.6 (J = 8.3 Hz), 134.9, 130.9, 127.0, 117.6-117.2 (J = 21.7 Hz); MS (IE) m/e 434 (MI), 307, 231, 202, 183, 127, 108.

Synthesis of 4,4'-Bis(4-fluorophenylthio)triphenylcarbinol 3.5. Product **3.3** (26.0 g, 0.06 mol) previously dried, and sodium-dried ether (600 mL) were placed into a 1000 mL flask, fitted with a magnetic stirrer, a Claisen adapter with a rubber stopper and an efficient double surface condenser with a nitrogen inlet. The apparatus was arranged so that the flask could be heated with a heating plate. All parts of the apparatus were thoroughly dried. The diethyl ether could be distillated in to the 1000 mL flask previously charged with the dried product **3.3**. The reaction mixture was placed under nitrogen for 0.5 h and the phenyl magnesium bromide **3.4** (3M solution in diethyl ether, 24 mL, 0.072 mol) was then introduced, in two fractions separated by 0.5 h, through the rubber stopper with a syringe. When the reaction was finished, approximately 2.5 h later (the reaction was followed by HPLC), it was cooled and poured into a 30% aqueous sulfuric acid solution (350 mL) to dissolve the magnesium hydroxide. The ethereal phase was separated and dried with anhydrous magnesium sulfate. The solution was filtered and the ether evaporated under vacuum. A green-yellow viscous liquid was separated and used in this form in the synthesis of **3.7**. After the workup, 22.45 g of **3.5** was obtained (yield = 73%, purity of the isolated product by HPLC = 77%). **3.5** could be purified by chromatographic column using hexane:ethyl acetate (8.5:1.5 in volume) and silica gel 60 (0.040 mm - 0.063 mm): ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.50-7.10 (m), 6.57 (s); ^{13}C NMR (50 MHz, $CDCl_3$) δ 165.0-160.1 (J = 245.3 Hz), 146.4, 145.1, 136.5, 135.2-135.0 (J = 8.0 Hz), 129.6-129.5 (J = 3.7 Hz), 129.0, 128.9, 128.4, 128.1, 127.9, 117.2-116.8 (J = 21.9 Hz), 82.4.

Synthesis of p-[4,4'-Bis(4-fluorophenylthio)]triphenylmethyl phenol 3.7. A mixture of phenol **3.6** (188.2 g, 2.0 mol), product **3.5** (29.22 g, 0.057 mol) and a catalytic amount of sulfuric acid was placed in a 1000 mL flask equipped with a condenser at 75°C for 24 h (the reaction was followed by HPLC). When the reaction finished, water (500 mL) was added and the reaction mixture was stirred for one half hour. The water phase was separated and the organic phase (a viscous liquid) was diluted with diethyl ether and extracted with 20% aqueous sodium hydroxide until the color faded in the aqueous phase. After that, the ethereal phase was washed several times with water, dried with anhydrous magnesium sulfate, filtered, and the ether evaporated under vacuum. The brown viscous liquid (purity by HPLC = 78%) separated was purified using flash chromatography, 5 g of sample, a column of 12 cm x 5 cm, hexane:ethyl acetate (8.5:1.5 in volume), and silica gel 60 (0.040 mm-0.063 mm). After the workup 24.37 g of **3.7** was obtained (purity of the isolated product by HPLC = 92%). The yield of the product after purification was 70%: ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.40 (s, 1.1H), 7.47-7.42 (m, 3.4H), 7.28-7.20 (m, 5.8H), 7.19-7.13 (m, 1.2H), 7.13-7.02 (m, 10.2H), 6.87-6.82 (d, 2.3H), 6.66-6.62:d (2); ^{13}C NMR (50 MHz, $CDCl_3$) δ 164.9-160.0 (J = 245.3 Hz), 154.2, 146.6, 145.4, 138.2, 135.1-134.9 (J = 8.0 Hz), 134.7, 132.4, 132.0, 131.2, 129.7-129.6 (J = 3.3 Hz), 128.4, 127.9, 126.4, 117.1-116.7 (J = 21.8 Hz), 114.9, 61.8; MS (IE) m/e 588 (MI), 511, 494, 461, 385, 257, 181, 127, 108; MALDI m/e 512.8 (MI-77), 496.6.

Dendrimer syntheses.

First generation fluoro poly(arylether sulfide) 1GFS. The sodium salt was prepared by treating **3.7** (29.44 g, 0.05 mol) in ethyl ether (1000 mL) with excess of NaH (1.80 g, 0.075 mol). The solution was filtered to removed excess NaH. The ether was removed in vacuum to obtain 27.48 g of the sodium salt of **3.7** (yield = 100%, purity of the isolated product by HPLC = 90%).

To a 250 mL round bottomed flask, fitted with a condenser and a nitrogen inlet, there was added 4,4'-difluorodiphenyl sulfone **3.8** (1.27 g, 5.00 mmol), the sodium salt of **3.7** (6.72 g, 11.00 mmol by HPLC) and DMAc (110 mL).The mixture was stirred vigorously and maintained under reflux for 3 h. The reaction was followed by SEC. When the reaction was finished it was cooled, poured into methanol (440 mL) and filtered. The solid recovered was dissolved in DMAc (110 mL), coagulated in 2% aqueous hydrochloric acid (440 mL), filtered and dried overnight at 70°C under vacuum. In general the volumes of methanol and acid solution were four times the volume of DMAc used in the reaction and the volume of DMAc for the separation procedure was the same as that used in the reaction. The crude product (6.75 g, isolated yield = 97%) was purified by fractional precipitation by dissolving the sample in chloroform (15-20 mL/g) and using methanol as the nonsolvent. After the workup 5.22 g of **1GFS** was obtained (isolated yield after purification = 75%): ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.92-7.86 (d, calc'd 4, found 4), 7.48-7.44 (m, calc'd 8, found 6), 7.32-7.27 (t, calc'd 4, found 5), 7.24-7.08 (m, calc'd 38, found 39), 7.04-7.00 (d, calc'd 4, found 4); ^{13}C NMR (50 MHz, $CDCl_3$) δ 165.0-160.1 (J = 245.7 Hz), 161.4, 153.2, 146.1, 144.7, 143.1, 135.9, 135.4-

135.3 (J = 8.1 Hz), 132.9, 131.9, 131.1, 130.1, 129.3 (J = 3.2 Hz), 128.3, 128.1, 126.7, 119.5, 118.5, 117.2-116.8 (J = 21.7 Hz), 65.00; MS (MALDI(Li)) m/e 1396.8 (MI); TG: 91°C (10°C/min, N_2), 5% weight loss = 487°C (10°C/min, N_2); n_{inh} = 0.05 dL/g (NMP, 0.5 g/dL, 25°C).

First generation fluoro poly(aryl ether sulfone) 1GFSO$_2$. Wet alumina was prepared by adding water (10 mL) to the alumina (50 g; Brockman grade I, 200 mesh) and shaking until a free flowing homogeneous powder was obtained.

The first generation fluoro poly(aryl ether sulfide) **1GFS**, (4.87 g, 3.50 mmol) was added to a vigorously stirred suspension of wet alumina (14.00 g) and Oxone (25.90 g, 42.00 mmol) in chloroform (175 mL). The mixture was heated at reflux for 24 h. When the reaction finished, it was cooled, filtered and the solids washed thoroughly with chloroform. The solution was concentrated, coagulated in methanol (350 mL), and the solid separated was dried overnight at 100°C under vacuum. After the workup 4.87 g of **1GFSO$_2$** was obtained (isolated yield = 92%): ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.04-7.99 (m, calc'd 8, found 7), 7.92-7.87 (m, calc'd 12, found 12), 7.46-7.40 (m, calc'd 16, found 16), 7.33-7.28 (t, calc'd 4, found 4), 7.25-7.20 (t, calc'd 2, found 2), 7.18-7.10 (m, calc'd 12, found 13), 7.05-7.01.d (calc'd 4, found 4); ^{13}C NMR (50 MHz, $CDCl_3$) δ 168.0-162.9 (J = 253.3 Hz), 161.1, 153.8, 151.4, 144.4, 141.3, 139.9, 137.5-137.4 (J = 3.2 Hz), 136.2, 132.6, 131.9, 131.1-130.9 (d, J = 9.6 Hz), 138.8, 130.1, 128.6, 127.5, 127.3, 119.8, 118.7, 117.4-117.0 (J = 22.2 Hz), 65.8; MS (MALDI(Li)) m/e 1525.1; Tg = 165°C (10°C/min, N_2), 5% weight loss = 501°C (10°C/min, N_2); n_{inh} = 0.05 dL/g (NMP, 0.5 g/dL, 25°C).

Second generation fluoro poly(aryl ether sulfide) 2GFS. The reaction was carried out using a procedure similar to that employed for the synthesis of **1GFS** using **1GFSO$_2$** (1.52 g, 1.00 mmol), sodium salt of **3.7** (2.44 g, 4.00 mmol), DMAc (40 mL) and temperatures of 96°C (reaction time = 3 h) and 155°C (reaction time = 2 h). The separated solid 3.60 g (isolated yield = 95%) was purified by fractional precipitation and dried overnight at 100°C under vacuum. After the workup 2.16 g of **2GFS** was obtained (isolated yield after purification = 57%): ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.92-7.80 (d, calc'd 20, found 19), 7.46-7.36 (m, calc'd 24, found 23), 7.30-7.04 (m, calc'd 102, found 104), 7.04-6.95 (d, calc'd 12, found 12); ^{13}C NMR (50 MHz, $CDCl_3$) δ 165.0-160.1 (J = 245.7 Hz), 161.8, 161.1, 153.8, 153.0, 151.1, 146.0, 144.7, 143.3, 141.4, 140.4, 136.2, 135.4-135.2 (J = 8.0 Hz), 134.9, 133.0, 132.7, 131.9, 131.8, 131.1, 130.8, 130.5, 130.2, 129.3-129.2 (J = 3.2 Hz), 128.6, 128.3, 128.1, 127.3, 126.7, 119.8, 119.6, 118.7, 118.4, 117.2-116.8 (J = 21.9 Hz), 65.8, 64.9; MS (MALDI(Li)) m/e 3804.1, 3234.7, 2665.7; Tg = 148°C (10°C/min, N_2), 5% weight loss = 490°C (10°C/min, N_2); n_{inh} = 0.07 dL/g (NMP, 0.5 g/dL, 25°C).

Second generation fluoro poly(aryl ether sulfone) 2GFSO$_2$. A procedure similar to that used to synthesize **1GFSO$_2$** was employed using **2GFS** (2.85 g, 0.75 mmol), wet alumina (6.00 g) and Oxone (11.10 g, 18.00 mmol) in chloroform (40 mL). The solution was concentrated and coagulated in methanol (75 mL) to afford 2.97 g of **2GFSO$_2$** (isolated yield = 98%): ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.04-7.98 (m, calc'd 16, found 15), 7.94-7.84 (m, calc'd 36, found 34), 7.46-7.38 (m, calc'd 40, found 41), 7.33-7.26 (m, calc'd 12, found 14), 7.24-7.10 (m, calc'd 42, found 44), 7.06-7.00 (m, calc'd 12, found 12); ^{13}C NMR (50 MHz, $CDCl_3$) δ 168.0-162.9 (J = 253.3 Hz), 161.4, 153.6, 151.4, 151.2, 144.4, 141.4, 140.2, 139.9, 135.3, 132.7, 131.9, 131.1-130.9 (J = 9.6 Hz), 130.8, 130.5, 130.1, 128.6, 127.5, 127.4, 120.0, 119.8, 118.7, 118.6, 117.4-117.0 (J = 22.4 Hz), 65.9, 65.8; MS (MALDI(Li)) m/e 4056.6, 3423.7, 2790.8; Tg = 205°C (10°C/min, N_2), 5% weight loss = 510°C (10°C/min, N_2); n_{inh} = 0.07 dL/g (NMP, 0.5 g/dL, 25°C).

Third generation fluoro poly(aryl ether sulfide) 3GFS. The reaction was carried out using a procedure similar to that employed to synthesize **1GFS** using **2GFSO$_2$** (1.62 g, 0.40 mmol), sodium salt of **3.7** (1.95 g, 3.20 mmol), DMAc (40 mL), and temperatures of 94°C (reaction time = 3.0 h) and 115°C (reaction time = 1.5 h). The separated solid (3.03 g, isolated yield = 88%) was purified by fractional precipitation and dried overnight at 100°C under vacuum. After the workup 2.24 g of **3GFS** was obtained (isolated yield after purification = 65%): ^{1}H NMR (500 MHz, DMSO-d$_6$) δ 7.90-7.76 (m, calc'd 52, found 49), 7.44-7.30 (m, calc'd 56, found 55), 7.28-6.70 (m, calc'd 222, found 225), 6.98-6.86 (m, calc'd 28, found 29); ^{13}C NMR (50 MHz, CDCl$_3$) δ 165.0-160.1 (J = 245.9 Hz), 161.8, 161.4, 153.6, 153.0, 151.2, 151.1, 146.0, 144.7, 144.6, 143.3, 141.5, 140.4, 140.3, 135.4-135.3 (J = 7.9 Hz), 134.9, 133.0, 132.7, 132.6, 131.9, 131.1, 130.8, 130.5, 130.2, 129.6, 128.6, 128.3, 128.1, 127.4, 126.7, 119.9, 119.6, 118.7, 118.4, 117.2-116.8 (J = 21.8 Hz), 65.8, 64.9; Tg = 177°C (10°C/min, N$_2$), 5% weight loss =.475°C (10°C/min, N$_2$); n_{inh} = 0.08 dL/g (NMP, 0.5 g/dL, 25°C).

Third generation fluoro poly(aryl ether sulfone) 3GFSO$_2$. A procedure similar to that used to synthesize **1GFSO$_2$** was employed, using **3GFS** (2.58 g, 0.30 mmol), wet alumina (4.80 g), and Oxone (8.88 g, 14.40 mmol) in chloroform (30 mL). The solution was concentrated and coagulated in methanol (50 mL) to afford 2.40 g of **3GFSO$_2$** (isolated yield = 88%): ^{1}H NMR (500 MHz, DMSO-d$_6$) δ 8.02-7.96 (m, calc'd 32, found 30), 7.96-7.82 (m, calc'd 84, found 79), 7.46-7.36 (m, calc'd 88, found 89), 7.30-7.06 (m, calc'd 126, found 132), 7.06-6.96 (m, calc'd 28, found 28); ^{13}C NMR (50 MHz, CDCl$_3$) δ 167.9-162.9 (J = 253.4 Hz), 161.4, 153.6, 151.4, 151.2, 144.4, 141.4, 140.2, 139.9, 135.3, 132.7, 131.9, 131.1-130.9 (J = 9.6 Hz), 130.8, 130.5, 128.6, 127.5, 127.4, 119.9, 118.7, 117.4-117.0 (J = 22.4 Hz), 65.9, 65.8; MS (MALDI(Ag)) m/e 8586.1, 7954.3, 7322.0, 6689.8, 6057.1, 5423.9, 4788.8; Tg = 221°C (10°C/min, N$_2$), 5% weight loss = 497°C (10°C/min, N$_2$); n_{inh} = 0.08 dL/g (NMP, 0.5 g/dL, 25°C).

Fourth generation fluoro poly(aryl ether sulfide) 4GFS. The reaction was carried out using a procedure similar to that employed to synthesize **1GFS** using **$3GFSO_2$** (1.82 g, 0.20 mmol), sodium salt of **3.7** (1.95 g, 3.20 mmol), DMAc (64 mL), and temperatures of 75°C (reaction time = 3 h) and 128°C (reaction time = 1 h). The solid separated was dried overnight at 100°C under vacuum. After the workup 3.06 g of **4GFS** was obtained (isolated yield = 84%): ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.90-7.74 (m, calc'd 116, found 115), 7.44-7.30 (m, calc'd 120, found 124), 7.26-6.98 (m, calc'd 462, found 455), 6.98-6.82 (m, calc'd 60, found 64); ^{13}C NMR (50 MHz, $CDCl_3$) δ 144.7, 135.4-135.2 (d, J=8.1 cps), 132.9, 132.7, 131.9, 131.1, 130.8, 130.5, 128.6, 128.3, 128.1, 127.3, 126.7, 119.9, 119.5, 118.7, 118.4, 117.2-116.8 (d, J=21.7 cps), 65.8, 64.9; Tg = 186°C (10°C/min, N_2), 5% weight loss = 491°C (10°C/min, N_2); n_{inh} = 0.09 dL/g (NMP, 0.5 g/dL, 25°C).

Fourth generation fluoro poly(aryl ether sulfone) $4GFSO_2$. A procedure similar to that used to synthesize **$1GFSO_2$** was employed, using **4GFS** (2.19 g, 0.12 mmol), wet alumina (3.84 g), and Oxone (7.10 g, 11.52 mmol) in chloroform (40 mL). The solution was concentrated and coagulated in methanol (40 mL) to afford 2.19 g of **$4GFSO_2$** (isolated yield = 95%): ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.02-7.96 (m, calc'd 64, found 65), 7.92-7.80 (m, calc'd 180, found 171), 7.44-7.34 (m, calc'd 184, found 188), 7.30-7.02 (m, calc'd 270, found 275), 7.02-6.90 (m, calc'd 60, found 58); ^{13}C NMR (50 MHz, $CDCl_3$) δ 168.0-162.9 (d, J=253.5 cps), 161.4, 153.6, 151.4, 151.2, 144.5, 144.4, 141.5, 141.4, 140.2, 139.9, 137.4 (d), 135.2, 132.7, 131.9, 131.1-130.9 (d, J=9.5 cps), 130.9, 130.8, 130.5, 128.6, 127.5, 127.4, 119.9, 118.7, 117.4-117.0 (d, J=22.5 cps), 65.8; Tg = 228°C (10°C/min, N_2), 5% weight loss = 507°C (10°C/min, N_2); n_{inh} = 0.10 dL/g (NMP, 0.5 g/dL, 25°C).

Fifth generation fluoro poly(aryl ether sulfide) 5GFS. The reaction was carried out using a procedure similar to that employed to synthesize **1GFS** using **$4GFSO_2$** (1.54 g, 0.08 mmol), sodium salt of 3.7 (1.56 g, 2.56 mmol), DMAc (15 mL), and temperatures of 93°C (reaction time = 2 h) and 126°C (reaction time = 1 h). The separated solid (2.54 g) was purified by fractional precipitation and dried overnight at 100°C under vacuum. After the workup 2.10 g of **5GFS** was obtained (isolated yield after purification = 70%): ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.86-7.68 (m, calc'd 244, found 246), 7.40-7.24 (m, calc'd 248, found 262), 7.22-6.92 (m, calc'd 942, found 925), 6.90-6.74 (m, calc'd 124, found 125); ^{13}C NMR (50 MHz, $CDCl_3$) δ 144.7, 135.4-135.2 (d, J=7.8 cps), 133.0, 132.7, 131.9, 131.1, 130.8, 130.5, 128.6, 128.3, 128.1, 127.3, 126.7, 119.9, 119.5, 118.7, 118.4, 117.2-116.8 (d, J=21.6 cps), 65.8, 64.9; Tg = 194°C (10°C/min, N_2), 5% weight loss = 497°C (10°C/min, N_2); n_{inh} = 0.11 dL/g (NMP, 0.5 g/dL, 25°C).

3.9 References

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Chapter 4

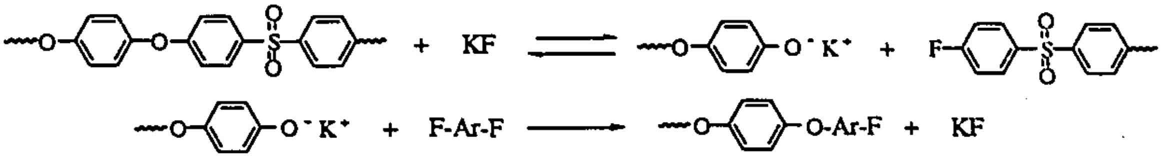
Synthesis of fluoro poly(aryl ether) dendrimers using an organic carbonate and mixtures of metal carbonates and metal hydroxides.

4.1 Introduction.

The phenolate is the active species during the displacement reaction with activated aryl halides. As we described in Chapter 2, the phenolate ions are formed either by reacting the phenol with, for example, alkali metal hydroxides and removing the water of reaction by azeotropic distillation or by adding alkali metal carbonates or bicarbonates to the condensation mixture. Sodium or potassium carbonate used commonly. Lithium carbonate is said to have a low reactivity, while rubidium carbonate and cesium carbonate, which are very effective, are less preferable for price reasons. Combinations of metal carbonates have also been used. High molecular weight polyethers have been obtained when a mixture of metal carbonates comprising a) lithium and/or alkaline earth metal carbonate and b) sodium, potassium, rubidium and/or cesium carbonate were used. Surprisingly the activity of the carbonates of group a) themselves are very low. (1)

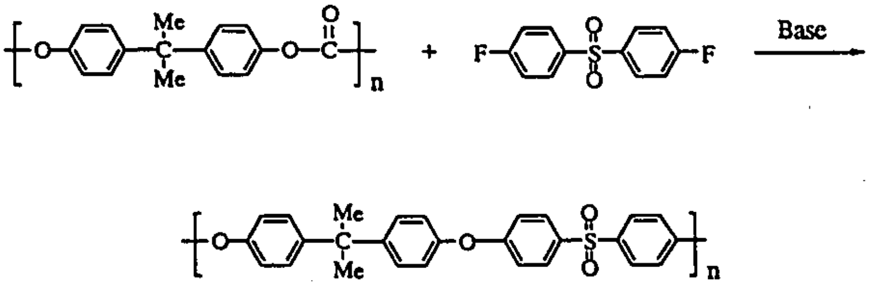
Attwood (2) showed that polysulfones are cleaved at the ether linkages by fluoride ions. The addition of potassium fluoride to a polysulfone resulted in the equilibration to a lower molecular weight. With excess 4,4'-difluorodiphenyl sulfone, F-Ar-F, also present, rapid depolymerization took place (Scheme 4.1). The phenolate end group reacts with F-Ar-F instead of reforming the polymer. Poly(aryl ether ketone)s also undergo molecular weight reduction in the presence of, for example, potassium fluoride and an end capping reagent. To control the molecular weight of the poly(aryl ether ketone)s an effective amount of an alkali, alkaline earth, or lanthanide metal salt is used in the polycondensation reaction. (3)

Scheme 4.1



Masked phenols, such as organic carbonates, can also be used in the synthesis of poly(aryl ether sulfone)s. This methodology relies on the fact that, at temperatures (155°C - 165°C) at which the polymerization reaction occurs, organic carbonates are rapidly cleaved by a metal carbonate to generate the phenolate ions *in situ.*

Scheme 4.2



The volatile by-product carbon dioxide is easily removed from the reaction system. The reaction time is shorter, since there is no water formed, hence the dehydration step is eliminated. In comparison, a period of at least 2 hours is needed to generate the phenolate ion by azeotroping off water when a phenol is used as the monomer. (4) In this manner polysulfone has been synthesized from bisphenol A polycarbonate by reaction with 4,4'-difluorodiphenyl sulfone in the presence of base (Scheme 4.2).

4.1.1 Strategy and goals

The objective of this section is the synthesis of fluoro poly(aryl ether sulfide) dendrimers from a masked phenol, using mixtures of metal carbonates and metal hydroxides.

We have seen that in the synthesis of fluoro poly(aryl ether) dendrimers there is incomplete reaction and the formation of high molecular weight by-products. The strategy that will be used to overcome these limitations includes:

a) Control of the concentration of fluoride in the reaction medium, by using alkaline earth cations such as calcium or magnesium ions. It is proposed that they would improve the reaction by removal of fluoride ions from the reaction mixture, since the corresponding metal fluorides are very insoluble.

b) Use a more active nucleophilic polycondensation agent such as Cs_2CO_3 along with metal hydroxides.

c) Employ a masked phenol to rapid generation of the phenolate ion *in situ*.

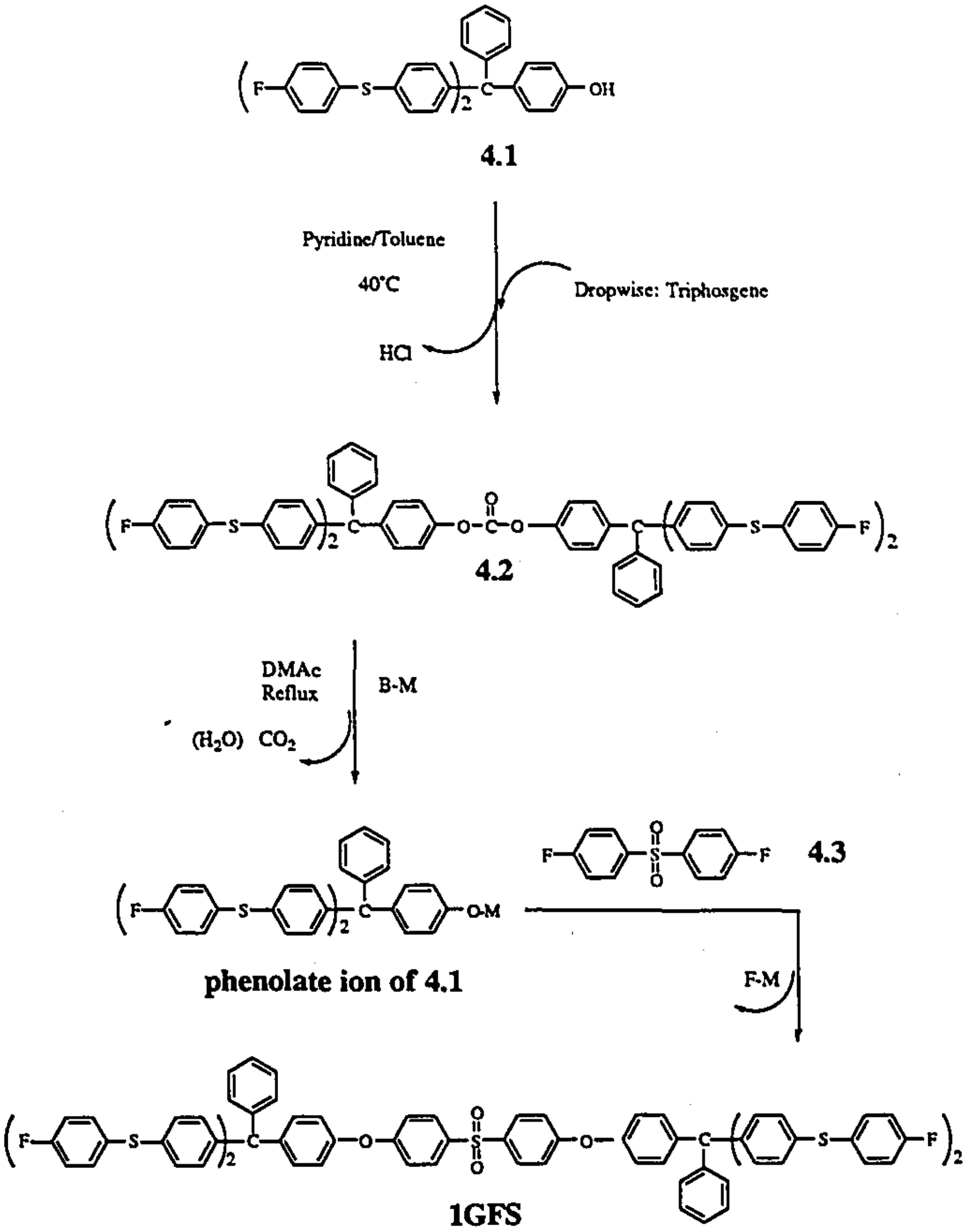
The synthesis of fluoro poly(aryl ether) dendrimers will be carried out using the *divergent initiator core method* based on the condensation/activation sequence that we described in Chapter 1, Part 1.6. The general strategy for the synthesis is shown in Scheme 1.4.

In our dendrimer synthesis, 4,4'-difluorodiphenyl sulfone **4.3** was chosen as the core precursor. The masked phenol is an organic carbonate **4.2,** which can be obtained in high yield from phenol **4.1.** The relatively high molecular weight of phenol **4.1** allows the formation, in a few generations, of high molecular weight dendrimer.

4.2 Preparation of the organic carbonate.

The organic carbonate **4.2,** was synthesized from phenol **4.1** (Chapter 3, Part 3.2) and triphosgene in pyridine/toluene at 40°C (Scheme 4.3). (5) The isolated yield after fractional precipitation of the crude product was 64 %.

Scheme 4.3


4.1
Pyridine/Toluene
40°C
Dropwise: Triphosgene
HCl
4.2
DMAc
Reflux
B-M
(H2O) CO2
4.3
phenolate ion of 4.1
F-M
1GFS

Nuclear magnetic resonance, NMR, supported the proposed structure for **4.2** and thin liquid chromatography, TLC, suggested that the fractionated product was a high purity sample. However, high pressure liquid chromatography, HPLC, and matrix-assisted laser desorption ionization time-of-flight mass spectrometry, MALDI-TOF-MS, indicated the presence of an impurity. Details of the characterization will be given later.

4.3 Preparation of fluoro poly(aryl ether) dendrimers.

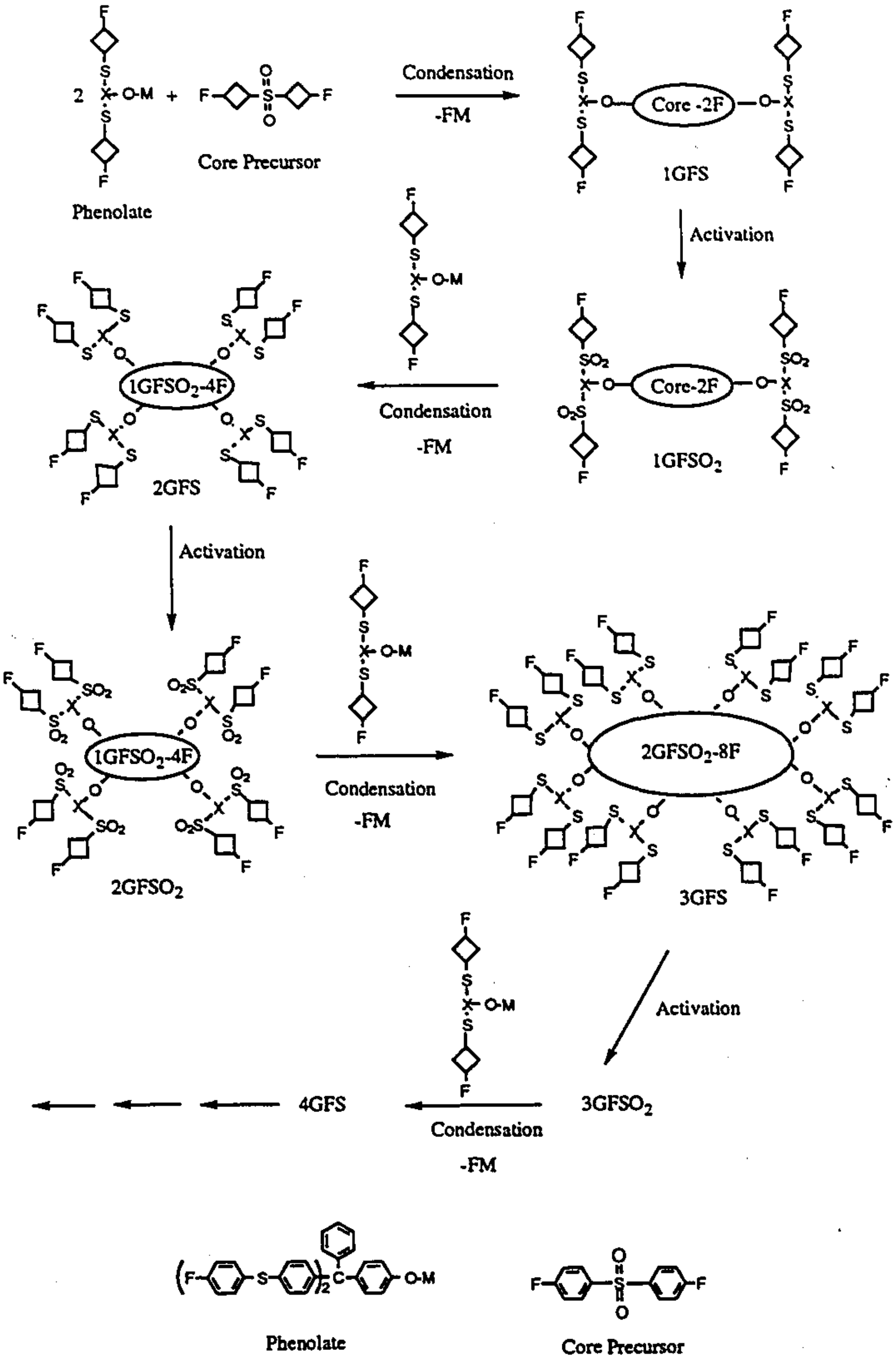
The synthetic strategy that we used led to two dendrimer families, both containing two different functionalities in the terminal units, aryl sulfide and aryl sulfone. Our nomenclature gives the dendrimer generation (1G, 2G, etc.) followed by letters denoting the nature of the terminal units (F = fluoro, S = sulfide, SO_2 = sulfone).

The synthesis of first generation fluoro poly(aryl ether sulfide) **1GFS**, as shown in Scheme 4.3, starts with the cleavage of the organic carbonate **4.2**, by a condensation agent, BM. Polycondensation of the phenolate ions with 4,4'-difluorodiphenyl sulfone **4.3**, in DMAc under reflux conditions gave **1GFS** as the main product.

The activation reactions, in which the sulfide atoms are oxidized to produce fluoro poly(aryl ether sulfone) dendrimers were carried out under similar conditions for all generations. The product of the condensation reaction is dissolved in chloroform and the solution added to a stirred mixture of Oxone, wet alumina and chloroform at room temperature. (6) Reflux condition and a reaction time of 24 hours are employed.

Higher generations of dendrimers (Scheme 4.4) were synthesized according to the procedure described previously. For example, in the synthesis of second generation fluoro poly(aryl ether sulfide) **2GFS,** the first step was the oxidation of the aryl sulfide terminal units of **1GFS** to obtain aryl sulfone groups followed by the cleavage of **4.2** by B-M and the subsequent polycondensation of the phenolate ion of **4.1** with the activated first generation fluoro poly(aryl ether sulfone) **1GFSO$_2$.**

Scheme 4.4


2
O-M
Phenolate
Core Precursor
Condensation
-FM
Core -2F
1GFS
Activation
Core-2F
1GFSO$_2$
1GFSO$_2$-4F
2GFS
2GFSO$_2$
2GFSO$_2$-8F
3GFS
3GFSO$_2$
4GFS
Phenolate
Core Precursor

The main product of the last reaction was the second generation fluoro poly(aryl ether sulfide) **2GFS**. The reactions were followed by HPLC and the products characterized by size exclusion chromatography, SEC, HPLC, MNR and MALDI. Details of the characterization will be given later. The isolated yields for the oxidation reactions were relatively high (86%-94%). Those of the condensation reactions, after purification of the samples, were only about 53%-72% (Table 4.6).

4.4 Effect of condensation agent on the dendrimer preparation.

Different mixtures of metal carbonates and metal hyroxides were used: a) calcium carbonate and alkali metal (Cs, K) carbonates, b) calcium hydroxide and potassium hydroxide, and c) alkaline earth metal (Ca, Mg) hydroxides and cesium carbonate. The effect of changing the following variables on the reaction was studied: a) molar ratio of alkaline earth metal (Mg^{++}, Ca^{++}) to alkali metal (K^+, Cs^+), and b) concentration of cesium or potassium in the reaction mixture. In this notation, $CO_3^=$, OC, OH^-, K, Cs, Mg, and Ca, represent the moles of metal carbonate, organic carbonate, metal hydroxide, and potassium, cesium, magnesium, and calcium ions, respectively. In all experiments the concentrations of **4.2** and core precursor, 4,4'-difluorodiphenyl sulfone **4.3**, were maintained constant. The effective concentration of **4.2** was controlled by the concentration of K_2CO_3 used, and it was always higher than the concentration of the core precursor, a necessary condition to reach a 100 % conversion.

4.4.1 Preparation of first generation fluoro poly(aryl ether sulfide) 1GFS.

4.4.1.1 Mixtures of $CaCO_3$ and Cs_2CO_3. The reactions were followed by size exclusion chromatography, SEC, and the reaction conditions are shown in Table 4.1. A relatively high concentration of calcium with respect to cesium (Ca/Cs = 2) was used in the synthesis of **1GFS-1**.

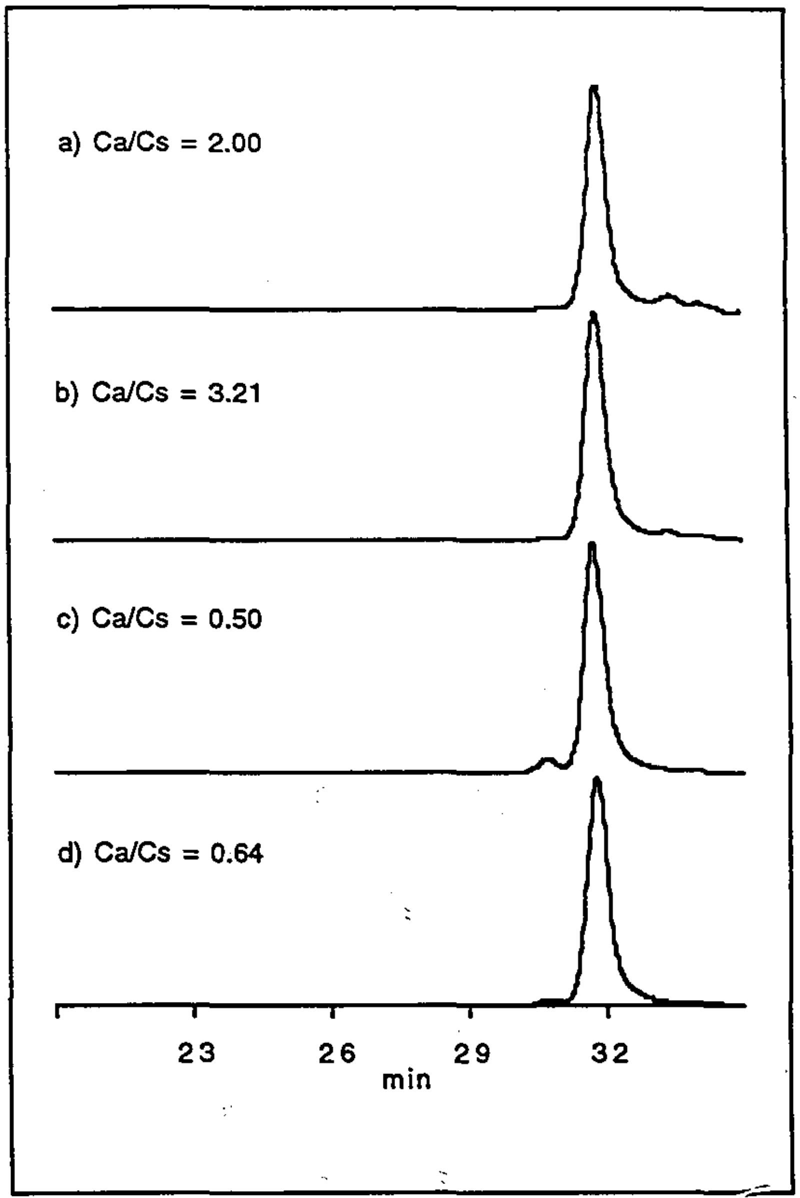


Figure 4.1. SEC chromatograms of reaction mixtures of first generation fluoro poly(aryl ether sulfide) **1GFS**: a) **1**, b) **2**, c) **3**, and d) **5**. Reaction conditions in **Table 4.1.**

Table 4.1. Conditions for the synthesis of first generation fluoro poly(aryl ether sulfide) 1GFS, using mixtures of $CaCO_3$ and Cs_2CO_3 a)

1GFS	1	2	3	4	5	6
t (h)	5.00	5.00	1.00	1.75	1.00	1.00
$CO_3^{=}$ / OC	0.86	1.27	1.11	0.89	1.02	1.27
Ca/Cs	2.00	3.21	0.50	0.50	0.64	0.93
Cs/OC	0.34	0.34	1.12	0.89	0.89	0.89

a) 0.885 mmol **4.2**, 0.680 mmol 4,4'-difluorodiphenyl sulfone, **4.3**, 15 mL DMAc, reflux, nitrogen. Isolated yield before purification = 99%.

The chromatogram of the reaction mixture, after a reaction time of 5 hours (Fig. 4.1a), showed some monosubstituted product, MS, remained in the reaction medium. MS is the intermediate product obtained when only one fluoride of the core precursor is displaced. A small amount of a lower retention time by-product was also detected.

To increase the rate of the reaction, the total concentration of metal carbonate (calcium carbonate plus cesium carbonate) was increased in the synthesis of **1GFS-2**, using a higher amount of $CaCO_3$ (Ca/Cs = 3.21) and keeping constant the concentration of cesium carbonate. The chromatogram of the reaction mixture (Fig. 4.1b) showed a small increase in the rate of the reaction but some monosubstituted product was still present. However, there was an improvement in the selectivity of the reaction since only traces of the lower retention time by-product were observed.

As we mentioned before, the synthesis of cascade polymers must ideally be quantitative, otherwise imperfections can be introduced in the polymer structure and side reactions can cause purification problems. Since we have a multistep reaction, the overall yield could also be very low. To overcome this limitation, in the synthesis of **1GFS-3** the concentration of the most active alkali metal carbonate was increased (Cs/OC = 1.12), keeping approximately constant the total concentration of metal carbonate. The chromatogram of the reaction mixture, after 1 hour of reaction (Fig. 4.1c), suggested that the reaction was complete. However, there was an increase in the intensity of the lower retention time peak, which was previously detected only in very small amount. Consequently, the reaction was faster but less selective.

In the synthesis of **1GFS-4** we tried to reach a compromise. We decreased the total concentration of metal carbonate by decreasing the concentration of the very active cesium carbonate (Cs/OC = 0.89) but we maintained the same ratio of Ca/Cs used in the synthesis of **1GFS-3**. After about 2 hours, the reaction seems to be complete. The concentration of lower retention time by-product was lower. Under these conditions a better compromise between reactivity and selectivity was reached.

It is apparent that to obtain a complete elimination of the by-product a relatively high concentration of calcium ions would be needed. However the reactions would then be very slow. The reactions must ideally be quantitative in as short time as possible to avoid equilibration and side reactions.

In the synthesis of **1GFS-5** we maintained the same concentration of Cs_2CO_3 used in the synthesis of **1GFS-4** but we increased the concentration of metal carbonate using a higher amount of calcium carbonate (Ca/Cs = 0.64). The chromatogram of the reaction mixture, after a reaction time of 1 hour (Fig. 4.1d), showed a slight improvement in the selectivity of the reaction and suggests that the reaction was complete in only 1 hour. The short reaction time is desirable.

In the synthesis of **1GFS-6** a further increase in the concentration of calcium carbonate showed no apparent improvement in the selectivity or reactivity of the reaction.

4.4.1.2 Mixture of $CaCO_3$ and K_2CO_3. The reaction was carried out without (synthesis of **1GFS-7**) and with (synthesis of **1GFS-8**) calcium carbonate present (Table 4.2). The chromatogram of the reaction mixture, after 2 hours of reaction and without $CaCO_3$ present (Fig. 4.2a), showed a high concentration of the by-product and also that the reaction was not totally complete.

Addition of calcium carbonate causes an improvement in selectivity of the reaction but a subsequent decrease in reactivity since elimination of the monosubstituted product took more than 5 hours (Fig. 4.2b)

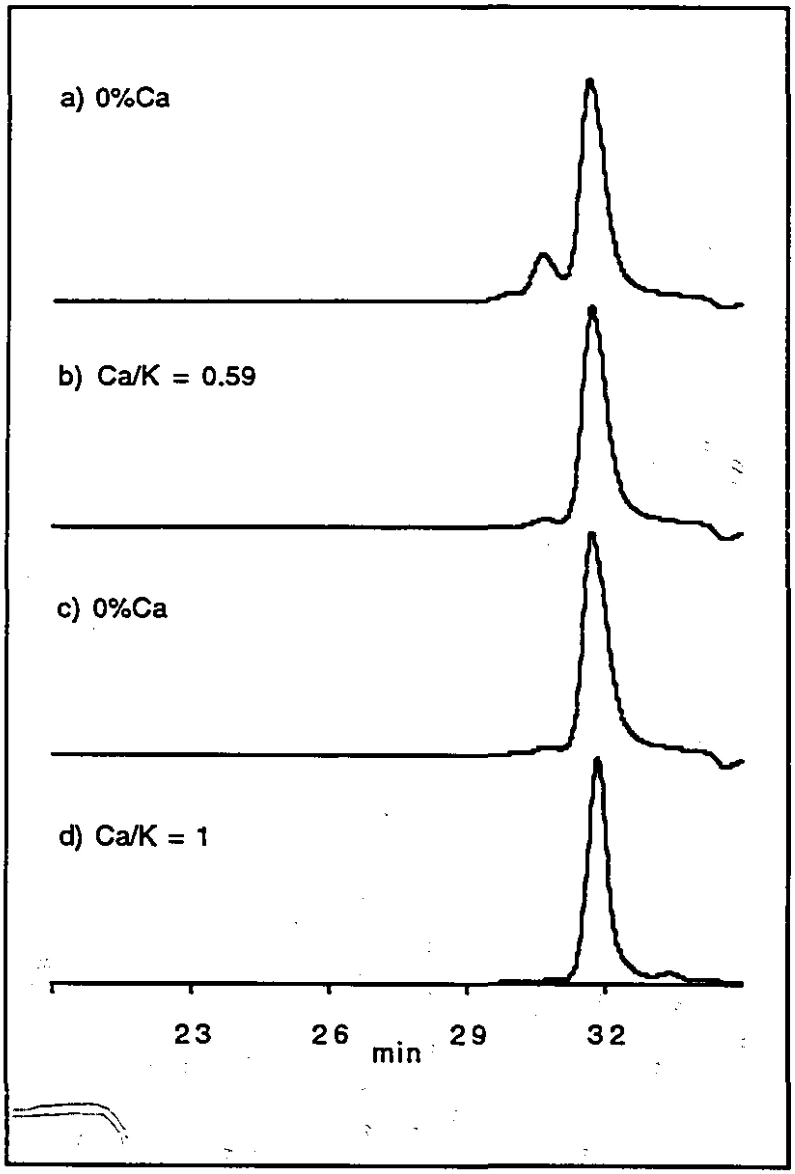


Figure 4.2. SEC chromatograms of reaction mixtures of first generation fluoro poly(aryl ether sulfide) **1GFS**: a) **7**, b) **8**, c) **9**, and d) **10**. Reaction conditions in **Table 4.2.**

Table 4.2. Conditions for the synthesis of first generation fluoro poly(aryl ether sulfide) 1GFS, using mixtures of $CaCO_3$:K_2CO_3, and KOH:$Ca(OH)_2$ a)

1GFS	7	8	9	10
t (h)	2	5	2	4
$CO_3^{=}$ / OC	0.93	1.21	-	-
Ca/K	0.00	0.59	0.00	1.00
K/OC	1.86	1.11	1.86	0.58
OH^- /OC	-	-	1.86	1.74

a) 0.885 mmol **4.2**, 0.680 mmol 4,4'-difluorodiphenyl sulfone **4.3**, 15 mL DMAc, reflux, nitrogen. Isolated yield before purification = 99%.

4.4.1.3 Mixture of $Ca(OH)_2$ and KOH. A similar procedure to that used with the mixture of $CaCO_3$ and K_2CO_3 was employed. The conditions of the reactions are given in Table 4.2.

The reactions were performed without (synthesis of **1GFS-9**) and with (synthesis of **1GFS-10**) calcium hydroxide present. The results were similar to those found previously; however, the concentration of the by-product was lower. Addition of $Ca(OH)_2$ increased selectivity of the reaction (Fig. 4.2d) but reactivity decreased since after 4 hours some monosubstituted product was still present.

This data indicated that the combination of calcium carbonate and cesium carbonate used in the synthesis of **1GFS-5** was the most reactive, with a comparatively short 1 hour reaction time and selectivity comparable to those of $CaCO_3$:K_2CO_3 and $Ca(OH)_2$:KOH mixtures.

4.4.2 Preparation of second generation fluoro poly(aryl ether sulfide) 2GFS.

A procedure similar to that used previously in the synthesis of **1GFS** was employed, but the reactions were followed by high pressure liquid chromatography, HPLC.

We have found that HPLC is a better technique for analysis of **2GFS**. It allows us to monitor the presence of reaction intermediates not detectable by SEC.

Three different mixtures were used in the first series of experiments (Table 4.3), starting with the cesium and calcium carbonate combination found to be best for the synthesis of **1GFS**. The HPLC chromatogram of the reaction mixture, after 1 hour of reaction (Fig. 4.3a), showed an intense peak corresponding to **2GFS-1** with overlay peaks at lower retention times. A higher retention time peak, was also detected in low concentration.

Since the lower retention time peak can be explained in part by an incomplete reaction we decided to use $Mg(OH)_2$:Cs_2CO_3 instead of $CaCO_3$:Cs_2CO_3, keeping the concentrations of cesium and alkaline earth metals the same (synthesis of **2GFS-2**). The mixture may be more reactive due to the presence of hydroxide. The chromatogram of the reaction mixture, after a reaction time of 1 hour (Fig. 4.3b), showed a lower concentration of lower retention time species.

Table 4.3. Conditions for the synthesis of second generation fluoro poly(aryl ether sulfide) 2GFS, using mixtures of $CaCO_3$:Cs_2CO_3 and $Mg(OH)_2$:Cs_2CO_3 [a)]

2GFS	1	2	3
t (h)	1	1	1
$CO_3^{=}$ / OC	1.02	0.45	0.31
OH^- / OC	-	1.14	1.42
Ca/Cs	0.64	-	-
Cs/OC	0.89	0.89	0.61
Mg/Cs	-	0.64	1.17

a) 0.59 mmol **4.2**, 0.25 mmol **1GFSO2**, 10 mL DMAc, reflux, nitrogen. Isolated yield before purification = 98%

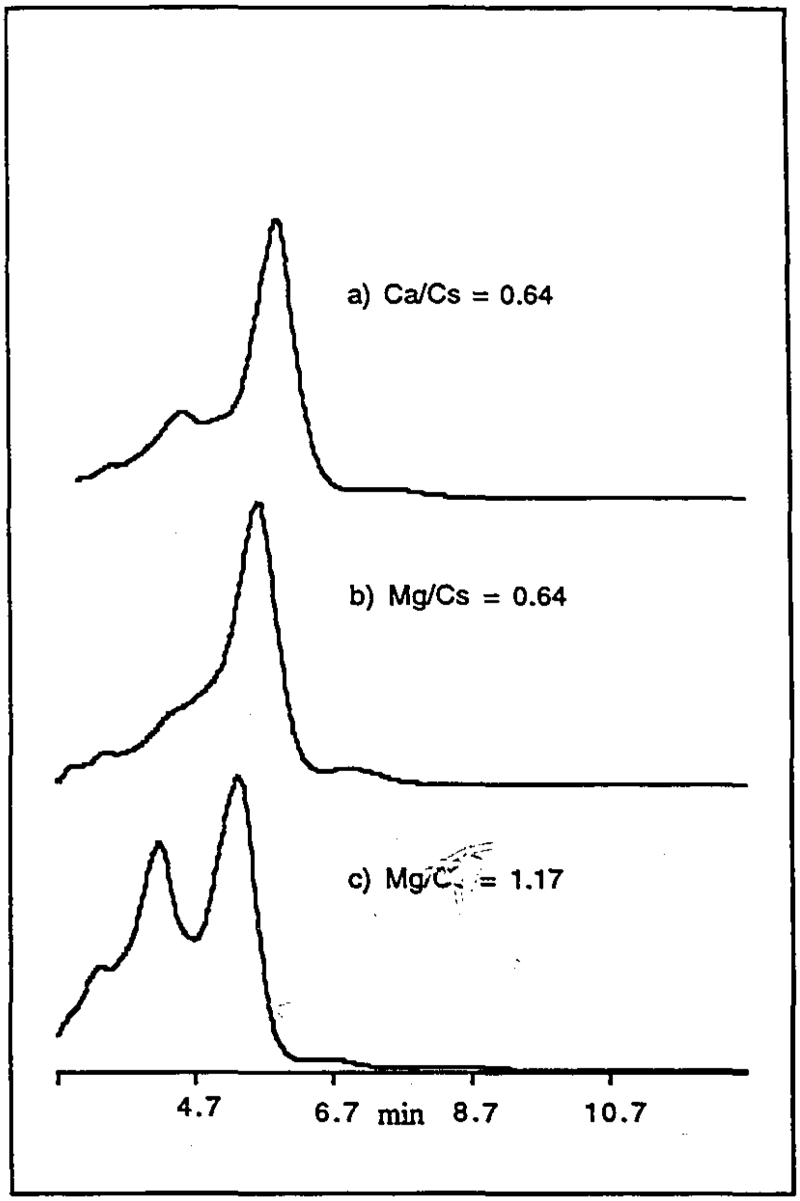


Figure 4.3. HPLC chromatograms of reaction mixtures of second generation fluoro poly(aryl ether sulfide) **2GFS**: a) **1**, b) **2**, and c) **3**. Reaction conditions in **Table 4.3.** HPLC solvent: THF/H_2O (80/20).

In the synthesis of **2GFS-3** we decreased the concentration of Cs_2CO_3. The chromatogram of the reaction mixture (Fig. 4.3c), shows that after 5 hours the reaction was incomplete.

This result and the previous data found for **1GFS** indicate the use of less than 0.9 atom of Cs per molecule of the organic carbonate **4.2** decreases the rate of the reaction considerable which is not desirable. The best compromise between reactivity and selectivity of the system was reached when the $Mg(OH)_2$:Cs_2CO_3 mixture was used under the conditions given in the synthesis of **2GFS-2.** The dehydration step was not required.

In the second series of experiments, we decided to study the effect of calcium hydroxide in our system (Table 4.4). The $Ca(OH)_2$:Cs_2CO_3 mixture may be more active than the $Mg(OH)_2$:Cs_2CO_3 mixture. There are two factors that can contribute to this. The larger size of a calcium ion makes the calcium phenolate more reactive than the magnesium phenolate, combined with the probable higher solubility of $Ca(OH)_2$ in the reaction mixture compared with $Mg(OH)_2$.

Table 4.4. Conditions for the synthesis of second generation fluoro poly(aryl ether sulfide) 2GFS, using mixtures of $M(OH)_2$:Cs_2CO_3, M = Mg, Ca $^{a)}$

2GFS	4	5	6
t (h)	3.0	2.5	2.0
$CO_3^{=}$ / OC	0.45	0.45	0.45
OH^- / OC	1.14	1.14	1.78
Ca/Cs	0.64	-	-
Cs/OC	0.89	0.89	0.89
Mg/Cs	-	0.64	1.00

a) 0.59 mmol **4.2**, 0.25 mmol **1GFSO$_2$**, 10 mL DMAc. Reflux conditions and argon. Isolated yield before purification = 99%

Argon, as inert atmosphere instead of nitrogen, was used in these experiments to eliminate any possibility of oxidation reactions involving the phenoxide ions. The reaction times were longer to improve the reaction conversion.

The chromatograms for dendrimers **2GFS-4** (Fig. 4.4a) and **2GFS-5** (Fig. 4.4b) are similar to those found previously for **2GFS-1** and **2GFS-2**. However, a relatively lower amount of higher retention time species was detected in the dendrimer **2GFS-5**. In the synthesis of dendrimer **2GFS-6** a higher concentration of magnesium hydroxide was used to increase the rate of the reaction. There was no significant decrease in the lower retention time products and the concentration of by-products was higher (Fig. 4.4c). According to these results, magnesium ions resulted in more efficient elimination of fluorides since the $Mg(OH)_2$:Cs_2CO_3 mixture, under the conditions given in the synthesis of **2GFS-5**, gave the most selective reaction. The HPLC chromatogram of purified dendrimer **2GFS-5** is given in Figure 4.6b. Complete purification by fractional precipitation was not possible.

4.4.3 Preparation of third generation fluoro poly(aryl ether sulfide) 3GFS.

Three different mixtures were used (Table 4.5), starting again with the cesium carbonate and calcium carbonate combination found to be the best for the synthesis of **1GFS**. The reaction was carried out under nitrogen. The HPLC chromatogram of the reaction mixture after 5 hours indicates that the reaction is incomplete.

To increase the rate of the reaction we decided to use $Mg(OH)_2$:Cs_2CO_3 in the synthesis of **3GFS-2** keeping constant the concentrations of cesium and alkaline earth metals. The reaction was relatively faster since no changes were detected after 2.5 hours (Fig. 4.5a). However, this analysis also suggests that the sample contains more than one compound. In the synthesis of **3GFS-3** we increased the concentration of Cs_2CO_3. The reaction was faster but less selective since new peaks appeared in the HPLC analysis (Fig. 4.5b).

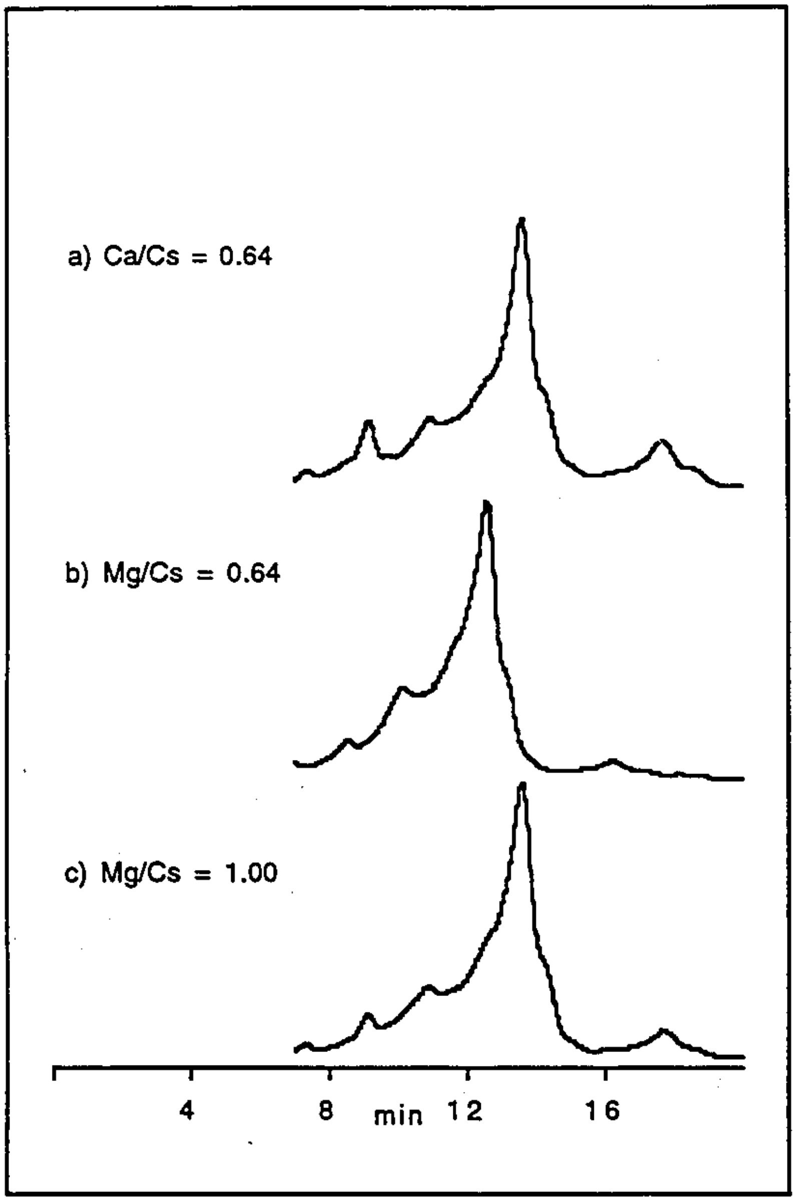


Figure 4.4. HPLC chromatograms of second generation poly(aryl ether sulfide) **2GFS**: a) **4**, b) **5**, and c) **6**. Crude products. Reaction conditions in **Table 4.4.** HPLC solvent: THF/H_2O (78/22).

Table 4.5. Conditions for the synthesis of third generation fluoro poly(aryl ether sulfide) 3GFS, using mixtures of $CaCO_3$:Cs_2CO_3 and $Mg(OH)_2$:Cs_2CO_3 a)

3GFS	1	2	3
t (h)	21.5	2.5	2.0
$CO_3^{=}$ / OC	1.02	0.45	0.71
OH^- / OC	-	1.14	0.61
Ca/Cs	0.64	-	-
Cs/OC	0.89	0.89	1.42
Mg/Cs	-	0.64	0.21

a) 0.590 mmol **4.2**, 0.125 mmol **2GFSO$_2$**, 10 mL DMAc, reflux, and nitrogen. Isolated yield before purification = 99%.

The conditions used in the synthesis of **3GFS-2**, which seem to be the most convenient, were repeated for the synthesis of **3GFS-4**, except for the fact that the reaction was carried out under argon The use of argon instead of nitrogen caused some improvement in the reaction. Unfortunately, it was not possible to purify **3GFS** by fractional precipitation.

4.4.4 Preparation of fourth generation fluoro poly(aryl ether sulfide) 4GFS.

The synthesis of **4GFS** was carried out with the cesium carbonate and magnesium hydroxide combination found to be the best for the synthesis of **3GFS**: argon, reaction time 3 hours, $Mg(OH)_2$:Cs_2CO_3 mixture, Cs/OC = 0.89, and Mg/Cs = 0.64. The HPLC chromatograms of the reaction mixture showed a broad signal formed by overlay peaks. A good separation was not possible due to the high molecular weight of the sample.

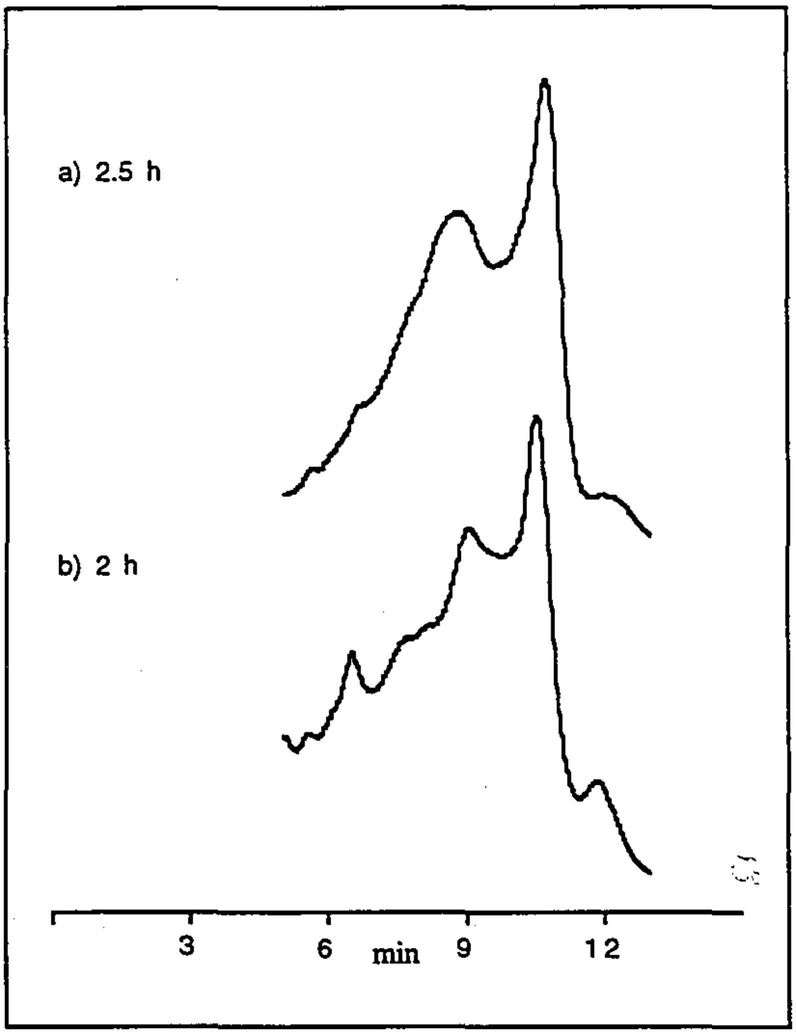


Figure 4.5. HPLC chromatograms of the reaction mixtures of third generation fluoro poly(aryl ether sulfide) **3GFS**: a) 2 and b) 3. Reaction conditions in **Table 4.5.** HPLC solvent: THF/H_2O (82/18).

4.5 Molecular characteristics.

Molecular characterization of the dendrimers was carried out using those samples obtained under the best conditions as described in the previous discussion.

4.5.1 Chromatography.

HPLC chromatograms of the purified dendrimers are shown in Figures 4.6. As we indicated before, HPLC was a better technique to monitor the degree of completion of the reaction for second and third generation fluoro poly(aryl ether sulfide)s and consequently to characterize the products. The first generation dendrimer **1GFS**, gave a HPLC chromatogram (Fig. 4.6a) that corresponded basically to a single compound. A low intensity-higher retention time by-product was also detected. The second generation, **2GFS** (Fig. 4.6b), and third generation **3GFS** (Fig. 4.6c) dendrimers gave HPLC chromatograms that showed a main signal overlapped with other lower intensity-lower retention time peaks. Very similar molecular structures make separation of the components very difficult.

The SEC characterization data are given in Table 4.6 and Figures 4.7. Molecular weights, Mw's, increase with the generation number from 738 to 15275, but polydispersities, PD's, remain close to 1, as is expected for almost monodisperse materials.

The difference between the weight average molecular weights and the formula weights (FW's) can be explained if we assume that dendrimer structures are more compact than those of the polystyrene standards used in the calibration curve.

The first, second, and third generation fluoro poly(aryl ether sulfide)s give SEC results similar to those found for the fluoro poly(aryl ether sulfone)s dendrimers of comparable molecular weight. It suggests that no significant side reactions occurs during the oxidation of the sulfide atoms.

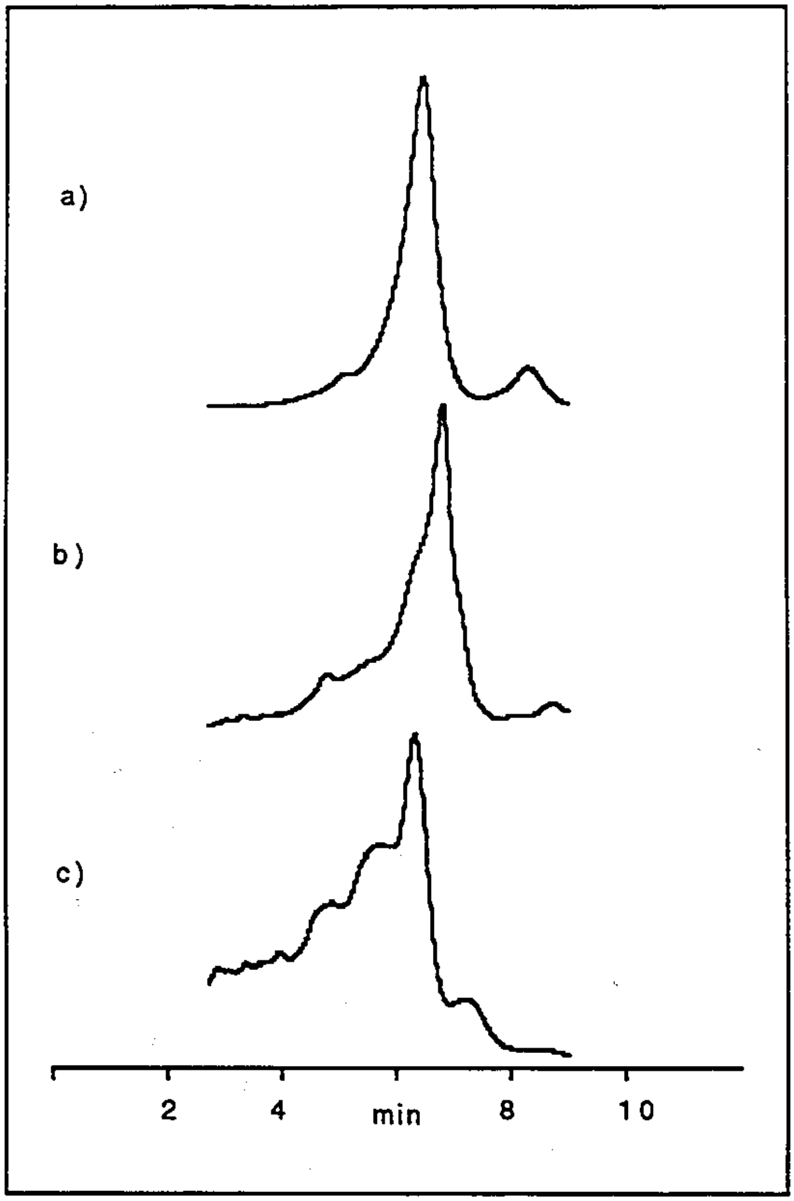


Figure 4.6. HPLC chromatograms of purified fluoro poly(aryl ether sulfide) dendrimers: a) **1GFS** (THF:H_2O, 70:30), b) **2GFS** (THF:H_2O, 78:22), and c) **3GFS** (THF:H_2O, 82:18).

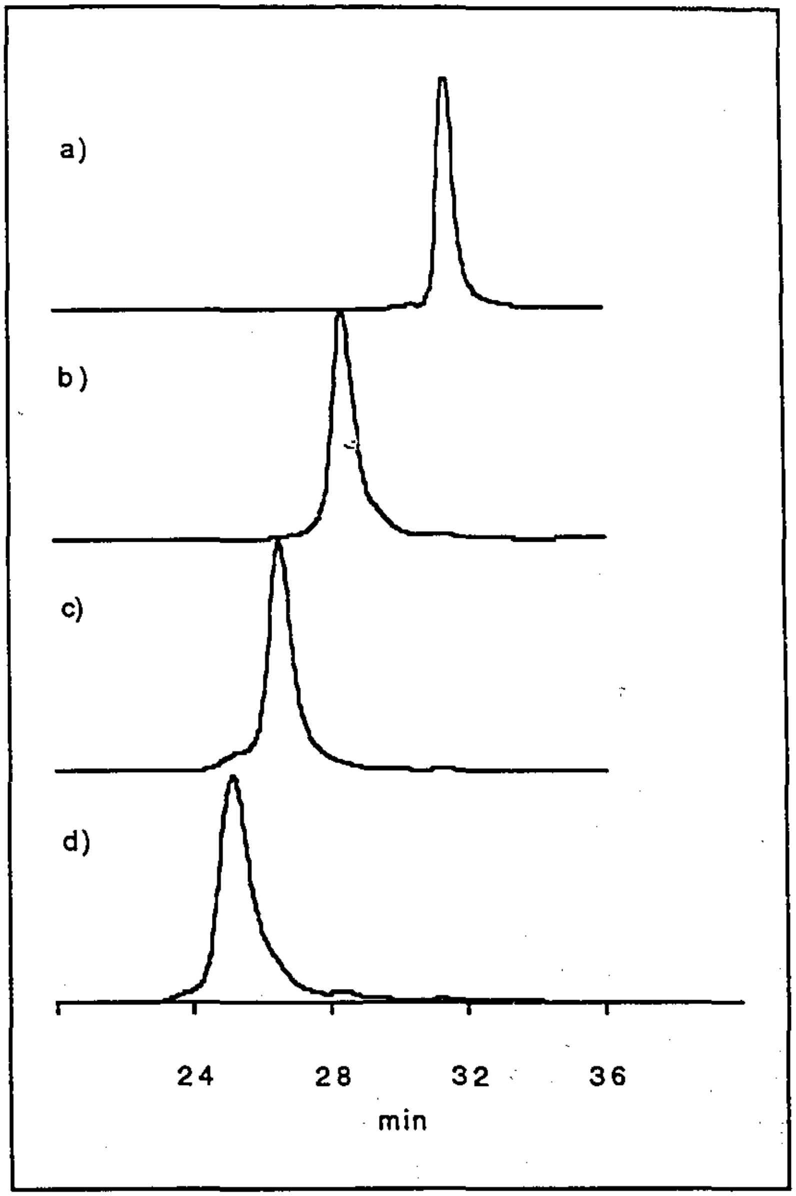


Figure 4.7. SEC chromatograms of fluoro poly(aryl ether sulfide) dendrimers: a) **1GFS**, b) **2GFS**, c) **3GFS**, and d) **4GFS**. Analysis conditions in **Table 4.6.**

Table 4.6. Some characteristics and properties of fluoro poly(aryl ether) dendrimers

Dendrimer	1GFS	1GFSO$_2$	2GFS	2GFSO$_2$	3GFS	3GFSO$_2$	4GFS	4GFSO$_2$
FW (g/mol)	1392	1520	3795	4051	8601	9113	18212	19239
Mw (g/mol) a)	738	956	3345	3605	8606	9008	15275	13078
PD a)	1.05	1.07	1.16	1.15	1.13	1.15	1.30	1.32
n_{inh} (dL/g) b)	0.05	0.05	0.07	0.07	0.09	0.09	0.10	0.10
Tg (°C) c)	92	170	154	215	185	230	183	231
Td (°C) d)	490	506	496	504	485	500	487	495
Yield (%)	53	94	56	94	66	86	72	87

a) SEC, based on polystyrene standards, chloroform, 1mL/min, RT, UV-detector. b) NMP, 0.5 g/dL, 25°C. c) 10°C/min, nitrogen. d) 5% weight loss, 10°C/min, nitrogen.

The activation reaction for the fourth generation poly(aryl ether sulfide) however had to be repeated to get reasonable SEC data for the oxidation product **4GFSO$_2$**. The high molecular weight of this dendrimer can be the cause of the incomplete reaction.

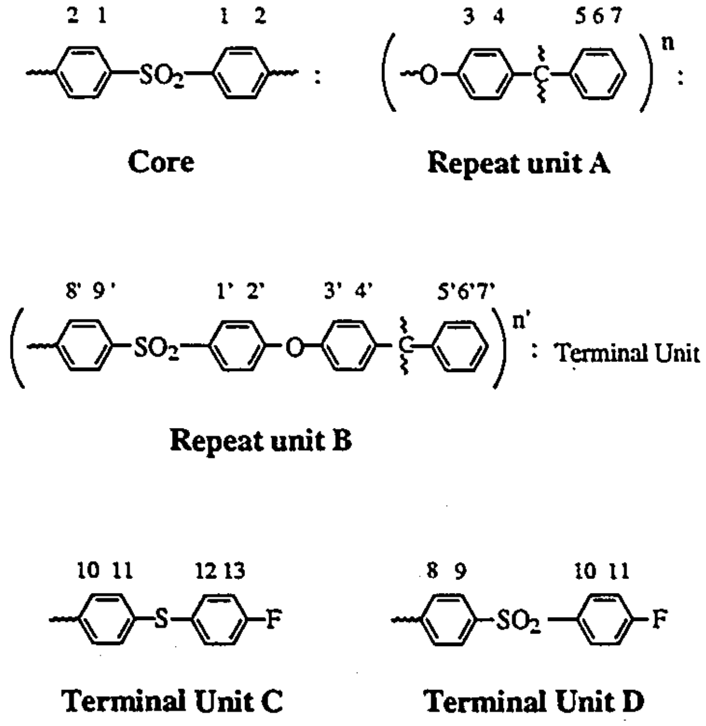
All SEC chromatograms showed a main signal and a low intensity-lower retention time peak. Complete purification by fractional precipitation was not possible.

4.5.2 Nuclear magnetic resonance.

The schematic representation of the different structural blocks that form fluoro poly(aryl ether) dendrimers is shown in Scheme 4.5. Each of these blocks can be identified in the ideal structures of **1GFSO$_2$**, **2GFSO$_2$**, and **3GFS** given in Scheme 3.2 For more details see Chapter 1: Part 1.1 and Chapter 2: Part 2.5.2.

The ^{1}H NMR spectra (G = 1, 2, and 3: 200 MHz; G = 4: 500 MHz) of these polymers are given in Figures 4.8 - 4.11. Cosy experiments were carried out for the identification of the protons. The differences between the ^{1}H NMR spectra of poly(aryl ether sulfide) dendrimers, and those of poly(aryl ether sulfone) dendrimers, confirm that structural changes occurred during the oxidation or displacement reactions.

Scheme 4.5



Before the oxidation reaction protons H_{12} at the terminal units C absorbs at $\delta = 7.40$ ppm - 7.52 ppm (Fig. 4.8a); after the oxidation reaction these protons, which are now close to the new sulfone group (H_{10}), show resonances at $\delta = 8.00$ ppm - 8.12 ppm (Fig. 4.8b). The similarities observed in the spectra of fluoro poly(aryl ether) dendrimers are a consequence of common protons present in their structures (Scheme 4.5).

The ^{1}NMR data suggest that the reactions were complete since no resonances were detected in the spectra of fluoro poly(aryl ether sulfide) dendrimers around 8.05 ppm. Protons H_{10} in the starting materials (terminal unit D) absorb at about 8.10 ppm - 7.96 ppm.

In general, the peaks become broader as the generation number increases. Similar protons in different layers could absorb slightly different amounts of energy that can affect the width of the peaks. Theoretical (Cal) and experimental values (Fnd) of the integrals (Table 4.7) are in good agreement (differences < 5 %).

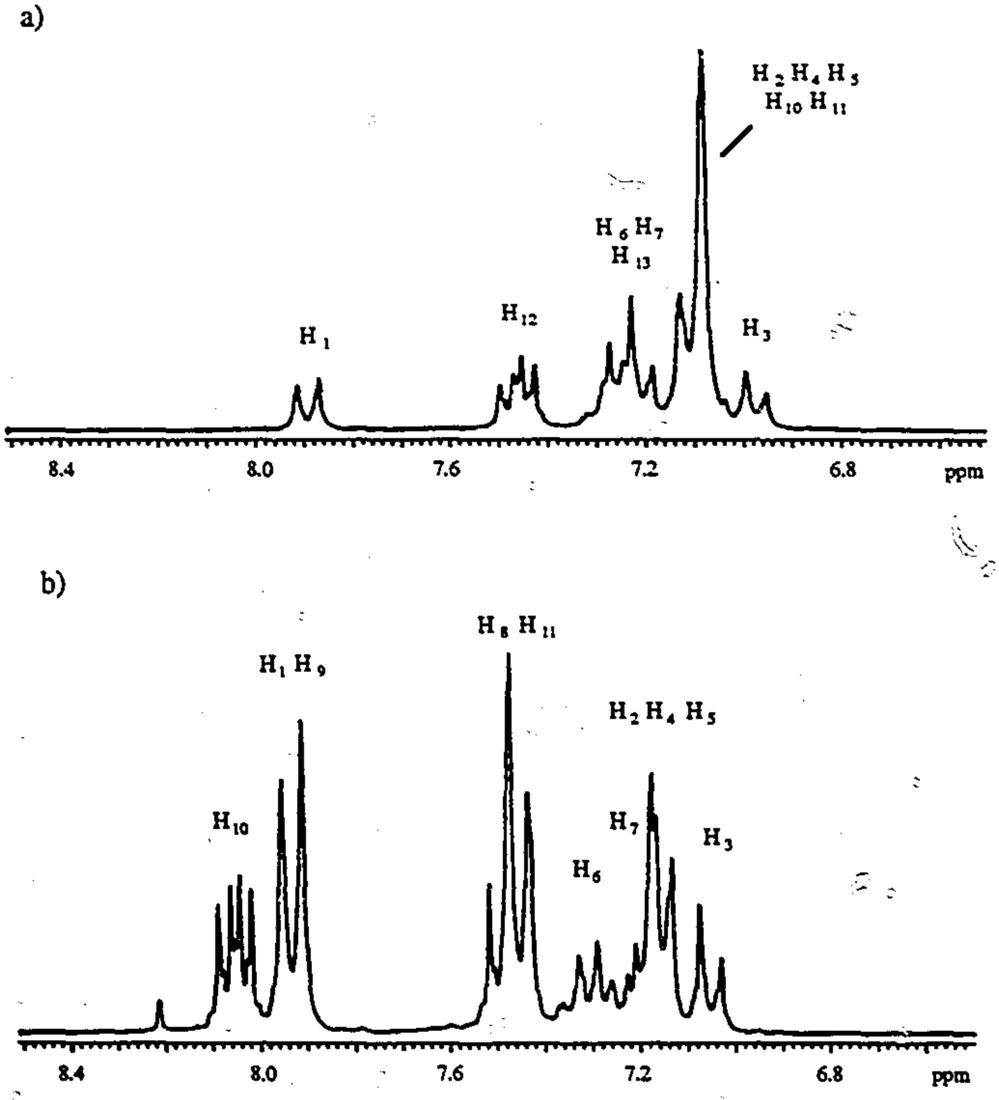


Figure 4.8. ^{1}H NMR spectra of first generation fluoro poly(aryl ether)s: a) **1GFS** and b) **1GFSO$_2$**.

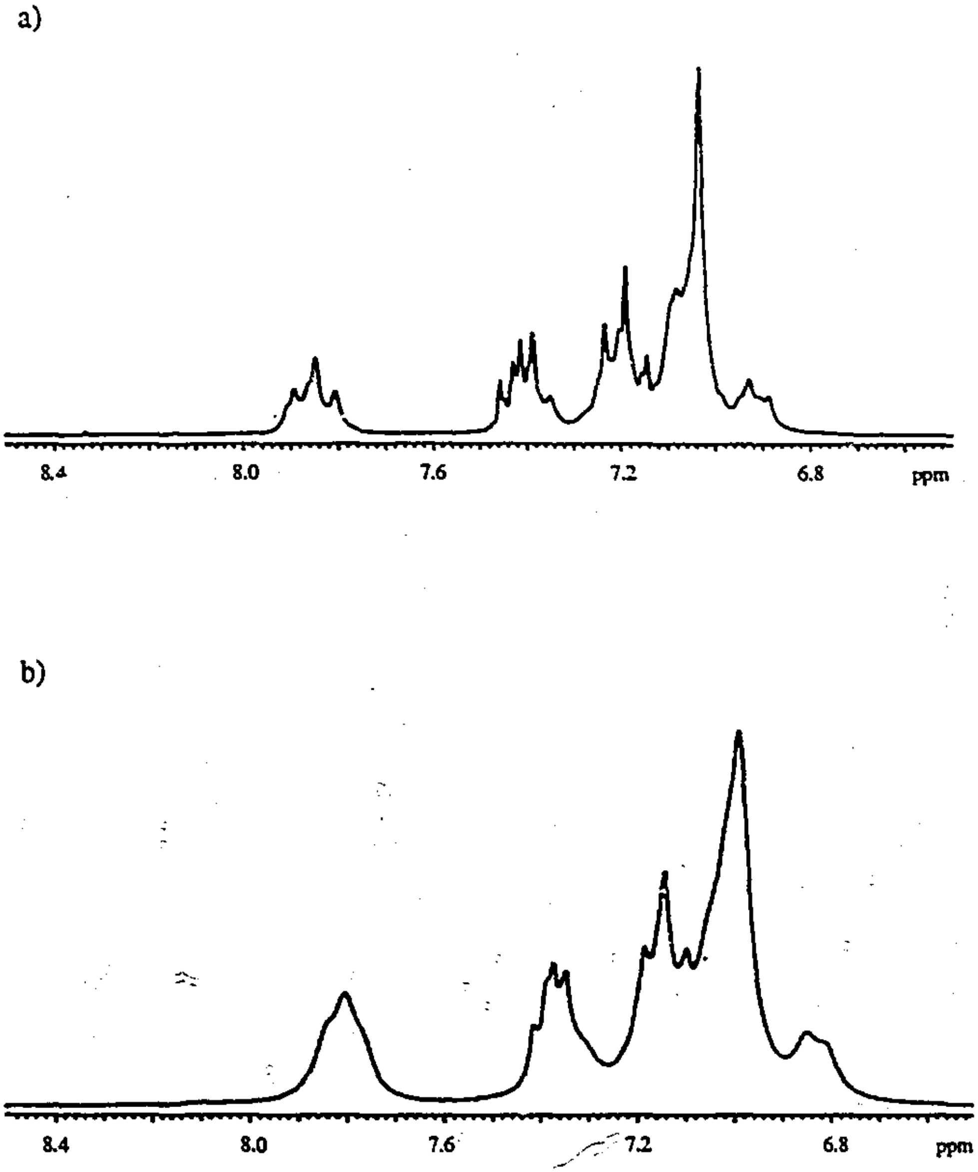


Figure 4.9. ^{1}H NMR spectra of fluoro poly(aryl ether sulfide) dendrimers: a) **2GFS** and b) **3GFS**. Peak identification in **Figure 3.4.**

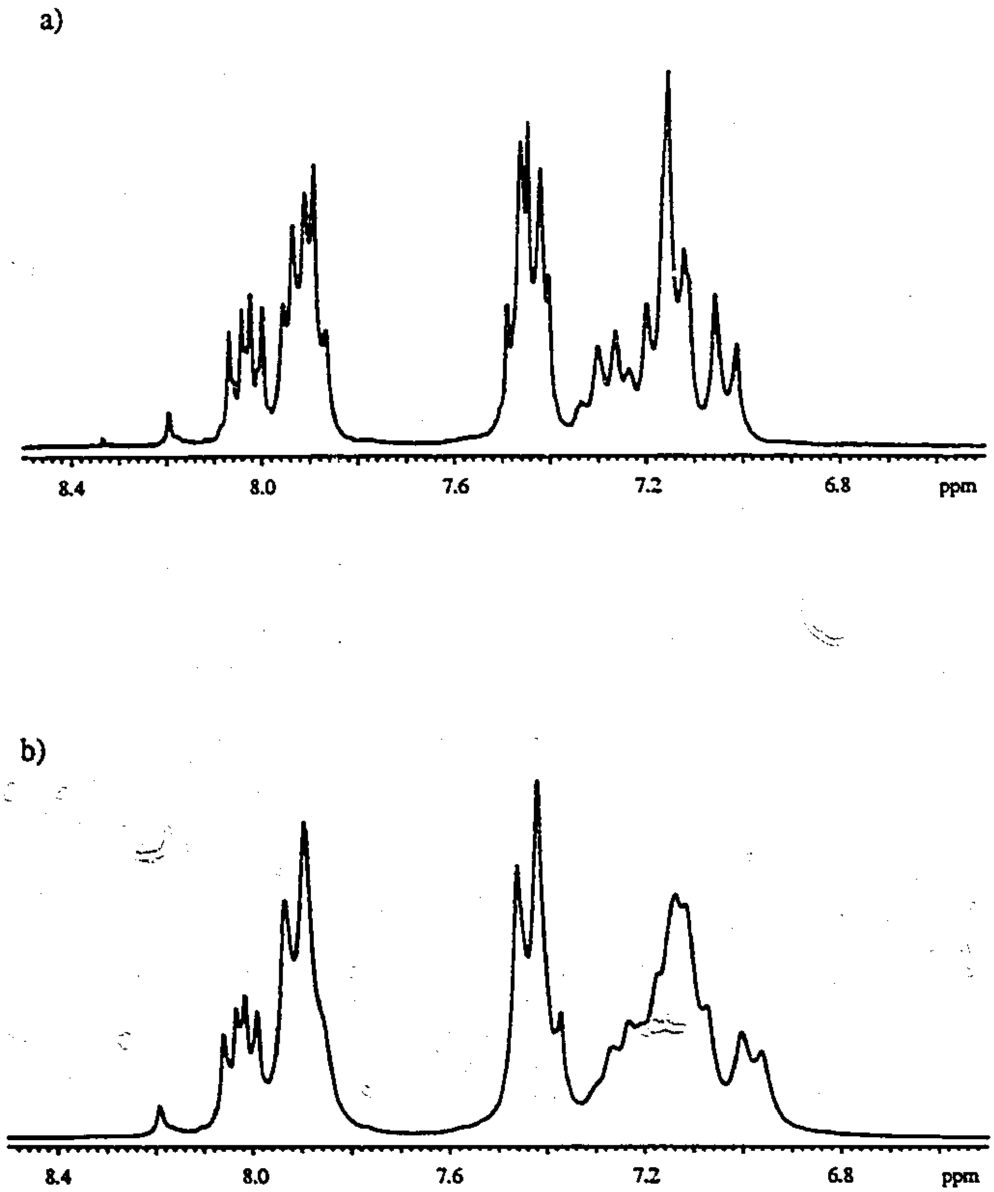
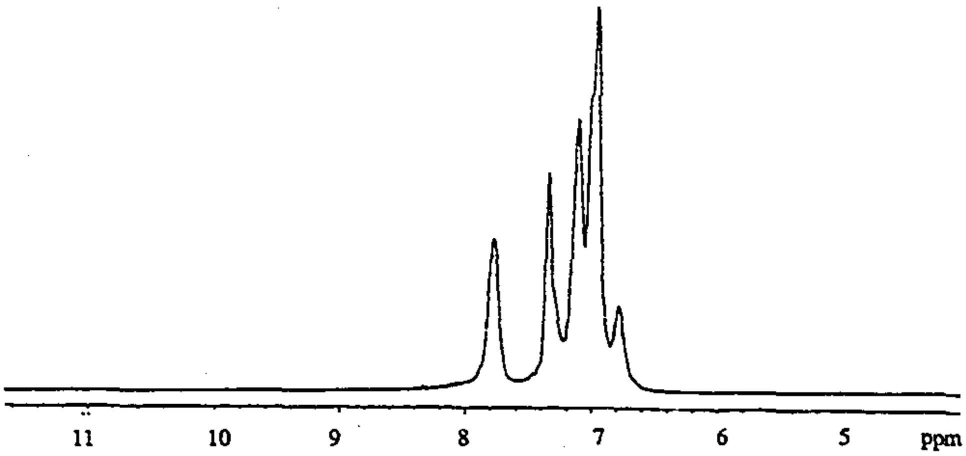


Figure 4.10. ^1H NMR spectra of fluoro poly(aryl ether sulfone) dendrimers: a) **2GFSO$_2$** and b) **3GFSO$_2$**. Peak identification in **Figure 3.6**

a)



b)

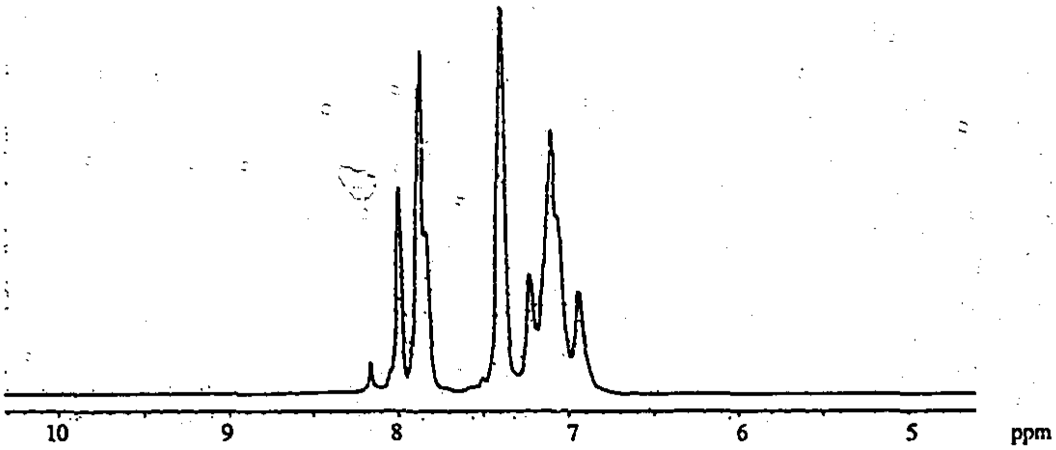


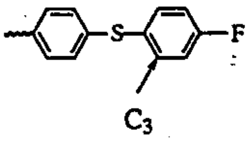
Figure 4.11. ^{1}H NMR spectra of fourth generation fluoro poly(aryl ether)s: a) **4GFS** and b) **4GFSO$_2$**. Peak identification in **Figures 3.4 and 3.6.**

Table 4.7. ^{1}H NMR integrations of fluoro poly(aryl ether) dendrimers

Dendrimer	Resonances				n' a)	Z b)
	$H_1+H_{1'}+H_9+H_{9'}$		$H_1+H_{1'}+H_9+H_{9'}+H_{10}$			
	Cal	Fnd	Cal	Fnd		
1GFS	4	4	-		0	4
1GFSO$_2$	-		20	20	0	4
2GFS	20	20	-		1	8
2GFSO$_2$	-		52	51	1	8
3GFS	52	52	-		2	16
3GFSO$_2$	-		116	114	2	16
4GFS	116	121	-		3	32
4GFSO$_2$	-		244	247	3	32

a) n' = number of layer with internal unit B; b) Z = number of terminal units.

The ^{13}C NMR spectra (50 MHz) are given in Figures 4.12 - 4.14 . The results were similar to those found previously. For example, before the oxidation reaction atoms C_3 at the **terminal unit C** absorb at $\delta = 135.4\text{-}135.2$ ppm (J = 8.1 Hz), (Fig. 4.12a). After the oxidation reaction these carbons, now close to the new sulfone group in the **terminal unit D,** show resonances at $\delta = 131.1\text{-}130.9$ ppm (J = 9.6 Hz) (Fig. 4.12b).



Since the number of peaks in each spectrum depends on the fact that similar carbons in different layers can absorb slight different amounts of energy, it is possible to see more than one peak for similar C's.

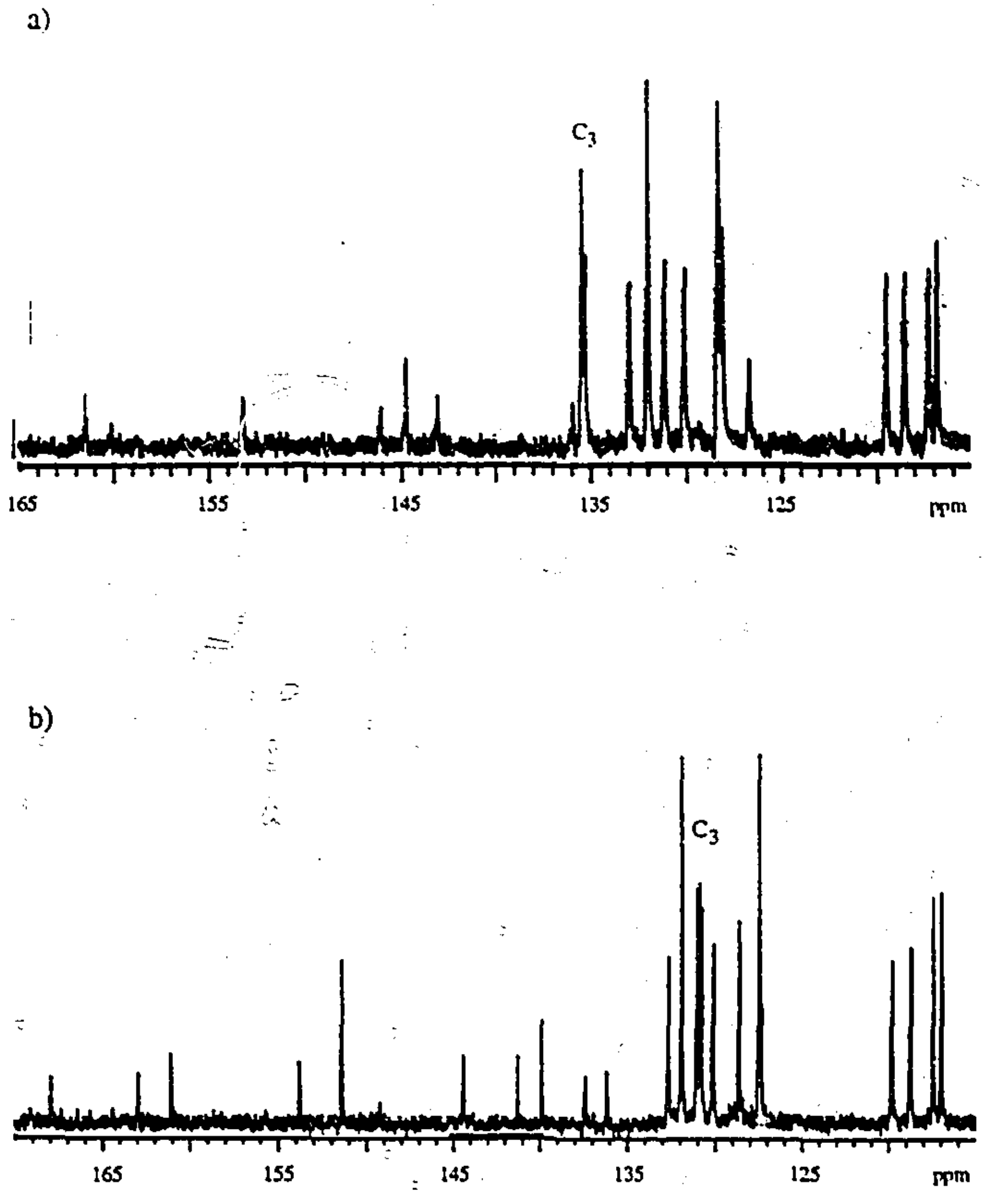


Figure 4.12. ^{13}C NMR spectra of first generation fluoro poly(aryl ether)s: a) **1GFS** and b) **$1GFSO_2$**.

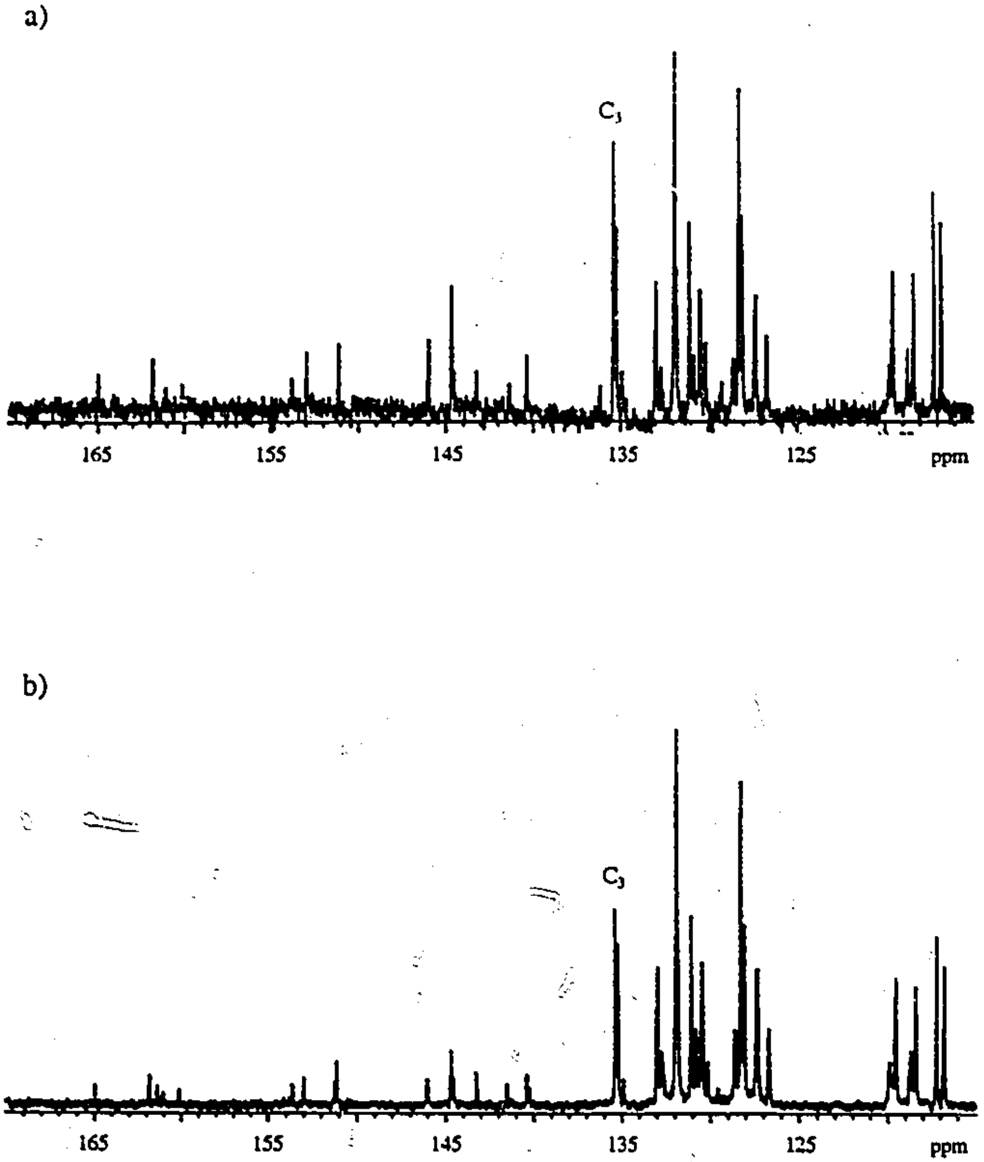


Figure 4.13. ^{13}C NMR spectra of fluoro poly(aryl ether sulfide) dendrimers: a) **2GFS** and b) **3GFS**.

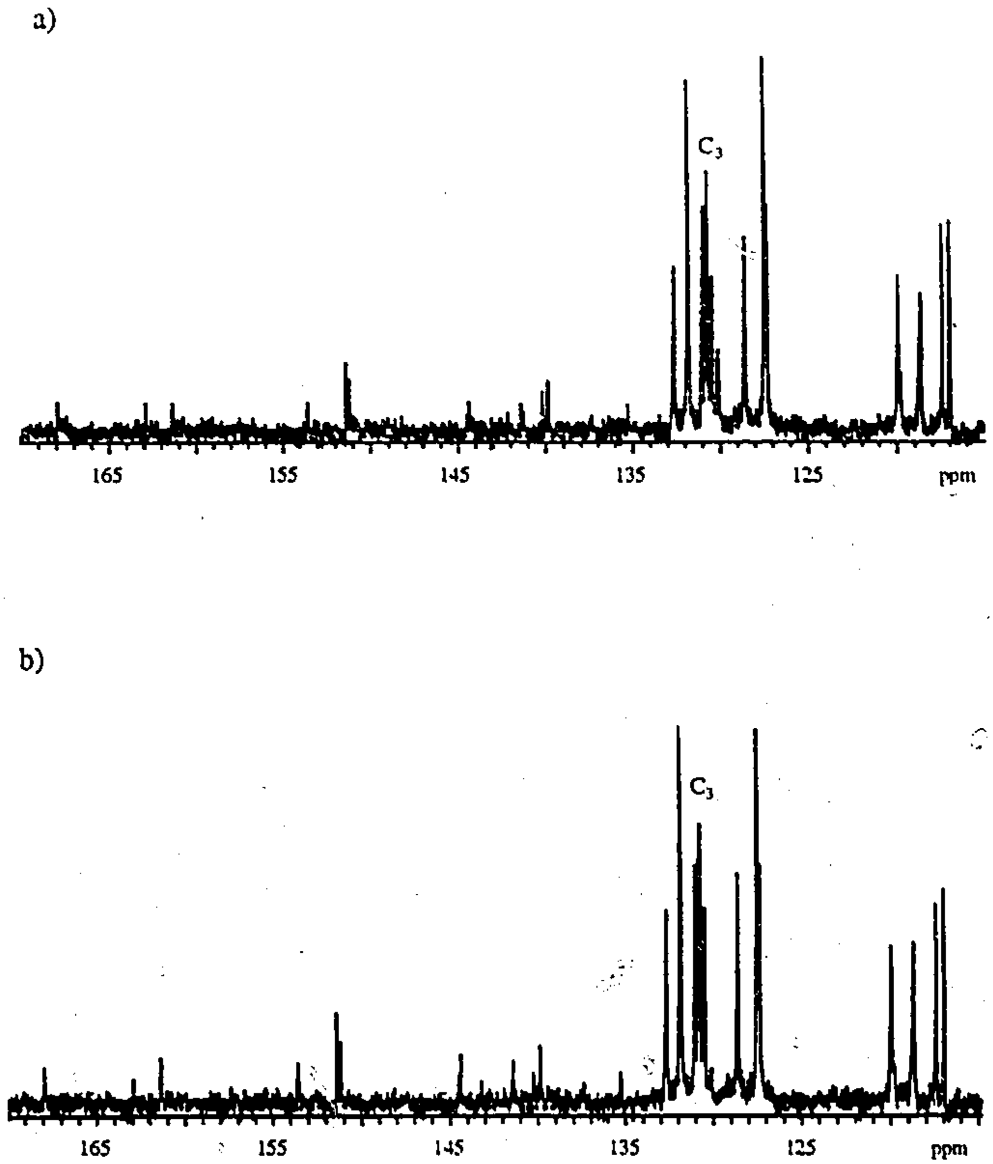


Figure 4.14. ^{13}C NMR spectra of fluoro poly(aryl ether sulfone) dendrimers: a) **2GFSO$_2$** and b) **3GFSO$_2$**.

4.5.3 MALDI mass spectrometry.

Matrix-assisted laser desorption ionization time-of-flight mass spectroscopy (MALDI-TOF-MS), a technique which is becoming of increasing importance for synthetic polymer chemistry, (7) was used for the mass determination of the poly(aryl ether) dendrimers.

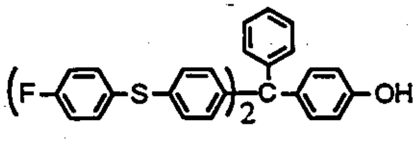
The analyses were carried out on a Kratos Compact MALDI III instrument in the reflectron mode using dithranol as the matrix. Silver trifluoroacetate was added to stabilize the system. The Figures 4.15 - 4.18 show the quality of the spectra achieved with excellent signal-to-noise ratio.

The molecular ion masses, MI's, of the poly(aryl ether sulfide) and poly(aryl ether sulfone) dendrimers (Table 4.8) were calculated using the following general equations, respectively:

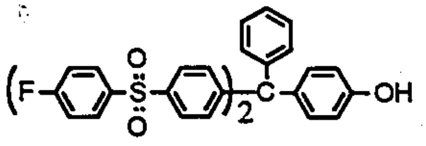
$$\mathrm{MI\,(iGFS)} = A + (B - D)\,(2^{i} - 2) + (C - D)\,2^{i}$$

$$\mathrm{MI\,(iGFSO_2)} = A + (B - D)\,(2^{i+1} - 2)$$

Where i represents the generation number (i = 1, 2, 3), A the molecular mass of the core precursor (254.25 Da) **4.3**, B the molecular mass of phenol **4.4** (652.73 Da), C the molecular mass of phenol **4.1** (588.73 Da), and D the molecular mass of HF (20.01Da):



4.1



4.4

HF is the small molecule eliminated during the condensation reaction. For example, the molecular mass of **2GFS** was obtained using i = 2, A = 254.25 Da, B = 652.73 Da, C = 588.73 Da, and D = 20.01 Da.

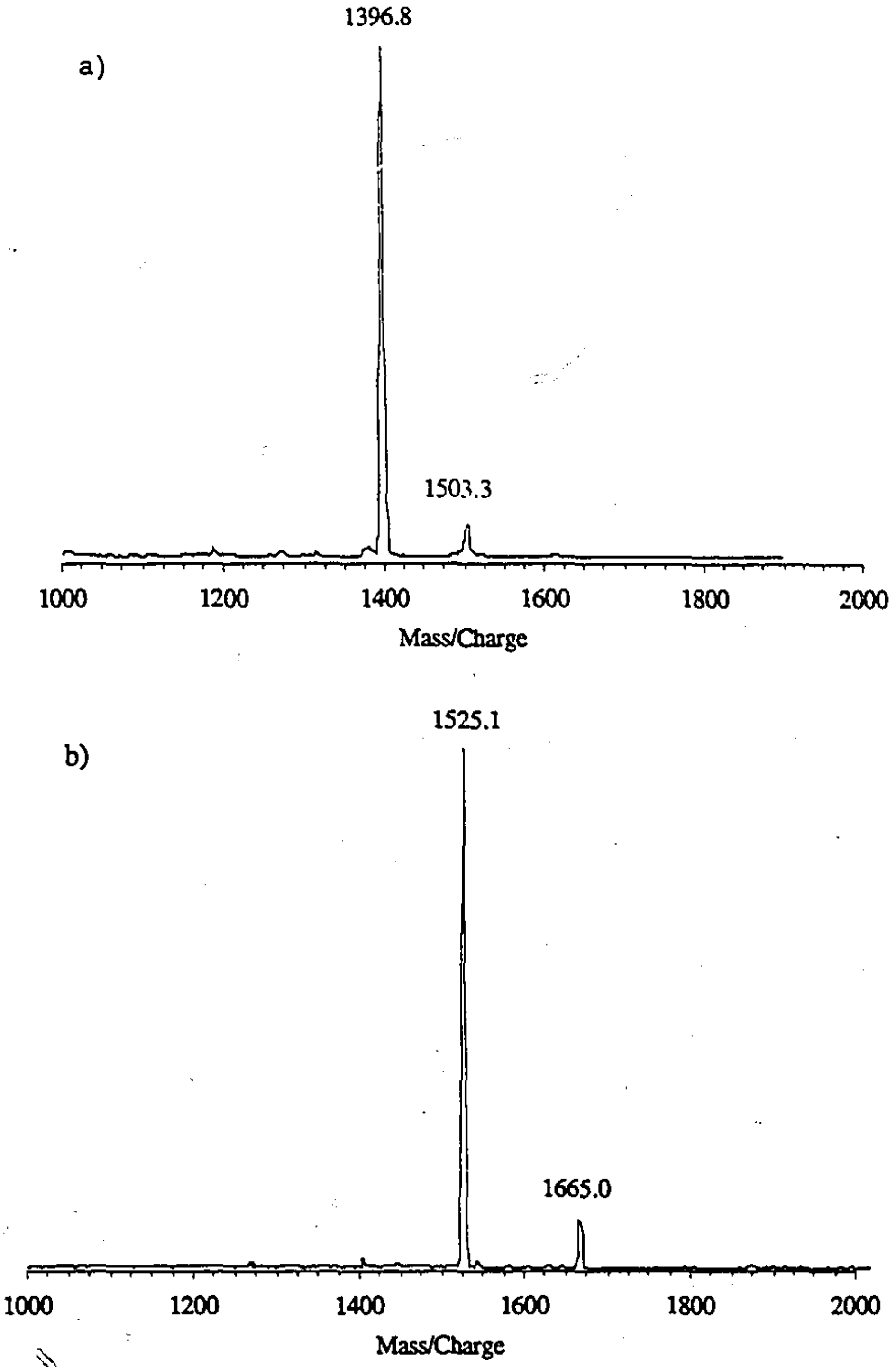


Figure 4.15. MALDI mass spectra of first generation fluoro poly(aryl ether)s: a) **1GFS** and b) **$1GFSO_2$**. Analysis conditions in **Table 4.8.**

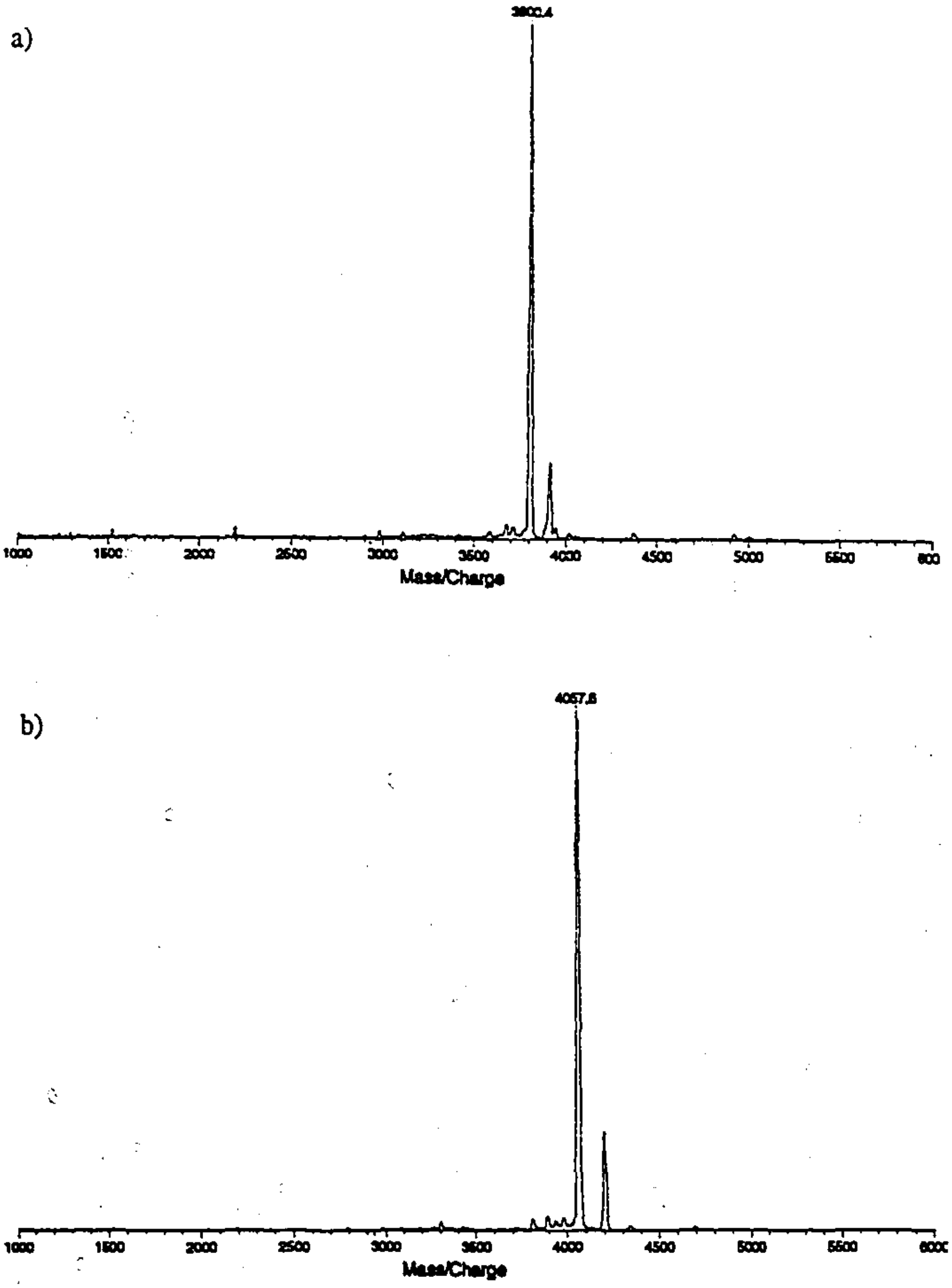


Figure 4.16. MALDI mass spectra of second generation fluoro poly(aryl ether sulfone)s: a) **2GFS** and b) **2GFSO$_2$**. Analysis conditions in **Table 4.8.**

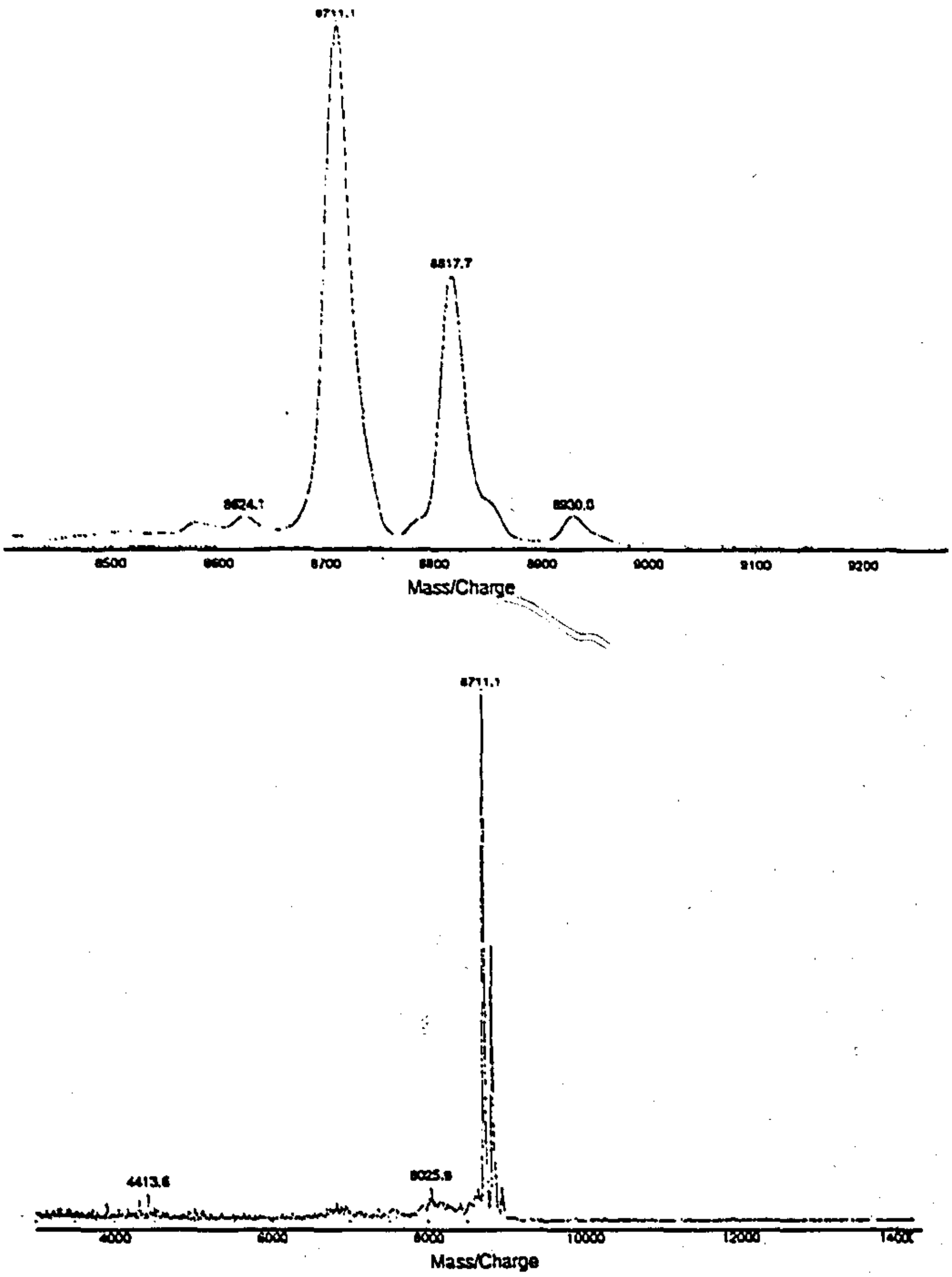


Figure 4.17. MALDI mass spectra of third generation fluoro poly (aryl ether sulfide) **3GFS**. Analysis conditions in **Table 4.8.**

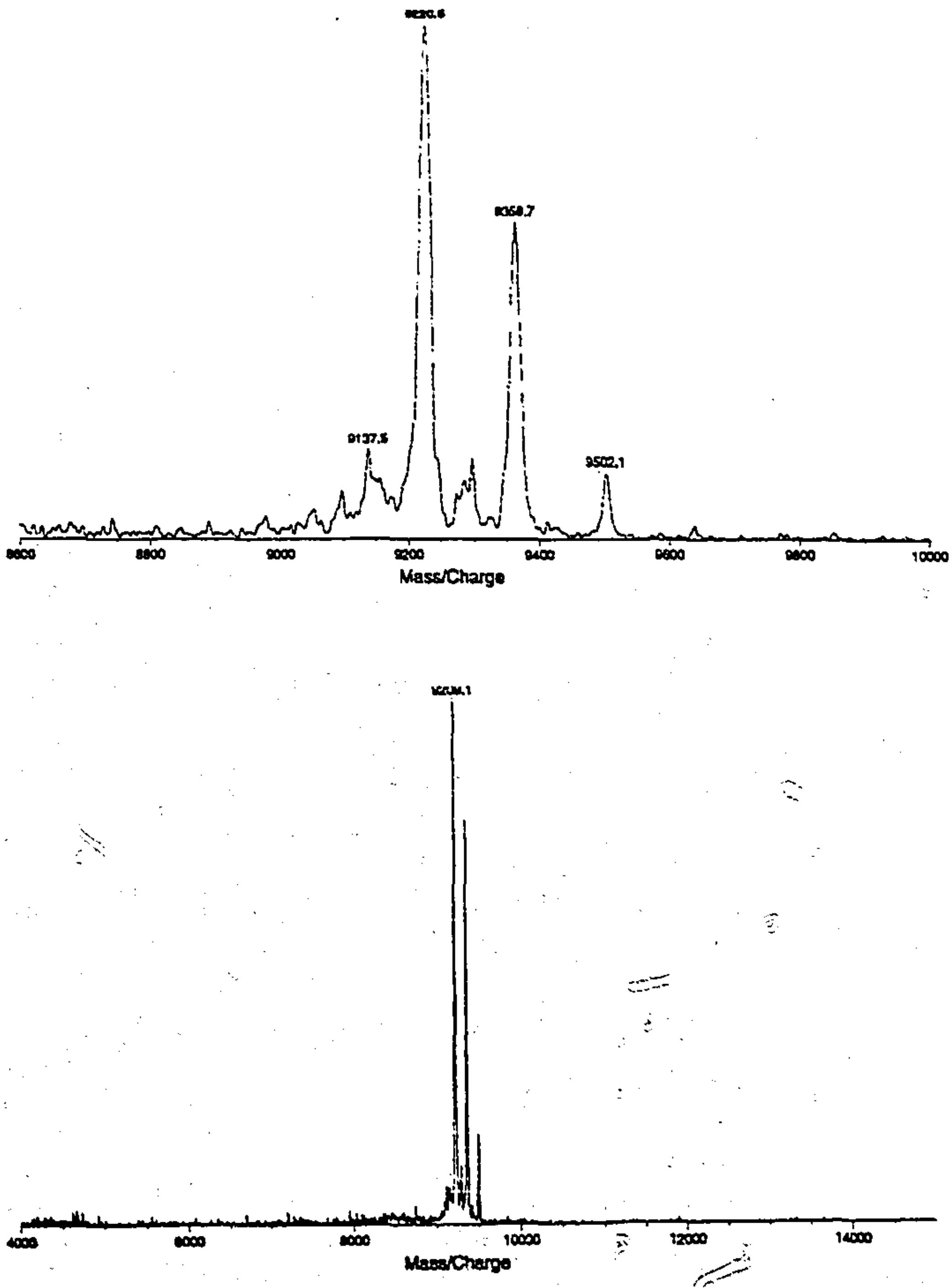


Figure 4.18. MALDI mass spectra of third generation fluoro poly(aryl ether sufone) **3GFSO$_2$**. Analysis conditions in **Table 4.8.**

Table 4.8. MALDI mass spectrometric analyses of fluoro poly(aryl ether) dendrimers [a)]

Dendrimer	MI (Da) [b)]	Mass/Charge		
		Peak 1	Peak 2	Peak 3
1GFS	1391.7	1396.8	1503.3	-
IGFSO$_2$	1519.7	1525.1	1665.0	-
2GFS	3794.6	3800.4	3908.9	-
2GFSO$_2$	4050.6	4057.6	4199.7	-
3GFS	8600.4	8711.1	8817.7	8930.0
3GFSO$_2$	9112.3	9220.5	9359.7	9502.1

a) First and second generation: dithranol:sample:CF_3CO_2Ag = 40:4:1; third generation: dithranol:sample:CF_3CO_2Ag = 40:4:2. b) MI = molecular ion mass.

Two signals were detected in the mass spectra for the first (Fig. 4.15) and second generation (Fig. 4.16) and three signals in the mass spectra of the third generation (Figs 4.17 and 4.18) products. The most intense signal in each spectrum (peak 1) corresponds to the molecular ion. The difference between the calculated and found MI values for the first and second generations are between 5.0 and 7.0 Da and for the third generation from 108 to 111 Da. These deviations can be explain assuming that a lithium cation (7 Da) or a silver cation (108 Da) is complexed with the sample. Lithium and silver cations can come from the metallic sample holder and from silver trifluoroacetate, respectively. Silver cations were not detected in the first and second generation, probably due to the low concentration of the CF_3CO_2Ag solution used.

The other signals (peak 1 and peak 2) can be related to the impurity found in the organic carbonate **4.2**, as we will discus below.

The mass spectra of the organic carbonate **4.2** showed two signals: one high intensity peak, corresponding to its molecular ion (a silver ion is complexed with each of the sample molecules), and one low intensity peak represented by **4.2-I** in Table 4.9.

Table 4.9. MALDI mass spectrometric analyses of organic carbonates [a)]

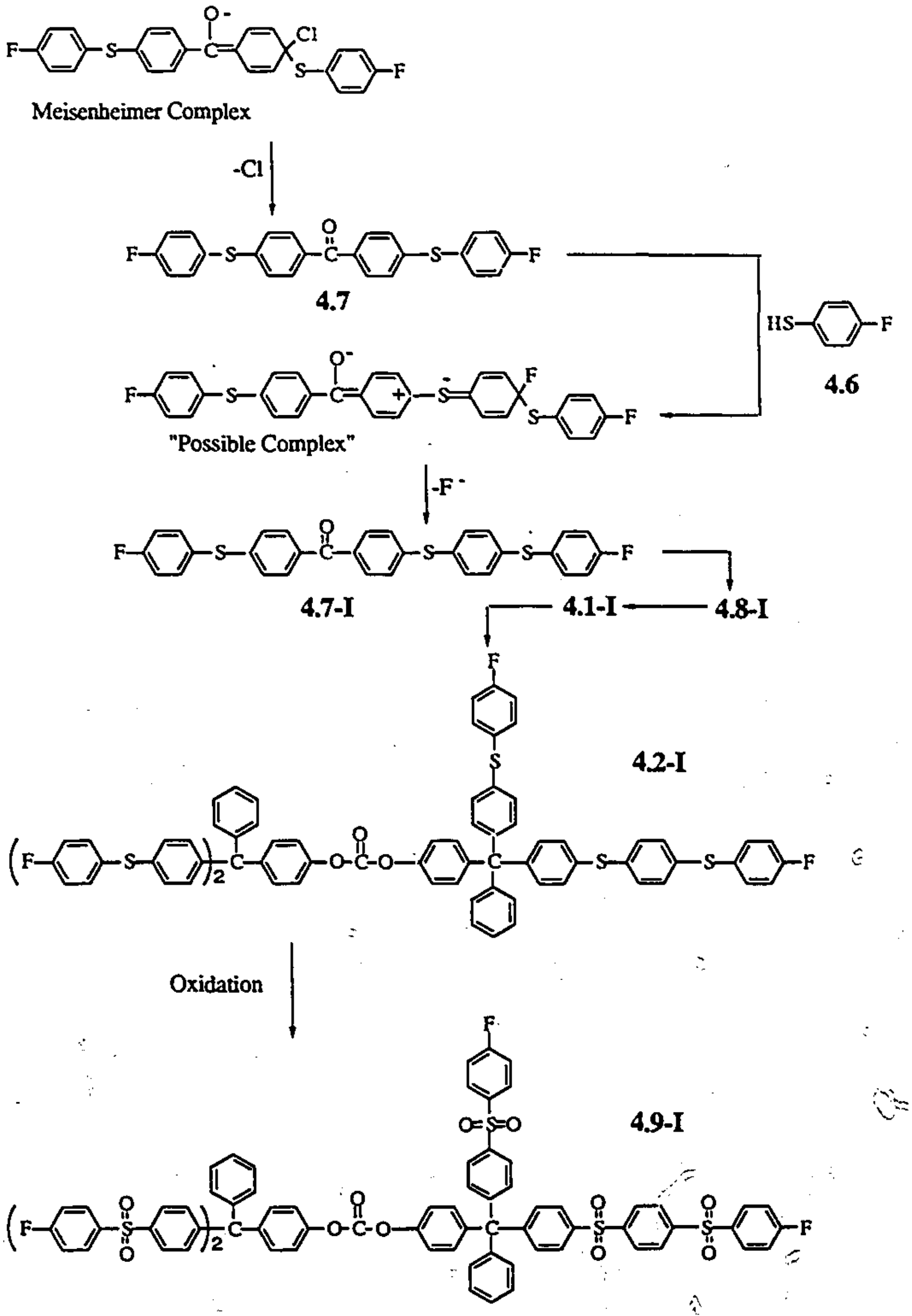
Organic Carbonate	$(M + Ag)^{+}$ [b)]	Mass/Charge
4.2	1311.5	1312.9
4.2-I	1419.5	1420.1
4.9	1439.5	1438.1
4.9-I	1579.5	1577.6

a) Dithranol:sample:CF_3CO_2Ag = 40:4:2. a) M = sample molecular mass, Da; Ag = silver atomic mass, Da.

The synthesis of phenol **4.1** (**3.7** in Scheme 3.1) included a displacement reaction in which chlorides of 4,4'-dichlorobenzophenone **4.5** (**3.1** in Scheme 3.1)), are displaced by two molecules of 4-fluorothiophenol **4.6** (**3.2** in Scheme 3.1) to obtain the product **4.7**. In the mechanism of this reaction the first step is the formation of the Meisenheimer complex which can be stabilized by electronwithdrawing groups such as keto or sulfone groups. Consequently, a by-product can be obtained if we assume that a similar complex is formed between 4-fluorothiophenol **4.6** and condensation product **4.7** (Scheme 4.6).

The mass difference between these two peaks, 108 units ($-C_6H_4S-$), suggested that this impurity can be represented by the structures **4.2-I** shown in Scheme 4.6. Only one of the possible resonance structures that contribute to the stablilization of this complex is shown; **4.8-I** and **4.1-I** represent the intermediate products formed between **4.7-I** and **4.2-I.**

Scheme 4.6


Meisenheimer Complex
-Cl
4.7
4.6
"Possible Complex"
-F⁻
4.7-I
4.1-I
4.8-I
4.2-I
Oxidation
4.9-I

The HPLC chromatograms of purified **4.7**, **4.8**, **4.1**, and **4.2**, also indicated that a low intensity - higher retention time impurity was present in all these samples. It could not be separated by recrystallization, chromatographic column, or fractional precipitation. The similarities in structure between the main product and the impurity made the purification difficult.

To obtain some conformation of our theory, we carried out the oxidation of **4.2** according to the procedure described in the Experimental Section. The results were similar. The MALDI mass spectrum of the oxidation product showed two peaks represented in Table 4.9 by **4.9** and **4.9-I**. The most intense signal corresponds to the molecular ion (a silver cation is complexed with the sample molecules). The difference found between both peaks is about 140 Da which corresponds to the molecular mass of $-C_6H_4SO_2-$. The structure of **4.9-I** is given in Scheme 4.6.

Differences between the molecular masses of peak 1 and peak 2 of fluoro poly (aryl ether sulfide)s and fluoro poly(aryl ether sulfone)s are about 108 Da and 140 Da, respectively, which confirms our previous suggestion. The same values are obtained for the mass differences between peak 2 and peak 3.

During the condensation reaction, **4.1-I** can react with the activated poly(aryl ether sulfone) and consequently be part of the structure of a few molecules of the dendrimer. Peak 2 corresponds to some molecules of the first and second generation with only one fragment of $-C_6H_4S-$ or $-C_6H_4SO_2-$ in their structures. Peak 3 corresponds to some third generation molecules which possess two of these fragments in their structure.

MALDI mass differences between the calculated values and the experimental values are around 0.1 %. Unfortunately, it was not possible to characterize the fourth generation and quantify the purity of our dendrimers using this technique. Variations in the peak intensities for a single sample analyzed several times were detected. It is known that the way the sample, matrix, and stabilizer interact and coprecipitate affects the characteristics of the spectra, beside other conditions such as beam power, shot number, area analyzed, and nature of the sample.

The data accumulated indicate that the condensation agent and conditions employed in the synthesis produce quantitative reactions since no signals were detected for the reaction intermediates and only the molecular ions were observed. The lower intensity peaks observed in HPLC chromatograms, described previously, could be a consequence of those impurities detected by MALDI mass spectrometry.

4.6 Organic carbonate versus sodium phenolate in the synthesis of fluoro poly(aryl ether sulfide) dendrimers.

The synthesis of fluoro poly(aryl ether) dendrimers using sodium phenolate was described in Chapter 3. It was demonstrated that the procedure used in those syntheses was efficient for the preparation of the first generation fluoro poly(aryl ether), but it showed some limitations in the synthesis of the higher generations of dendrimers. The sodium phenolate was not active enough to make the reactions of the higher generations quantitative.

In our present work, the use of a more active metal carbonate, such as cesium carbonate, in conjunction with magnesium hydroxide or calcium carbonate which removes some of the fluoride ions formed allowed us to overcome that limitation by reaching a better compromise between reactivity and selectivity.

The HPLC chromatograms of the second and third generation poly (aryl ether sulfide)s synthesized using the carbonate and sodium salt of phenol **4.1** are shown in Figures 4.19 and 4.20. The reaction with sodium phenolate is less selective and less reactive.

Cesium carbonate cleaves the organic carbonate relatively fast. The formation of the very active cesium phenolate makes the displacement of fluorides a fast reaction. However, the equilibration reactions associated with the displacemt of aryl phenoxide branches of dendrimers by fluorides and cesium phenolates can become competitive reactions.

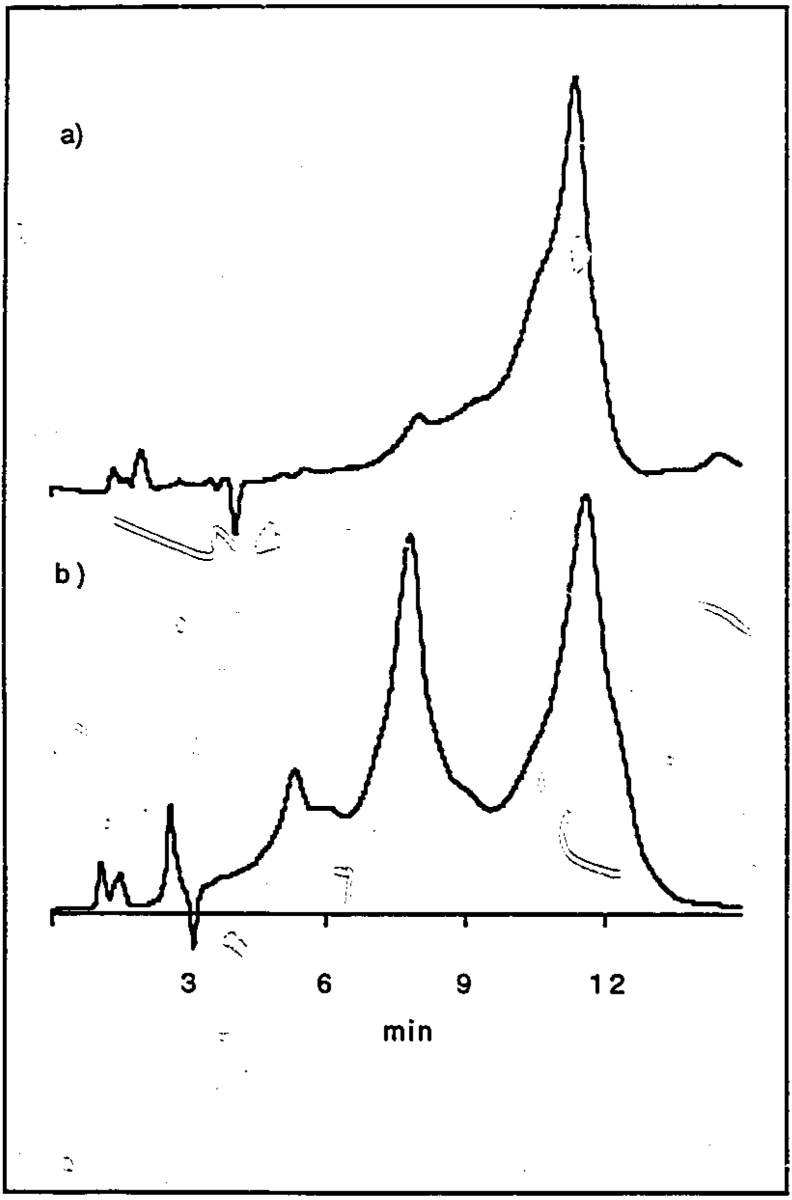


Figure 4.19. HPLC chromatograms of the second generation fluoro poly(aryl ether sulfide) **2GFS**, synthesized using: a) **organic carbonate,** $Mg(OH)_2$:Cs_2CO_3, and Ar and b) **sodium phenolate.** HPLC solvent: THF/H_2O (78/22).

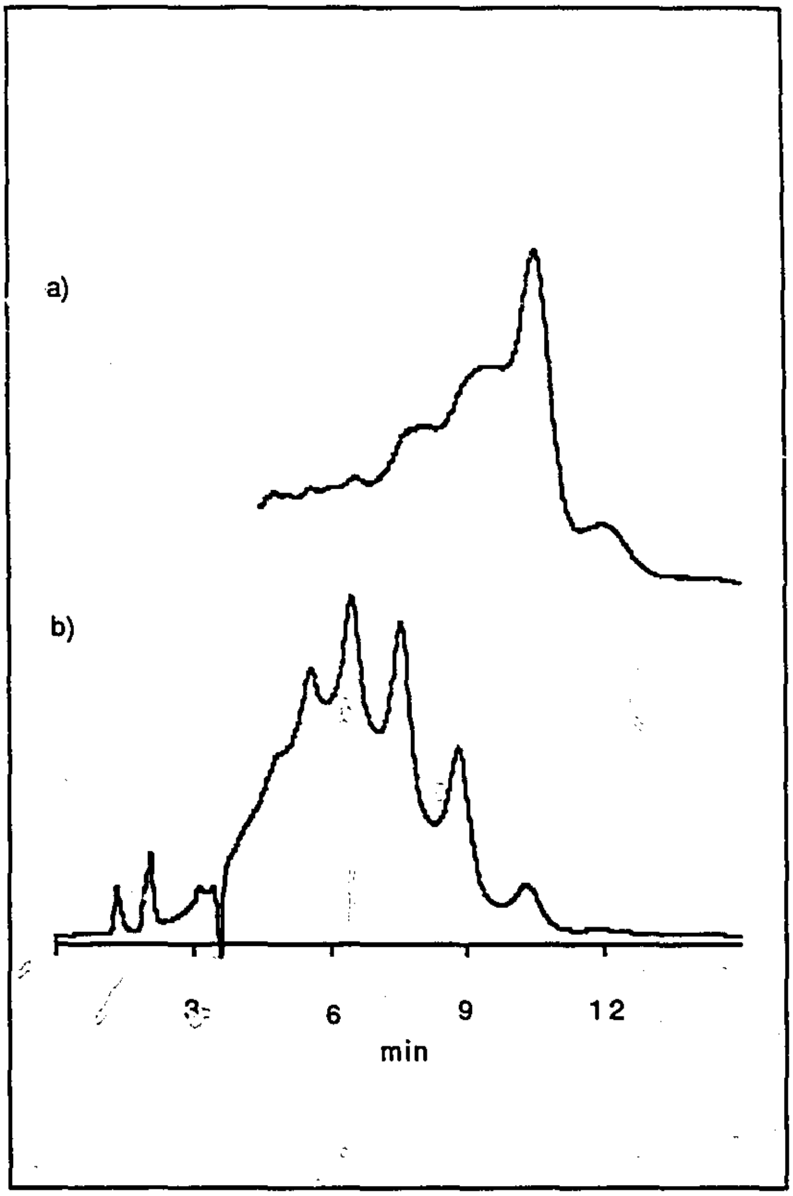


Figure 4.20. HPLC chromatograms of third generation fluoro poly(aryl ether sulfide) **3GFS**, synthesized using: a) **organic carbonate**, $Mg(OH)_2$:Cs_2CO_3, and Ar, and b) **sodium phenolate.** HPLC solvent: THF/H_2O (82/18).

The fact that Mg^{++} and Ca^{++} form insoluble salts with fluoride and that the phenolate ions of these metal are less reactive allows us keep control of the equilibration reactions associated with F^- and ArO^- and make the syntheses of the dendrimers essentially quantitative.

4.7 Physical properties.

The physical properties of these materials are given in Table 4.6. The glass transition temperature, Tg, of the fluoro poly(aryl ether) dendrimers increases with the generation number and molecular weight from 92°C - 231°C. Since a fluoro poly(aryl ether sulfone) dendrimer has a more polar structure, its Tg is higher than that of a poly(aryl ether sulfide) of comparable molecular weight. For example, for the first generation: Tg(1GFS) = 92°C and Tg($1GFSO_2$) = 170 °C. The inherent viscosity, n_{inh}, also increased with the generation number (0.05 dL/g - 0.10 dL/g).

All of these samples showed a high solubility in common organic solvents such as tetrahydrofuran, chloroform, N,N-dimethylacetamide, and dimethylsulfoxide, and all of them showed a high thermal stability (5 % weight loss = 485°C - 506°C by TGA).

The physical properties of fluoro poly(aryl ether) dendrimers synthesized from a organic carbonate were similar to those of fluoro and chloro poly(aryl ether) dendrimers synthesized from sodium phenolate.

4.8 Conclusions.

We have synthesized four generations of fluoro poly(aryl ether)s with activated aryl fluoride terminal functionality from 4,4'-difluorodiphenyl sulfone and a relatively high molecular weight bis(fluoroaryl)phenolate. An iterative procedure was employed that involved oxidation of the aryl sulfide moieties followed by the displacement of the fluorides activated by sulfone groups.

In these syntheses several combinations of metal carbonates and metal hydroxides under different reaction conditions were used: a) alkali metal (Cs, K) carbonates and calcium carbonate, b) potassium hydroxide and calcium hydroxide, and c) cesium carbonate and alkaline earth metal (Ca, Mg) hydroxides.

The data indicated that for the synthesis of the first generation poly(aryl ether sulfide) **1GFS** the combination of calcium and cesium carbonate (Table 4.1, **1GFS-5**) is the most reactive, with a selectivity comparable to those of $CaCO_3$:K_2CO_3 and $Ca(OH)_2$:KOH mixtures. For the synthesis of the higher generations of dendrimers the best compromise between reactivity and selectivity is reached with the $Mg(OH)_2$:Cs_2CO_3 mixture.

The best conditions in general are: a) slight excess of basic equivalents (metal carbonate, metal hydroxide) with respect to organic carbonate; b) around 30 % molar excess of $CaCO_3$ or $Mg(OH)_2$ to Cs_2CO_3, and c) about 0.9 mol of cesium per mol of organic carbonate. The use of argon instead of nitrogen is preferable.

Higher amounts of $CaCO_3$ or $Mg(OH)_2$ give more selective reactions but also longer reaction times are required. A contrary effect is observed for Cs_2CO_3. The formation of insoluble calcium fluoride or magnesium fluoride and the use of the more active nucleophilic polycondensation agent, Cs_2CO_3, can explain those results. The use of only K_2CO_3 is clearly unsatisfactory.

The characterization results indicated that the size and molecular weight of these molecules increase with the generation number and that there are changes in their structure during the condensation and activation reaction. The polydispersities of all these samples are close to one and the NMR data confirms the proposed structures. It also indicates that the condensation reactions are almost quantitative.

MALDI mass spectrometry, which was only available in the last stage of this research, was shown to be a very useful characterization technique. It confirms that the synthesis of the first, second, and third generation dendrimers are almost quantitative. The possible origin of the lower intensity peaks observed in HPLC chromatograms and mass spectra is associated with imperfections in some molecules of the dendrimers formed by reaction of the impurity found in the organic carbonate with the corresponding core precursor.

4.9 Experimental.

Materials. Anhydrous calcium carbonate (ACP), anhydrous cesium carbonate (Aldrich), anhydrous calcium hydroxide (Fisher), anhydrous magnesium hydroxide (Aldrich), anhydrous potassium hydroxide (Caledon), pyridine (BDH), and triphosgene (Aldrich), were used as obtained. For more details see Chapter 2: Part 2.8.

General methods. For details see Chapter 2: Part 2.8.

Dendrimer characterization. HPLC analyses were performed on a Milton Roy CM4000 with auto injector instrument using THF/H_2O as the mobile phase, a Primesphere 5uC8 column (250 mm x 4 mm), and an UV detector (Milton Roy Spectro Monitor 3100) at a wavelength of 254 nm. For more details see Chapter 2: Part 2.8.

Monomer synthesis.

Synthesis of p-[[4,4'-Bis(4-fluorophenylthio)]triphenylmethyl] phenol 4.1. For details see Chapter 3: Part 3.8.

Synthesis of p-[[4,4'-Bis(4-fluorophenylthio)]triphenylmethyl]phenyl carbonate 4.2. A mixture of phenol **4.1** (40 mmol, 23.55 g), pyridine (100 mL) and toluene (150 mL) was stirred under argon for 0.5 h at 40°C. Then, a solution of **bis(trichloromethyl) carbonate** (triphosgene, 10.00 mmol, 2.97 g) in toluene (50 mL) was added, under the same conditions, for a period of 1 h. When the reaction was finished, it was poured into methanol (1000 mL) and filtered. The solid recovered was dissolved in DMAc (150 mL), and the solution poured into 1% aqueous HCl, filtered and dried. The solid was purified by fractional precipitation dissolving the sample in chloroform (15 mL/g) and using methanol as the nonsolvent. After the workup 15.40 g of a white solid was obtained (isolated yield = 64%). The purity of the isolated product by HPLC was 85% (Column: C8, THF:H_2O, 85:15): ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.49-7.42 (m, 8H), 7.31-7.04 (m, 42H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 165.0-160.1 (d, J = 245.7 Hz), 149.1, 146.0, 144.7, 144.5, 135.4-135.2 (d, J = 8.0Hz), 132.3, 131.9, 131.1, 129.4-129.30 (d, J = 3.1 Hz), 128.3, 128.1, 126.7, 120.3, 117.2-116.8 (d, J = 21.8 Hz), 65.0; MS (EI) m/e 1202, 999, 495, 460, 303, 154, 137; MS (MALDI(Ag)) m/e 1312.9 (MI), 1420.1.

Synthesis of p-[[4,4'-Bis(4-fluorophenylsulfonyl)]triphenylmethyl]phenyl carbonate 4.9. Wet alumina was prepared by adding water (10 mL) to the alumina (50 g; Brockman grade I, 200 mesh) and shaking until a free flowing homogeneous powder was obtained.

Organic carbonate **4.2** (3.61 g, 3.00 mmol) was added to a vigorously stirred suspension of wet alumina (12.54 g) and Oxone (23.22 g, 36.00 mmol) in chloroform (30 mL). The mixture was heated at reflux for 8 h. When the reaction finished, it was cooled, filtered and the solids washed thoroughly with chloroform. The solution was concentrated and coagulated in methanol (60 mL) to afford 3.91 g of a white solid (isolated yield = 98 %): ^{1}H NMR (200 MHz, DMSO-d_6) δ 8.10-8.00 (m, 8H), 7.98-7.88 (d, 8H), 7.54-7.40 (m, 16H), 7.40-7.10 (m, 18H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 167.0-162.1 (J = 250.5

Hz), 151.1, 148.6, 144.4, 142.8, 138.8, 137.1-137.0 (J = 2.7 Hz), 131.4, 130.9-130.7 (J = 9.7 Hz), 130.1, 128.5, 127.4, 126.7, 121.1, 117.5-117.0 (J = 22.5 Hz), 65.3; MS (MALDI(Ag)) m/e 1441.3 (MI), 1580.9 (MI); Analysis calc'd for $C_{75}H_{50}S_4O_{11}F_4$: H, 3.79%; S, 9.63%; F, 5.71%; found: H, 3.70%; S, 9.75%; F, 5.55%.

Dendrimer synthesis.

First generation fluoro poly(aryl ether sulfide) 1GFS. To a 250 mL round bottomed flask, fitted with a condenser and a argon inlet, there was added 4,4'-difluorodiphenyl sulfone **4.3** (1.73 g, 6.80 mmol), **4.2** (10.65 g, 8.85 mmol), **cesium carbonate** (1.28 g, 3.94 mmol), **calcium carbonate** (0.51 g, 5.06 mmol), and DMAc (150 mL). No correction was made for the impurity present in **4.2**. The mixture was stirred vigorously and maintained under reflux for 1h. The reaction was followed by HPLC. When the reaction was finished, it was cooled, poured into methanol (800 mL) and filtered. The solid recovered was dissolved in DMAc (150 mL), coagulated in 2% aqueous HCl (600 mL), filtered and dried overnight at 70°C under vacuum. In general the volumes of methanol and acid solution were four times the volumes of DMAc used in the reaction, and the volume of DMAc for the separation procedure was the same as that used in the reaction. The precipitate (9.50 g) was purified by fractional precipitation by dissolving the sample in chloroform (15 mL/g) and using methanol as the nonsolvent. After the workup 5.02 g of **1GFS** was obtained (isolated yield after purification = 53%): ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.94-7.84 (d, calc'd 4, found 4), 7.52-7.40 (m, calc'd 8, found 8), 7.34-6.94 (m, calc'd 46, found 46); ^{13}C NMR (50 MHz, $CDCl_3$) δ 165.0-160.1 (J = 245.7 Hz), 161.4, 153.2, 146.1, 144.7, 143.1, 135.9, 135.4-135.2 (J = 8.1 Hz), 132.9, 131.9, 131.1, 130.1, 129.3 (J = 3.2 Hz), 128.3, 128.1, 126.7, 119.5, 118.5, 117.2-116.8 (J = 21.7 Hz), 65.9; MS (MALDI(Li)) m/e 1396.8 (MI), 1503.3; Tg = 92°C (10°C/min, N_2), 5% weight loss = 490C (10°C/min, N_2); n_{inh} = 0.05 dL/g (NMP, 0.5 g/dL, 25°C).

First generation fluoro poly(aryl ether sulfone) 1GFSO$_2$. The method is similar to that used for the synthesis of product 9. The first generation fluoro poly(aryl ether sulfide) **1GFS** (4.87 g, 3.50 mmol) was added to a vigorously stirred suspension of wet alumina (14.00 g) and Oxone (25.90 g, 42.00 mmol) in chloroform (175 mL). The mixture was heated at reflux for 24 h. When the reaction was finished, it was cooled, filtered and the solids washed thoroughly with chloroform. The solution was concentrated, coagulated in methanol (175 mL), and the solid separated was dried overnight at 100°C under vacuum. After the workup 5.00 g of **1GFSO$_2$** was obtained (isolated yield = 94%): ^{1}H NMR (200 MHz, DMSO-d$_6$) δ 8.12-8.00 (m, calc'd 8, found 8), 8.00-7.86 (m, calc'd 12, found 12), 7.54-7.40 (m, calc'd 16, found 16), 7.40-7.10 (m, calc'd 18, found 18), 7.10-7.00 (d, calc'd 4, found 4); ^{13}C NMR (50 MHz, CDCl$_3$) δ 168.0-162.9 (J = 253.4 Hz), 161.0, 153.8, 151.4, 144.4, 141.3, 139.9, 137.5-137.4 (J = 3.2 Hz), 136.2, 132.6, 131.9, 131.1-130.9 (J = 9.6 Hz), 130.8, 130.1, 128.6, 127.5, 127.3, 119.8, 118.7, 117.4-117.0 (J = 22.2 Hz), 65.8; MS (MALDI(Li)) m/e 1525.1 (MI), 1665.0; Analysis calc'd for $C_{86}H_{58}S_5F_4O_{12}$: C, 67.97%; H, 3.85%; S, 10.55%; F, 5.00%; found: C, 67.16%; H, 3.93%; S, 10.27%; F, 4.91%; Tg = 170°C (10°C/min, N$_2$), 5% weight loss = 506°C (10°C/min, N$_2$); η_{inh} = 0.05 dL/g (NMP, 0.5 g/dL, 25°C).

Second generation fluoro poly(arylether sulfide) 2GFS. The reaction was carried out using a procedure similar to that employed for the synthesis of **1GFS** using **1GFSO$_2$** (3.80 g, 2.50 mmol), **4.2** (7.10 g, 5.90 mmol), **cesium carbonate** (0.855 g, 2.625 mmol), **magnesium hydroxide** (0.197 g, 3.375 mmol), and DMAc (100 mL). The reaction time was 1.5 h. The precipitate (8.92 g, isolated yield = 94%) was purified by fractional precipitation dissolving the sample in chloroform (20 mL / g) and using methanol as the nonsolvent. The solid separated was dried overnight at 100°C under vacuum. After the workup 5.31 g of **2GFS** was obtained (isolated yield after purification = 56%): ^{1}H NMR (200 MHz, DMSO-d$_6$) δ 7.94-7.78 (m, calc'd 20, found 20), 7.48-7.30 (m, calc'd 24, found 25), 7.30-6.86 (m, calc'd 114, found 114); ^{13}C NMR (50 MHz, $CDCl_3$) δ 165.0-160.1 (J = 245.7 Hz), 161.8, 161.1, 153.8, 153.0, 151.1, 146.0, 144.7, 143.3, 141.4, 140.4, 136.2, 135.4-135.2 (J = 8.1 Hz), 134.9, 133.0, 132.7, 131.9, 131.8, 131.1, 130.8, 130.5, 130.2, 129.2, 128.6, 128.3, 128.1, 127.3, 126.7, 119.8, 119.6, 118.7, 118.4, 117.2-116.8 (J = 21.7 Hz), 65.8, 64.9; MS (MALDI(Li)) m/e 3800.9 (MI), 3908.9; Tg = 154°C (10°C/min, N_2), 5% weight loss = 496°C (10°C/min, N_2); n_{inh} = 0.07 dL/g (NMP, 0.5 g/dL, 25°C).

Second generation fluoro poly(aryl ether sulfone) 2GFSO$_2$. A procedure similar to that used to synthesize **1GFSO$_2$** was employed using **2GFS** (1.90 g, 0.50 mmol), wet alumina (4.00 g), and Oxone (7.40 g, 12.00 mmol) in chloroform (25 mL). The solution was concentrated and coagulated in methanol (25 mL) to afford 1.90 g of **2GFSO$_2$** (isolated yield = 94%): ^1H NMR (200 MHz, DMSO-d_6) δ 8.10-7.98 (m, calc'd 16, found 16), 7.98-7.84 (m, calc'd 36, found 35), 7.52-7.36 (m, calc'd 40, found 40), 7.36-6.98 (m, calc'd 66, found 67); ^{13}C NMR (50 MHz, $CDCl_3$) δ 168.0-162.9 (J = 253.4 Hz), 161.4, 153.6, 151.4, 151.2, 144.4, 141.4, 140.2, 139.9, 135.3, 132.7, 131.9, 131.1-130.9 (J = 9.6 Hz), 130.8, 130.5, 130.1, 128.6, 127.5, 127.4, 120.0, 119.8, 118.7, 118.6, 117.4-117.0 (J = 22.4Hz), 65.9, 65.8; MS (MALDI(Li)) m/e 4059.5 (MI), 4199.7; Analysis calc'd for $C_{234}H_{158}S_{13}F_8O_{32}$: H, 3.93%; S, 10.29%; F, 3.75%; found: H, 4.09 %; S, 10.23%; F, 3.70%; Tg = 215°C (10°C/min, N_2), 5% weight loss = 504°C (10°C/min, N_2); n_{inh} = 0.07 dL/g (NMP, 0.5 g/dL, 25°C).

Third generation fluoro poly(aryl ether sulfide) 3GFS. The reaction was carried out using a procedure similar to that employed to synthesize **1GFS** using **2GFSO$_2$** (0.506 g, 0.125 mmol), **4.2** (0.710 g, 0.590 mmol), **cesium carbonate** (0.086 g, 0.263 mmol), **magnesium hydroxide** (0.020 g, 0.338 mmol), and DMAc (10 mL). The reaction time was 2.5 h. The precipitate was purified by fractional precipitation dissolving the sample in chloroform (20 mL/g) and using methanol as the nonsolvent. The solid separated was dried overnight at 100°C under vacuum. After the workup 0.71 g of **3GFS** was obtained (isolated yield after purification = 66%): ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.92-7.70 (m, calc'd 52, found 52), 7.46-7.26 (m, calc'd 56, found 58), 7.26-6.74 (m, calc'd 250, found 248); ^{13}C NMR (50 MHz, $CDCl_3$) δ 165.0-160.1 (J = 245.7 Hz), 161.8, 161.4, 153.6, 153.0, 151.2, 151.1, 146.0, 144.7, 144.6, 143.3, 141.5, 140.4, 140.3, 135.4-135.2 (J = 8.2 Hz), 134.9, 133.0, 132.7, 132.6, 131.9, 131.1, 130.8, 130.5, 130.2, 129.6, 128.6, 128.3, 128.1, 127.4, 126.7, 119.9, 119.6, 118.7, 118.4, 117.2-116.8 (J = 21.7 Hz), 65.8, 64.9; MS (MALDI(Ag)) m/e 8705.4 (MI), 8812.7, 8921.4; Tg = 185°C (10°C/min, N_2), 5% weight loss = 485°C (10°C/min, N_2); n_{inh} = 0.09 dL/g (NMP, 0.5 g/dL, 25°C).

Third generation fluoro poly(aryl ether sulfone) 3GFSO$_2$. A procedure similar to that used to synthesize **1GFSO$_2$** was employed, using **3GFS** (0.86 g, 0.10 mmol), wet alumina (1.87 g), and Oxone (3.45 g, 5.60 mmol) in chloroform (10 mL). The solution was concentrated and coagulated in methanol (10 mL) to afford 0.78 g of **3GFSO$_2$** (isolated yield = 86%): ^{1}H NMR (200 MHz, DMSO-d_6) δ 8.10-7.97 (m, calc'd 32H, found 35H), 7.97-7.80 (m, calc'd 84H, found 79H), 7.54-7.34 (m, calc'd 88H, found 90 H), 7.34-6.90 (m, calc'd154 H, found 154H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 167.9-162.9 (J = 253.4 Hz), 161.4, 153.6, 151.4, 151.2, 144.4, 141.4, 140.2, 139.9, 135.3, 132.7, 131.9, 131.1-130.9 (J = 9.6 Hz), 130.8, 130.5, 128.6, 127.5, 127.4, 119.9, 118.7, 117.4-117.0 (J = 22.4 Hz), 65.9, 65.8; MS (MALDI(Ag)) m/e 9220.5 (MI), 9359.7, 9502.1; Analysis calc'd for $C_{530}H_{358}S_{29}F_{16}O_{72}$: H, 3.96%; S, 10.02%; F, 3.34%; found: H, 4.03%; S, 10.22%; F, 3.23%; Tg = 230°C (10°C/min, N_2), 5% weight loss = 500°C (10°C/min, N_2); n_{inh} = 0.09 dL/g (NMP, 0.5 g/dL, 25°C).

Fourth generation fluoro poly(aryl ether sulfide) 4GFS. The reaction was carried out using a procedure similar to that employed for the synthesis of **1GFS** using **3GFSO$_2$**

(0.91 g, 0.10 mmol), **4.2** (1.14 g, 0.80 mmol), **cesium carbonate** (0.14 g, 0.42 mmol), **magnesium hydroxide** (0.03 g, 0.54 mmol), and DMAc (10 mL). The reaction time was 3 h. The precipitate (1.61 g) was purified by fractional precipitation dissolving the sample in chloroform (20 mL/g) and using methanol as the nonsolvent. The solid separated was dried overnight at 100°C under vacuum. After the workup 1.31 g of **4GFS** was obtained (isolated yield after purification = 72%): ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.90-7.60 (m, calc'd 116, found 121), 7.40-6.60 (m, calc'd 642, found 637); Tg = 183°C (10°C/min, N_2), 5% weight loss = 487°C (10°C/min, N_2); n_{inh} = 0.10 dL/g (NMP, 0.5 g/dL, 25°C).

Fourth generation fluoro poly(aryl ether sulfone) 4GFSO$_2$. A procedure similar to that used to synthesize **1GFSO$_2$** was employed, using **4GFS** (0.91 g, 0.05 mmol), wet alumina (1.60 g), and Oxone (2.96 g, 4.80 mmol) in chloroform (40 mL). The solution was concentrated and coagulated in methanol (17 mL) to afford 0.83 g of **4GFSO$_2$** (isolated yield = 87%) : ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.10-7.77 (m, calc'd 244, found 247), 7.50-7.30 (s, calc'd 184, found 184), 7.30-6.85 (m, calc'd 330, found 327; Tg = 231 °C (10°C/min, N_2), 5% weight loss = 495°C (10°C/min, N_2); n_{inh} = 0.10 dL/g (NMP, 0.5 g/dL, 25°C).

4.9 References.

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Chapter 5

Preparation and characterization of aryl halide-terminated and phenol-terminated hyperbranched poly(aryl ether sulfone)s.

5.1 Introduction.

Research on synthesis, characterization, and properties of hyperbranched and/or dendritic macromolecules has steadily increased in the last several years. The synthetic methodology for preparing these spherical or globular shaped molecules is often difficult and laborious. For example, Tomalia, Hedestrand and Wilson (1) have synthesized well-defined multigeneration starburst poly(amido amine)s by a divergent process, which involves starting with a central core and attaching an increasing number of functional groups at each generation. Large excesses of reagents and rigorous separation/purification steps were required after each addition step. Some of these problems can be solved by using the convergent approach as described by Wooley, Hawker and Fréchet, (2) and Miller, Neenan and Bair. (3) They created, in a step-by-step synthesis, several generations of dendrons that can be attached to a central core to form much larger dendritic structures.

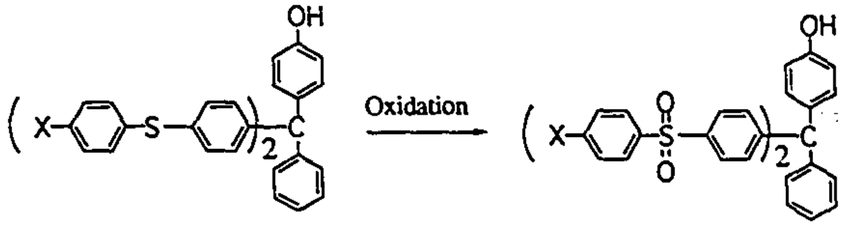
A much faster route to obtain highly branched polymer structures is the one-step reaction of A_xB monomers, where x is 2 or greater. Tomalia called this approach the *divergent uncontrolled method* (Chapter 1, Part 1.3). Flory (4) has predicted that highly branched but soluble polymers (noncrosslinked materials), with high molecular weight and broad molecular weight distributions should be obtained from these reactions. Assuming that all of the A functionalities react in an A_xB monomer, one would actually produce an ideal dendritic structure with one unreacted B functional group and n(x-1)+1 number of unreacted A functional groups at the surface of the polymer, where n is the degree of the polymerization. However, it is much more likely that the polymer structure has defects that result in a number of linear instead of branched units. Several examples of this type of condensation to form hyperbranched polymers have been reported. Kim and Webster (5) have prepared hyperbranched polyphenylenes, Hawker, Lee, and Fréchet (6) and Volt and Turner (7) have reported the synthesis of hyperbranched all aromatic polyesters, Miller, Neenan, Kwock and Stein, (8) and Uhrich, Hawker, Fréchet and Turner (9) have synthesized hyperbranched poly(aryl ether)s, and Suzuki, Ii and Saegusa (10) have produced a hyperbranched polyamine. All of them used A_2B type condensations. According to Kim and Webster (5) these highly branched polymers can be used as polymer rheology control agents as well as spherical multifunctional macromonomers.

5.1.1 Strategy and goals

The general objective of this section is the one-pot preparation of hyperbranched poly(aryl ether sulfone)s by polymerization of A_2B monomers. We proposed the synthesis of aryl halide-terminated and phenol-terminated hyperbranched poly(aryl ether sulfone)s using the *divergent uncontrolled method* and the etherification chemistry utilized by us previously in the preparation of almost monodisperse poly(aryl ether) dendrimers by the *divergent initiator core method*.

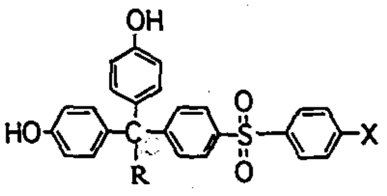
The *divergent initiator core method* relied on a stepwise condensation-activation procedure for polymer growth involving monomers **5.1**. In that process, phenols **5.1** are first condensed with a dendritic fragment and then the aryl sulfide groups are oxidized to give reactive aryl halides which can be condensed with other molecules of **5.1**. In the present case phenols **5.1** (Scheme 5.1) are activated, through the oxidation of the sulfide groups to sulfone groups to give phenols **5.4.** Each phenol molecule contains a single hydroxyl group and two aryl halides (Ar-Cl or Ar-F) which are activated toward nucleophilic displacement by sulfone moieties. These monomers can now undergo self-condensation to give aryl halide-terminated hyperbranched poly(aryl ether sulfone)s.

Scheme 5.1



5.1 : X = Cl, F

5.4 : X = Cl, F



5.15-a: R = CH_3, X = Cl

5.15-b: R = CH_3, X = F

5.26: R = Phenyl, X = F

In the synthesis of the aryl chloride-terminated hyperbranched polymer we proposed to use sodium phenolate as the starting material and generate the ether linkages by displacement of chlorides by the phenolate ions.

We observed in our previous work on the synthesis of starburst fluoro poly(aryl ether)s that the use of a mixture of cesium carbonate and magnesium hydroxide in combination with an organic carbonate gives faster and almost quantitative condensation reactions. The magnesium ions form insoluble salts with fluorides which suppresses the possible equilibration reactions of the poly(aryl ether) with fluorides. (11) At temperatures (155°-165°C) at which the polymerization reaction occurs the organic carbonates are rapidly cleaved by a metal carbonate or metal hydroxide to generate the phenolate ion in situ. (12) The volatile by-product, carbon dioxide, is easily removed from the reaction system.

Taking into account the above results we proposed to carried out the synthesis of the aryl fluoride-terminated hyperbranched polymers employing a different strategy which included generation of the phenolate ion from a carbonate, and to use a mixture of cesium carbonate and magnesium hydroxide as the condensation agent. In this kind of condensation reaction the displacement of fluorides is faster than the displacement of chlorides by phenols .

The phenol-terminated hyperbranched poly(aryl ether sulfone)s that we proposed to synthesize can be readily prepared by polycondensation of the monomers **5.15-a, 5.15-b,** and **5.26** (Scheme 5.1). These A_2B monomers are bisphenols which contain a single aryl halide (Ar-Cl or Ar-F) activated toward nucleophilic displacement by a sulfone moiety, and two phenolic groups. They can give hyperbranched polyethers by a self-condensation reaction. We proposed to generate *in situ* the phenolates using, as the condensation agent, potassium carbonate or a mixture of cesium carbonate and magnesium hydroxide.

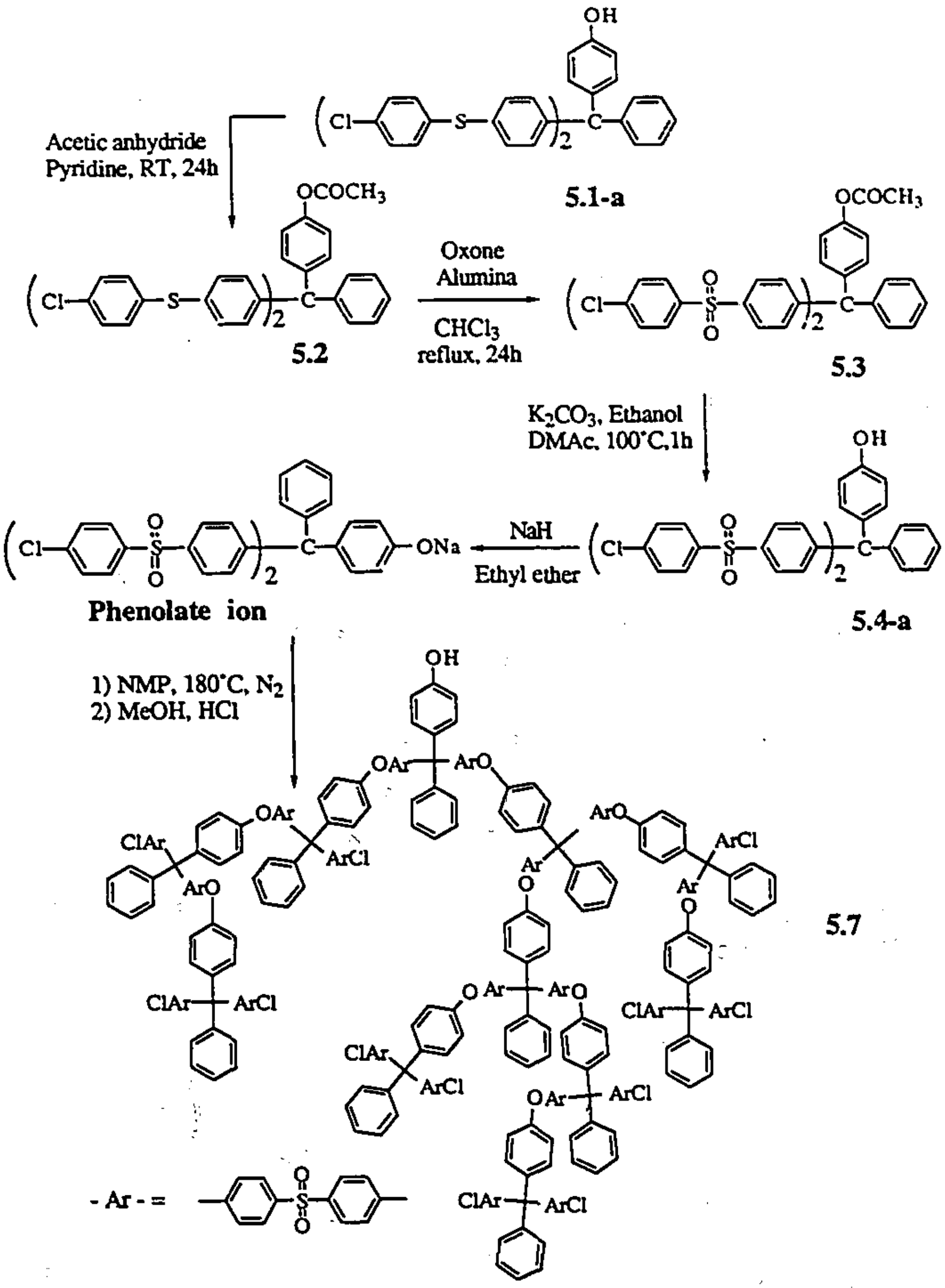
5.2 Aryl halide-terminated hyperbranched poly(aryl ether sulfone)s.

5.2.1 Preparation of activated monomer 5.4-a.

Phenol **5.1-a** was made according to the procedures described previously in Chapter 2, Part 2.2.

The synthesis of the activated monomer **5.4-a** is showed in Scheme 5.2. The reaction began with the acetylation (13) of the phenol **5.1-a** to protect the phenol and avoid its oxidation followed by the oxidation of the aryl sulfide groups by Oxone (14) to obtain **5.2** and **5.3**, respectively. The last reaction is the cleavage of the ester linkage (13) in **5.3** using potassium carbonate to obtain the activated monomer **5.4-a.**

Scheme 5.2


5.1-a
Acetic anhydride
Pyridine, RT, 24h
5.2
Oxone
Alumina
CHCl3
reflux, 24h
5.3
K2CO3, Ethanol
DMAc, 100°C,1h
5.4-a
NaH
Ethyl ether
Phenolate ion
1) NMP, 180°C, N2
2) MeOH, HCl
5.7
- Ar - =

The yield of **5.4-a** from **5.1-a**, was 56 %. NMR, and mass spectrometric characterization of each of these products confirmed the proposed structures (see Experimental Section).

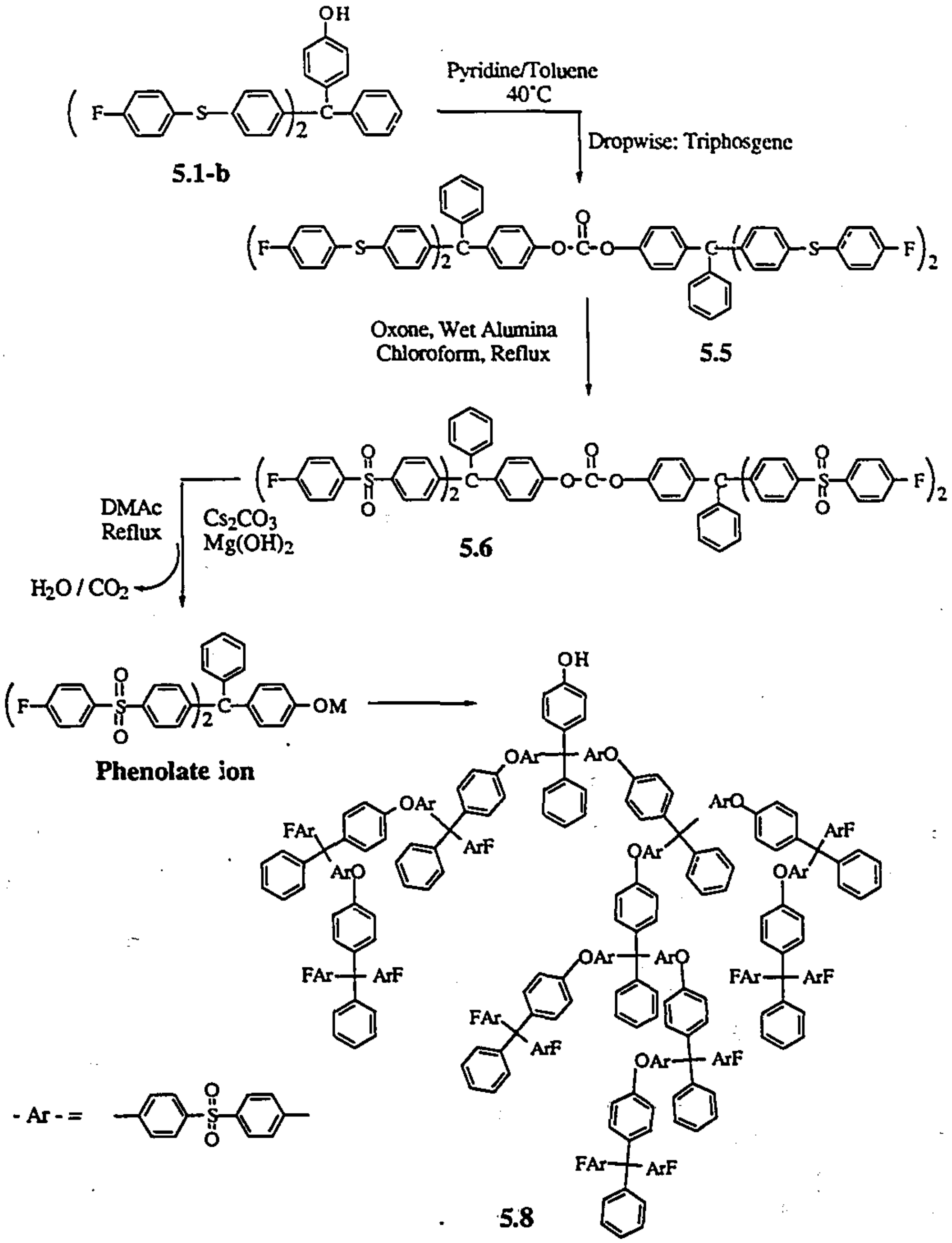
5.2.2 Preparation of organic carbonates 5.5 and 5.6.

Phenol **5.1-b** was made according to the procedures described in Chapter 3, Part 3.2.

The organic carbonate **5.5**, was synthesized from **5.1-b** and triphosgene in pyridine/toluene at 40°C (Scheme 5.3). (15) The crude product was purified by fractional precipitation using chloroform/methanol. The isolated yield after purification was 64 %. The activation reaction, in which the sulfide atoms are oxidized to produce the carbonate **5.6**, was carried out according to the general procedure used previously in the synthesis of starburst polymers. The purified carbonate **5.5** was dissolved in chloroform and the solution was then added to a stirred mixture of Oxone, wet alumina and chloroform at room temperature (14). The reaction was carried out during 8 hours under reflux conditions. The isolated yield from this reaction was 98 %.

Matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF-MS) (16) was used for the mass determination of **5.5** and **5.6**. The analyses were carried out on a Kratos Compact MALDI III instrument in the reflectron mode using dithranol as the matrix. Silver trifluoroacetate was added to stabilize the system. The mass spectrum of **5.5** showed a high intensity peak corresponding to the molecular ion of **5.5** (plus a silver ion) and a low intensity peak. A similar result was found for the oxidation product **5.6** (Fig. 5.1). The nature of these impurities, represented by **5.5-I** and **5.6-I** in Table 5.1 and Scheme 5.4, can be related to the impurity presents in phenol **5.1-b** as we described in Chapter 4, Part 4.5.3.

Scheme 5.3


OH
F
S
C
2
5.1-b
Pyridine/Toluene
40°C
Dropwise: Triphosgene
O
O-C-O
5.5
Oxone, Wet Alumina
Chloroform, Reflux
5.6
DMAc
Reflux
Cs2CO3
Mg(OH)2
H2O / CO2
OM
Phenolate ion
OAr
ArO
FAr
ArF
- Ar - =
5.8

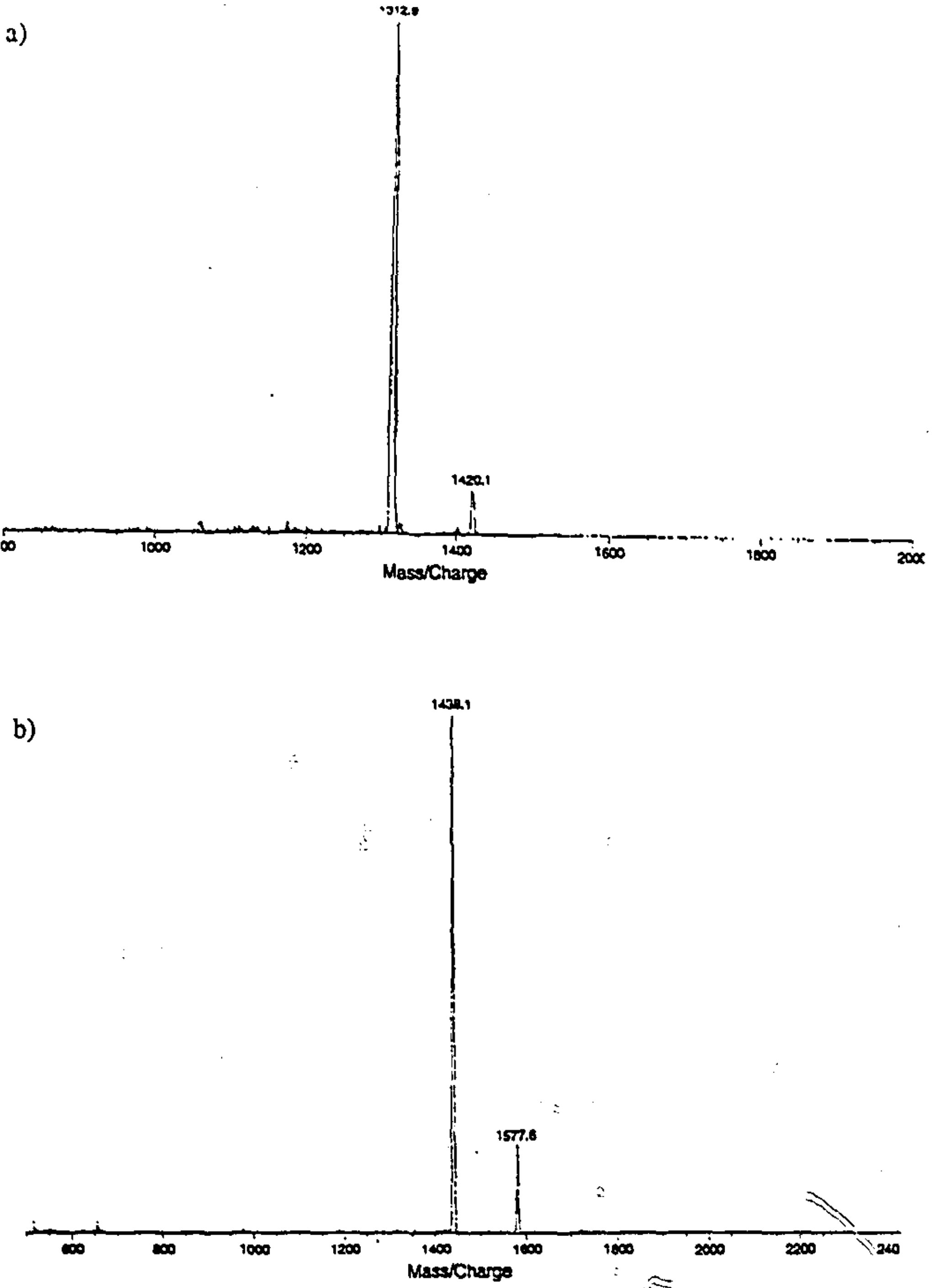
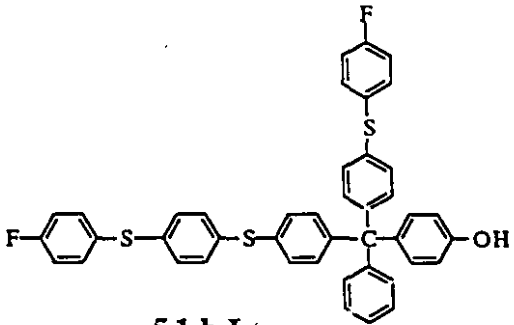
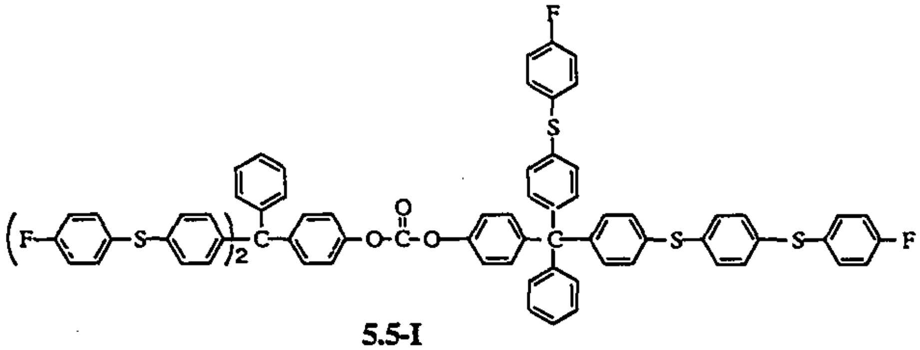


Figure 5.1. MALDI mass spectra of organic carbonates: a) **5.5** and b) **5.6.**

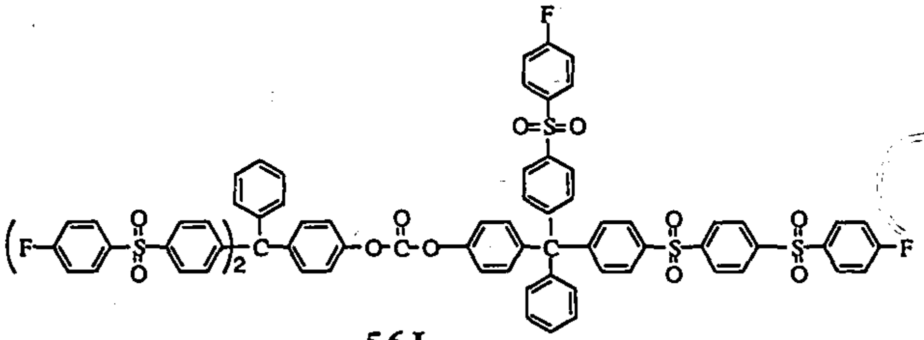
Scheme 5.4



5.1-b-I



5.5-I



5.6-I

Table 5.1. MALDI mass spectrometric analyses of organic carbonates a)

Organic Carbonate	$(M + Ag)^{+}$ b)	Mass/Charge
5.5	1311.5	1312.9
5.5-I	1419.5	1420.1
5.6	1439.5	1438.1
5.6-I	1579.5	1577.6

a) Dithranol:sample:CF_3CO_2Ag = 40:4:1. b) M = sample molecular mass, Da; Ag = silver atomic mass, Da.

5.2.3 Preparation of hyperbranched poly(aryl ether sulfone) 5.7.

The hyperbranched poly(aryl ether sulfone) **5.7** was readily prepared by polycondensation of the activated monomer **5.4-a** according to the procedure described in Scheme 5.2. Treatment of monomer **5.4-a** in ethyl ether with an excess of NaH yielded a solution of its sodium salt. (17) The solution was filtered to remove excess of NaH, ethyl ether was removed in vacuum, and NMP was added. Heating the resulting solution for 2-15 hours under reflux effected polymerization. The resulting reaction mixture was cooled, poured into acidified methanol with a few drops of HCl. The precipitated was filtered, dissolved in DMAc, and the solution filtered and coagulated in aqueous HCl. The polymer was filtered and dried. The isolated yield was 82%.

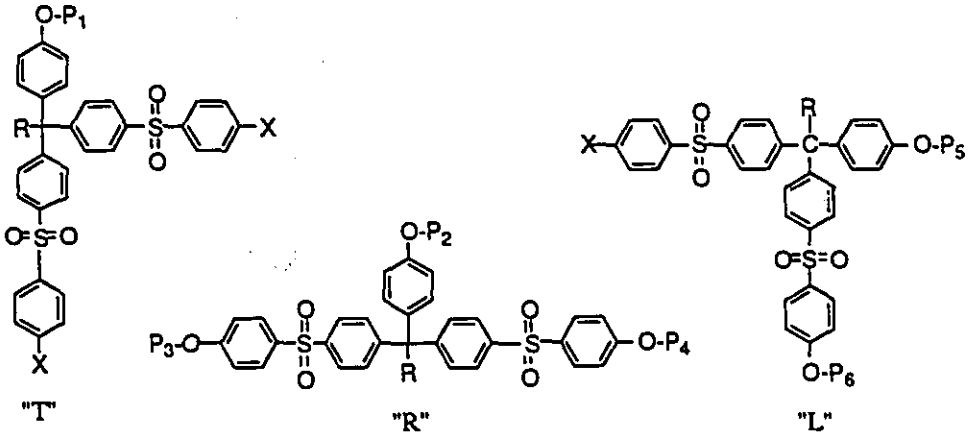
5.2.4 Preparation of hyperbranched poly(aryl ether sulfone) 5.8.

The synthesis of **5.8**, as shown in Scheme 5.3, started with the cleavage of the organic carbonate **5.6** by a mixture of cesium carbonate and magnesium hydroxide, using DMAc as the solvent of the reaction at 150°C-164°C for 1-2 hour. The phenolate ion generate in the first step, can undergo self-condensation and generate the hyperbranched polymer **5.8**. The yield of the reaction was 95%.

5.2.5 Molecular characterization.

For the discussion of the NMR characterization it is useful to describe the three building blocks that make up these polymers. The structure of the hyperbranched polymers consists of terminal units (T), lineal units (L), and branching points (R), as shown in Scheme 5.5. However, due to the complexity of these systems only a general assignation of the absorption to the different protons or carbons in these molecules was possible. The broad molecular size distribution of **5.7** and **5.8** led to significant peak broadening in their ^{1}H NMR spectra. To simplify this study, we chose the lineal block "L" to describe the NMR spectra. This is the only block that can generate all the different possible signals in the polymer.

Scheme 5.5



P = polymer segment, R = phenyl, X = Cl, F.

The ^{1}H NMR spectra and Cosy experiments obtained for monomers **5.4** and **5.6** (Figs. 5.2a and 5.2b) and those of the hyperbranched poly (aryl ether sulfone)s **5.7** and **5.8** confirm their general structures (Figs. 5.3a and 5.3b). Hyperbranched poly(aryl ether sulfone) **5.7** and **5.8** show signals that corresponded to those of the more regular dendritic poly(aryl ether sulfone)s prepared by us using the divergent- growth approach.

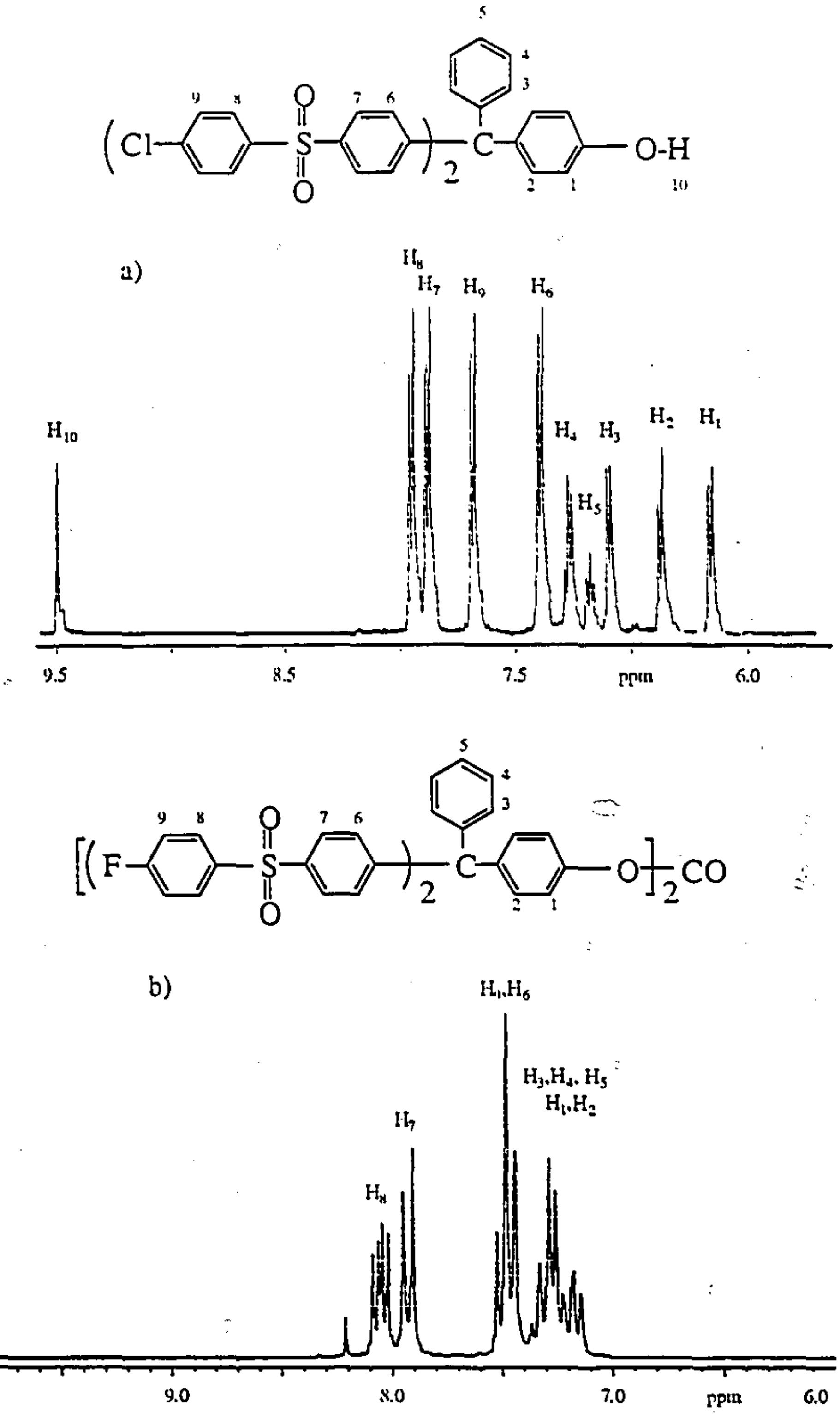


Figure 5.2. ^{1}H NMR spectra of monomers: a) 5.4 and b) 5.6.

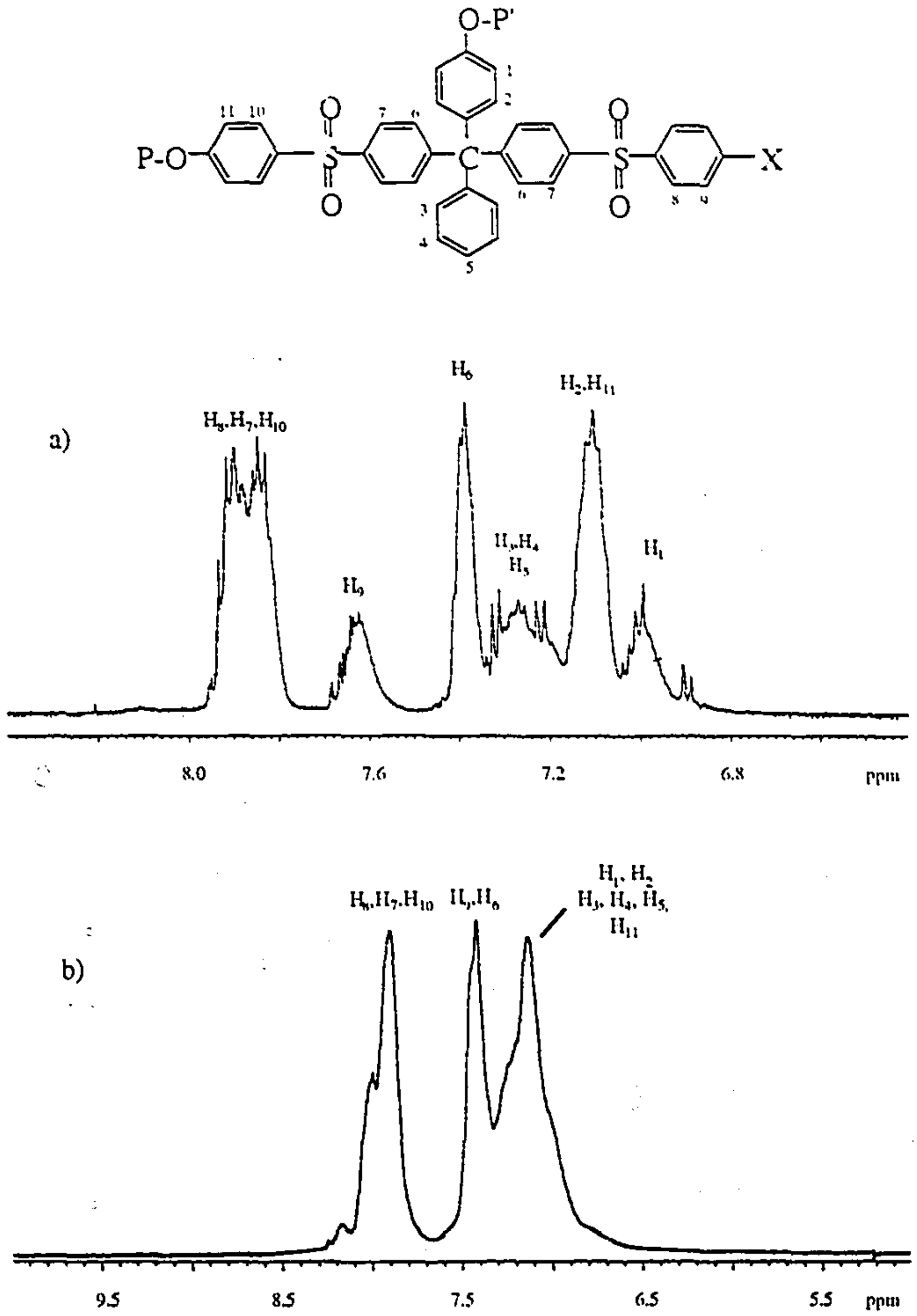


Figure 5.3. ^{1}H NMR spectra of hyperbranched poly(aryl ether sulfone)s: a) **5.7** (X = Cl) and b) **5.8** (X = F). P and P' are hyperbranched fragments of the polymer.

The structure numbers in the NMR figures represent the different hydrogen atoms on the molecule which were arbitrarily chosen.

For example, the aromatic protons ortho to the sulfone group (H_7, H_8, H_{10}) resonate at about 7.9 ppm and the aromatic protons ortho to the chloride or fluorides (H_9) resonate at about 7.6 and 7.4 ppm, respectively. The high intensity and broadness of the resonances of the aromatic protons close to the oxygen suggest that the displacement of the halides took place and that ether linkages were formed.

The same general conclusions are obtained from the ^{13}C NMR spectrum of poly (aryl ether sulfone)s **5.7** and **5.8** (Figs. 5.4a and 5.4b). For example, there are two important signals for C's at the ß positions from oxygen atoms (C_2, C_{20}) in the hyperbranched polymers **5.7** and **5.8** which resonate at about 118 ppm and 119 ppm, but there is only a single signal for carbons of that type in the monomer. This carbon (C_2) resonates at about 115 ppm (Figs. 5.5a and 5.5b). We can observe, very close to these signals, the resonances of the C_{16}'s (ß position from the fluoro atom) in the monomer **5.6** and in the hyperbranched polymer **5.8** .

Matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF-MS) (16) was used for the mass determination of **5.7** and **5.8**. The analysis was carried out on a Kratos Compact MALDI III instrument in the reflectron mode using dithranol as the matrix. Silver trifluoroacetate was added to stabilize the system. The Figure 5.6 shows the quality of the spectra achieved which have excellent signal-to-noise ratio. We see evidence for the formation of oligomers with degree of polymerization between 2 and 9. However, by this method we can not exclude the possibility that higher molecular weight material may have been formed.

The values of mass/charge found correspond to the oligomeric molecular ions (a silver cation is complexed with the oligomeric molecules).

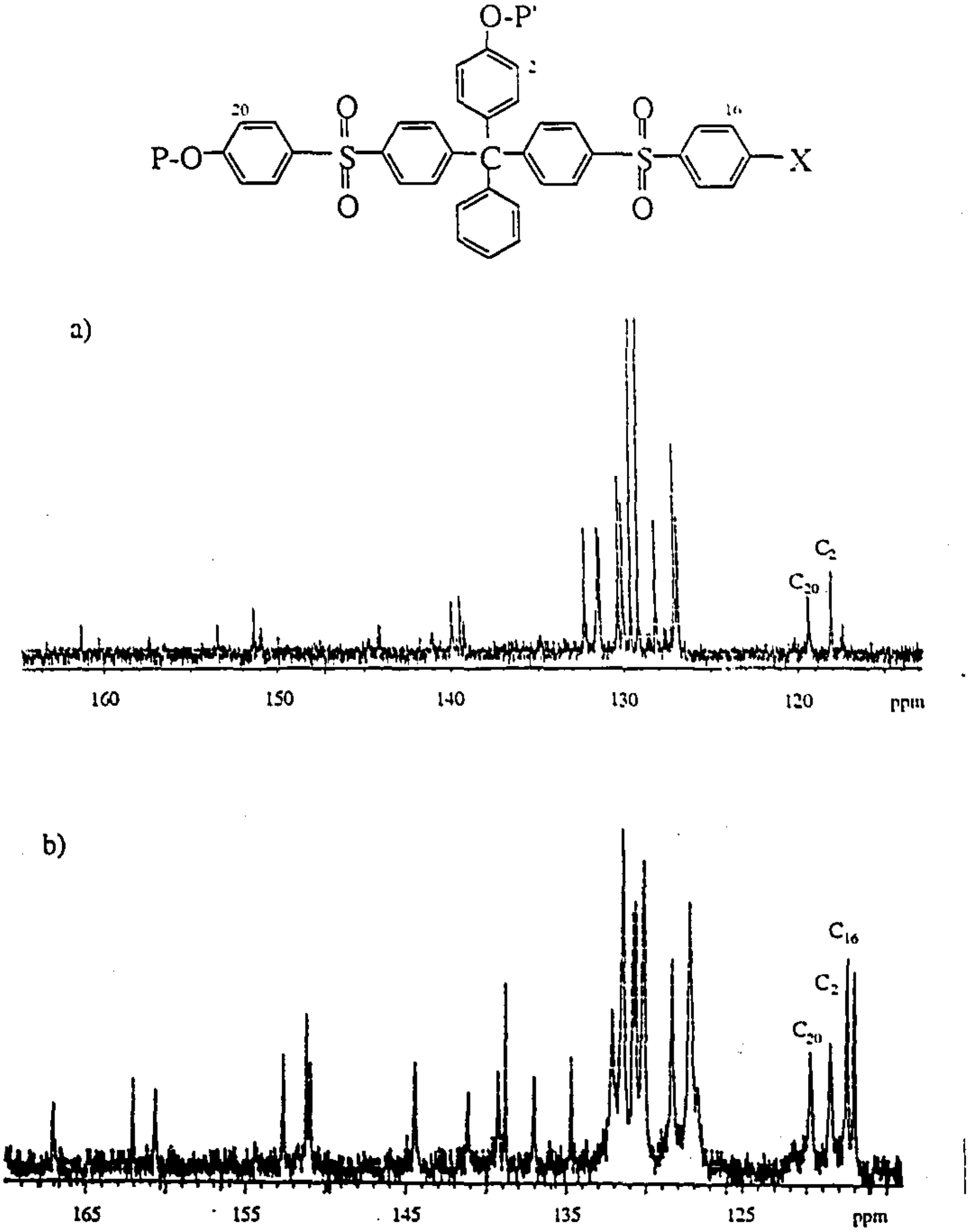


Figure 5.4. ^{13}C NMR spectra of hyperbranched poly(aryl ether sulfone)s: a) **5.7** (X = Cl) and b) **5.8** (X = F). P and P' are hyperbranched fragments of the polymer.

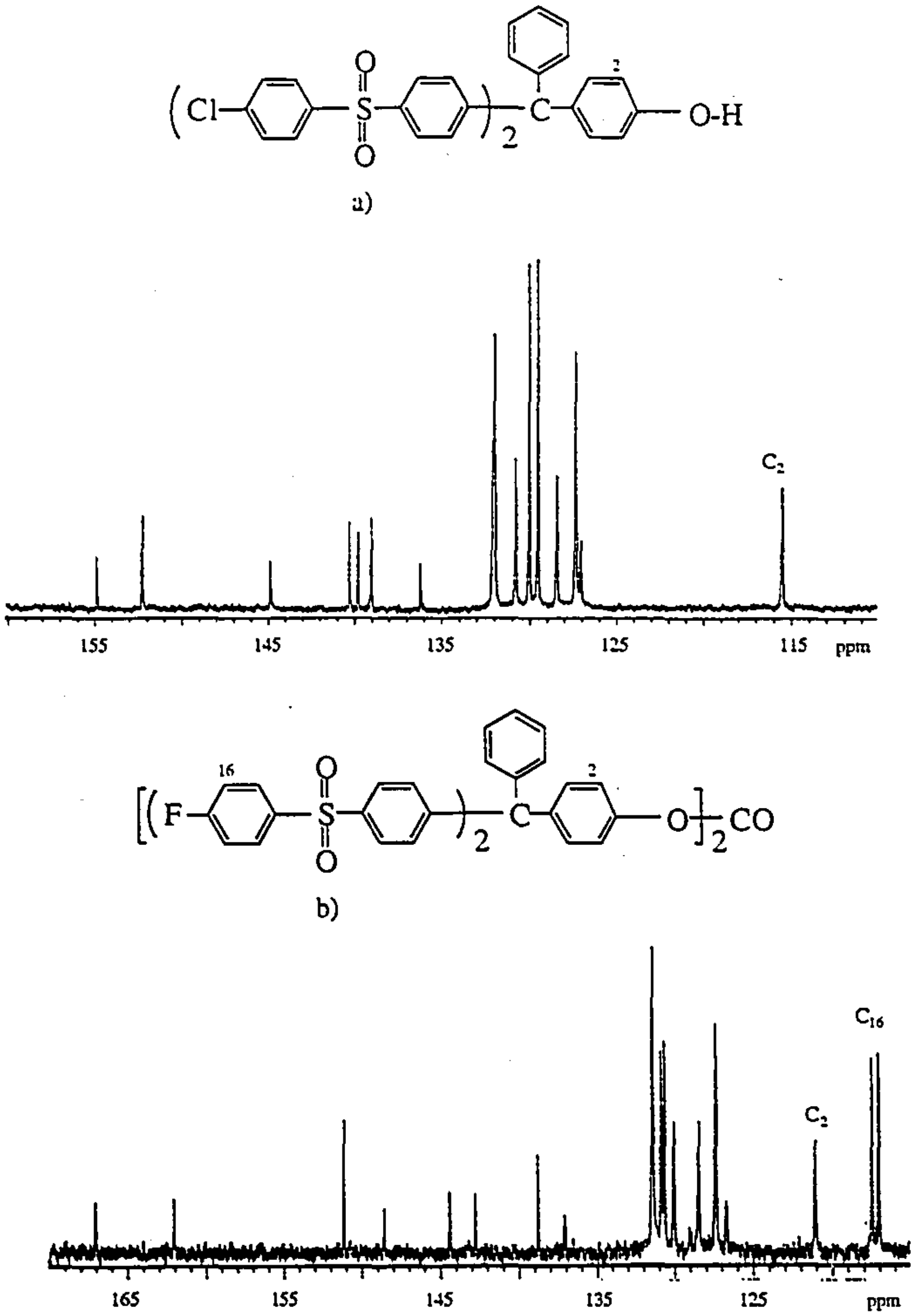


Figure 5.5. ^{13}C NMR spectra of monomers: a) 5.4 and b) 5.6.

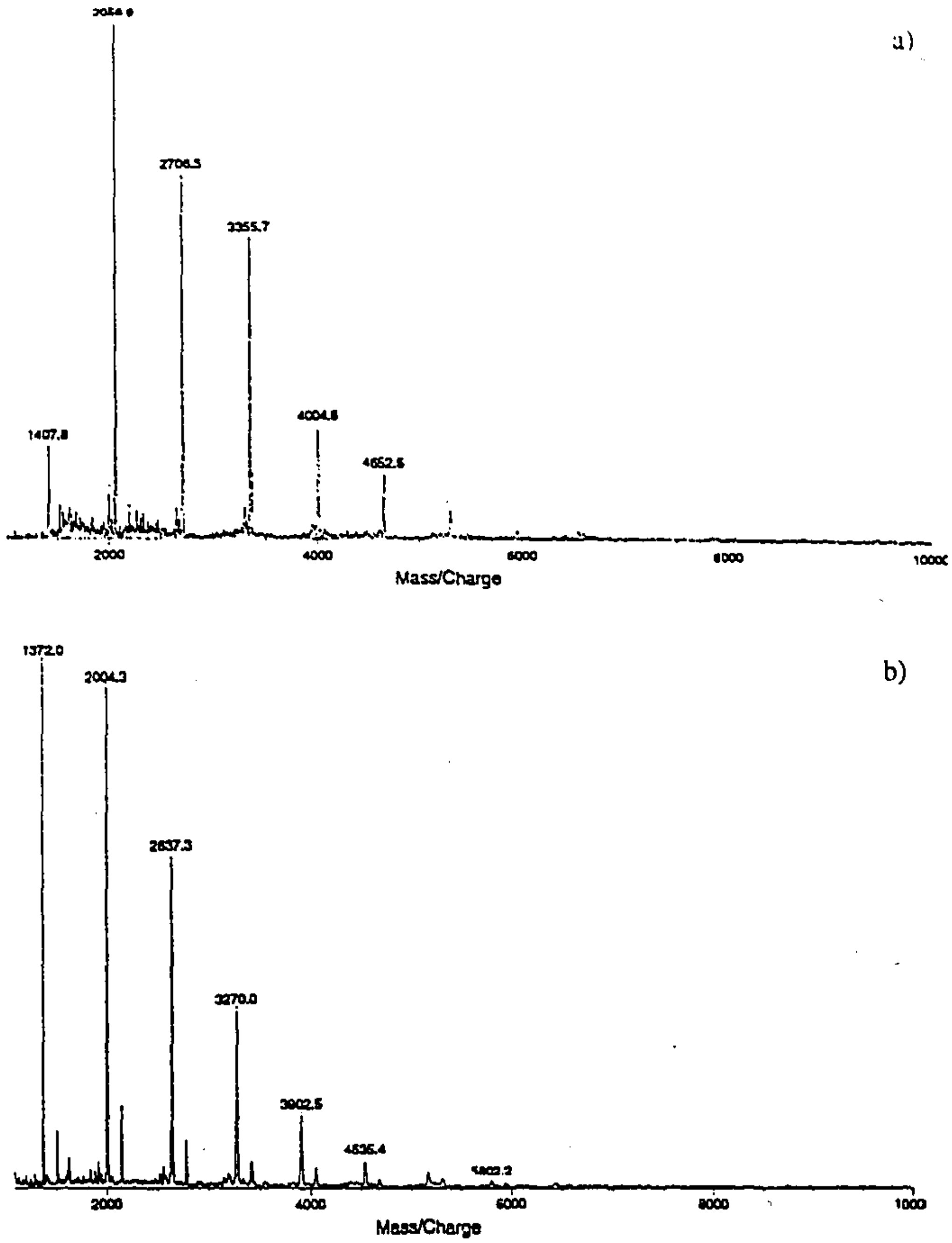


Figure 5.6. MALDI mass spectra of hyperbranched poly(aryl ether sulfone)s: a) **5.7** and b) **5.8**.

The molecular masses, M's, of the hyperbranched polymers **5.7** and **5.8** (Table 5.2) were calculated using the following general equation:

$$M\ (n) = n\ (A - B)\ \text{Da}$$

In this equation n represents the degree of polymerization of the oligomer, A is the molecular mass of the respective monomer (**5.4**: 685.7 Da, **5.6**: 652.7 Da), and B is the molecular mass of the small molecule eliminated during the condensation reaction (HCl for the hyperbranched polymer **5.7** and HF for the hyperbranched polymers **5.8**). For example, the molecular masses for the hyperbranched polymer **5.8** were obtained using A = 652.7 Da, B = 20 Da.

Table 5.2. MALDI mass spectrometric analyses of hyperbranched polymers a)

Dendrimer	**5.7**	**5.7**	**5.8**	**5.8**
n b)	$(M+Ag)^+$ c)	Mass/Charge	$(M+Ag)^+$ c)	Mass/Charge
2	1406.5	1407.8	1373.4	1372
3	2055.75	2056.9	2006.1	2004.3
4	2705	2706.5	2638.8	2637.3
5	3354.25	3355.7	3271.5	3270
6	4003.5	4004.6	3904.2	3902.5
7	4652.75	4652.6	4536.9	4535.4
8	5302	5301.5	5169.6	5167.9
9	5951.25	5950	5802.3	5802.2

a). Dithranol:sample:CF_3CO_2Ag = 40:4:2. b) n = grade of polymerization. c) MI = sample molecular mass, Da; Ag = silver atomic mass, Da.

In general, when n molecules react to generate n ether linkages, n - 1 molecules of HCl or HF are eliminated. Since the ^{1}H NMR spectrum of **5.7** and **5.8** did not show any evidence of a hydroxyl group in the hyperbranched polymer, the probable termination reaction is the displacement of a chloride or fluoride by the only hydroxyl group present in the molecule. It indicates that some internal cyclization probably took place, and it explains the fact that our system lost n and not n-1 molecules of HCl and HF.

However, reductive dechlorination can not be excluded as a possible side reaction since if an atom of chloro is displaced by an atom of hydrogen the differences between the calculated molecular masses and the experimental values of mass/charge are still reasonable.

The small peak that accompanies each of the intense signals of the MALDI mass spectrum of **5.8** can be a consequence of the impurity found in the monomer **5.6**, since the difference between the molecular masses is about 140 g/mol which could correspond to the molecular mass of -$C_6H_4SO_2$-.

The differences between the calculated and the experimental values are lower than 0.1%. The MALDI mass spectrometric data accumulated were very useful in the identification of the termination reactions and characterization of the lower molecular weight species formed in the polymerization reaction. Unfortunately, it was not possible to detect any special effects related to the nature of the monomers, condensation agent, or conditions employed in the polymerization reaction relative to the molecular weights obtained. The differences observed in the maximum values of masses detected for these samples are probably due to the technique itself. Even though the general mass spectra of these samples were all similar, we observed differences in the peak intensities and in the maximum molecular weight reached for a single sample analyzed several times. It is known that the way the sample, matrix, and stabilizer interact and coprecipitate affects the characteristics of the mass spectra as well as other conditions such as beam power, shot number, area analyzed, and nature of the sample.

5.2.6 Effect of polymerization reaction conditions on the characteristics and properties of hyperbranched poly(aryl ether sulfone)s.

The influence of factors such as monomer concentration, temperature, reaction time, and solvent on the condensation reaction was explored. The molecular masses of hyperbranched polymers were measured by SEC relative to polystyrene narrow molecular mass standards. The shape of the SEC chromatograms of hyperbranched polymers **5.7** and **5.8** (Figs. 5.7 and 5.8) showed overlay peaks which indicated that species with very different molecular weight and size were present in these samples. Since the chromatograms are not represented by Gaussian curves, the data obtained probably gives only a rough idea of the molecular characteristics of these polymers.

The weight average molecular weight, Mw, polydispersity, PD, and viscosity of fluoride-terminated hyperbranched polymer **5.8** were affected by the reaction conditions, as shown in Table 5.3. An increase in monomer concentration, under reflux conditions and using DMAc as the solvent of the reaction, caused an increase in Mw, PD, and viscosity. Concentrations higher than 0.6 mol/L produce some insoluble materials. The use of a higher concentration (0.63 mol/L) with a lower reaction temperature (150°C) was not practical since it generated a relatively low viscosity hyperbranched polymer. It suggests that temperatures lower than 164°C are not favorable for this synthesis.

The same general results are valid for the synthesis of the hyperbranched polymer **5.7** (Table 5.3). Concentrations higher than 0.2 mol/L, under reflux conditions and using NMP as the solvent, yielded some insoluble materials. The lower maximum concentration can be a consequence of the higher reaction temperature or a relatively lower rate of the termination reaction. A reaction time of 2 hours was sufficient for this reaction, since the characteristics and properties of the hyperbranched polymer **5.7** were not appreciably changed by a longer reaction time.

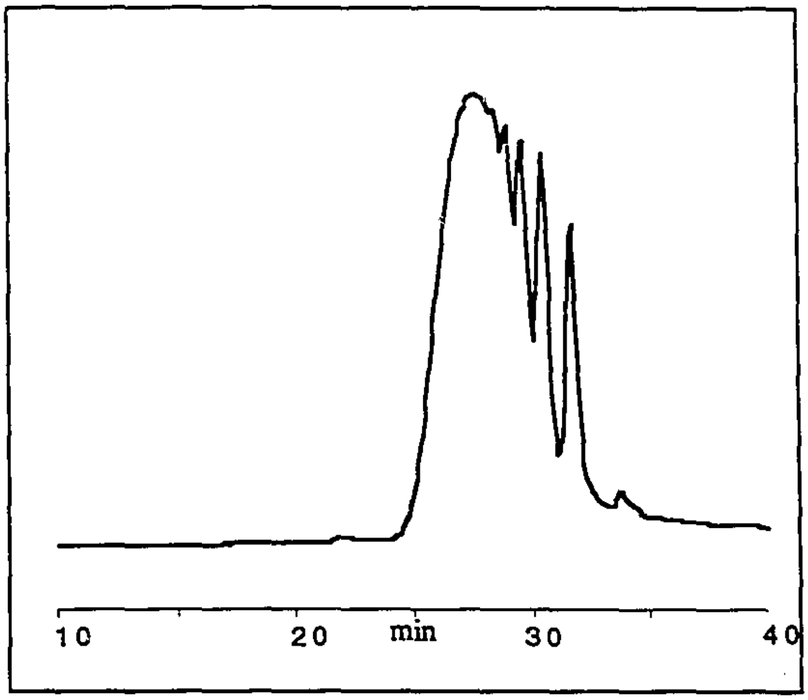


Figure **5.7**. SEC chromatogram of hyperbranched poly(aryl ether sulfone) **5.7**. Monomer concentration: 0.20 mol/L. Analysis conditions in **Table 5.3**.

The synthesis of hyperbranched polymer **5.8** was more efficient than that of hyperbranched polymer **5.7** since the resulting yield (95% vs 82%) and viscosity of **5.8** were higher when similar conditions were employed (compare **5.8-2** vs **5.7-3**). In the synthesis of **5.8** the condensation agent was a mixture of Cs_2CO_3 and $Mg(OH)_2$, the phenolate was generated *in situ* from a carbonate, and the displaced halide was a fluoride.

The analysis of our results indicated that relatively low monomer concentrations are not practical since intramolecular cyclizations cause the termination of the polymerization reaction, as was shown in the previous MALDI mass spectrometric study, with the consequent generation of a low molecular weight and low viscosity hyperbranched polymer. On the other hand, relatively high monomer concentrations favored bimolecular reaction which produce insoluble materials and high viscosity reaction mixtures which are difficult to stir.

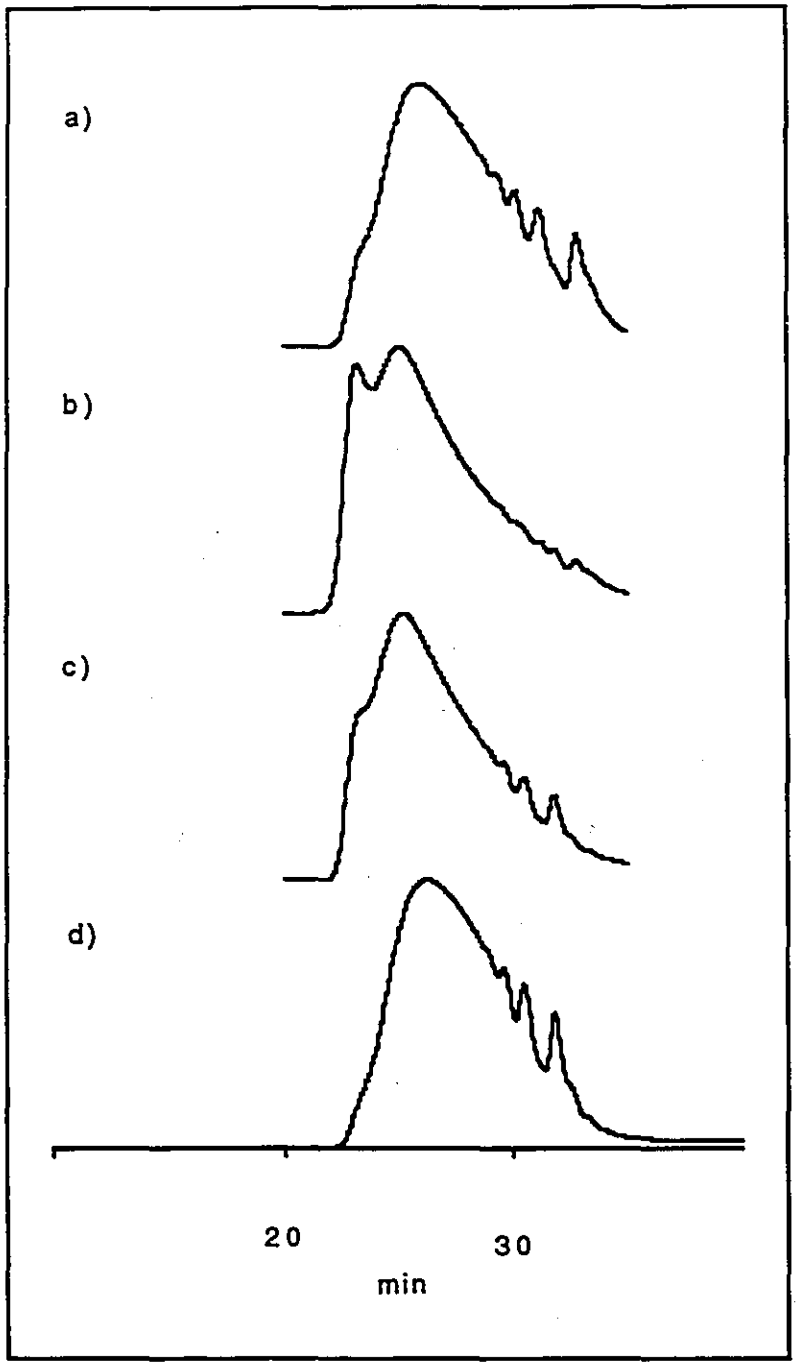


Figure 5.8. SEC chromatograms of hyperbranched poly(aryl ether sulfone) **5.8.** Monomer concentrations: a) 0.63 mol/L, b) 0.42 mol/L, c) 0.22 mol/L, and d) 0.13 mol/L. Analysis conditions in **Table 5.3.**

Table 5.3. Effect of the polymerization reaction conditions on the characteristics and properties of hyperbranched poly(aryl ether sulfone)s 5.7 and 5.8

Polymer	5.8-1	5.8-2	5.8-3	5.8-4	5.7-1	5.7-2	5.7-3
T (°C)	164	164	164	150	180	180	180
t (h)	2	1	1	1	15	6	2
C (mol/L)	0.13	0.22	0.42	0.63	0.15	0.20	0.20
ninh (dL/g) a)	0.10	0.13	0.18	0.09	0.09	0.09	0.10
Tg (°C) b)	-	-	239	-	239	229	226
Td (°C) c)	-	-	467	-	488	472	462
Mw (g/mol) d)	9545	16600	20833	10309	5535	4980	4770
PD	3.1	4.2	5.1	4.7	2.2	2.3	2.2

a) NMP, 0.5 g/dL, 25°C. b) Nitrogen, 10 °C/min. c) 5% weight loss, 10 °C/min, nitrogen. e) SEC, based on polystyrene standards, chloroform, 1mL/min, UV-Detector. d) NMP, 0.5 g/dL, 25 °C. c) Nitrogen, 10 °C/min. d) 5% Weight Loss, nitrogen, 10 °C/min.

5.2.7 Properties.

The hyperbranched poly(aryl ether sulfone)s **5.7** and **5.8** were soluble in common organic solvents (THF, $CHCl_3$, DMAc), and showed low inherent viscosities (not higher than 0.20 dL/g)).

Thermal properties were studied by differential scanning calorimetry (DSC) and thermogravimetric analysis (TGA), (Table 5.3). We observed a Tg but no evidence for melting or crystallization in the polymer. Polymers **5.7** and **5.8** have thermal properties and inherent viscosities similar to those of the more regular dendritic poly(aryl ether sulfone)s prepared by us by the divergent-growth approach. For example, glass transition temperature, Tg, for the third generation dendritic poly(aryl ether sulfone) was about 220°C.

Thermal gravimetry analyses under nitrogen at 10°C/min showed that 5.7 and 5.8 retain 95 % of their mass up to 470°C and have high thermal stability, as do regular dendritic poly(aryl ether sulfone)s as well as the linear poly(ether ketone)s and poly(ether sulfone)s.

5.3 Phenol - terminated hyperbranched poly(aryl ether sulfone)s

5.3.1 Preparation of activated monomers 5.15-a and 5.15-b.

The general synthesis of the monomers **5.15-a** and **5.15-b** is shown in Scheme 5.6. The reaction began with the displacement of the fluoride of 4-fluoroacetophenone by a molecule of 4-chlorothiophenol **5.9-a** or fluorothiophenol **5.9-b**, using K_2CO_3 under mild conditions (13, 18) to obtain the condensation product **5.10-a** or **5.10-b**, respectively.

In the following step the bis-phenols **5.12** (**a** and **b**) were formed by condensation of **5.10** (**a** and **b**) with two molecules of phenol **5.11** employing sulfuric acid and mercaptoacetic acid as catalyst at room temperature. (19)

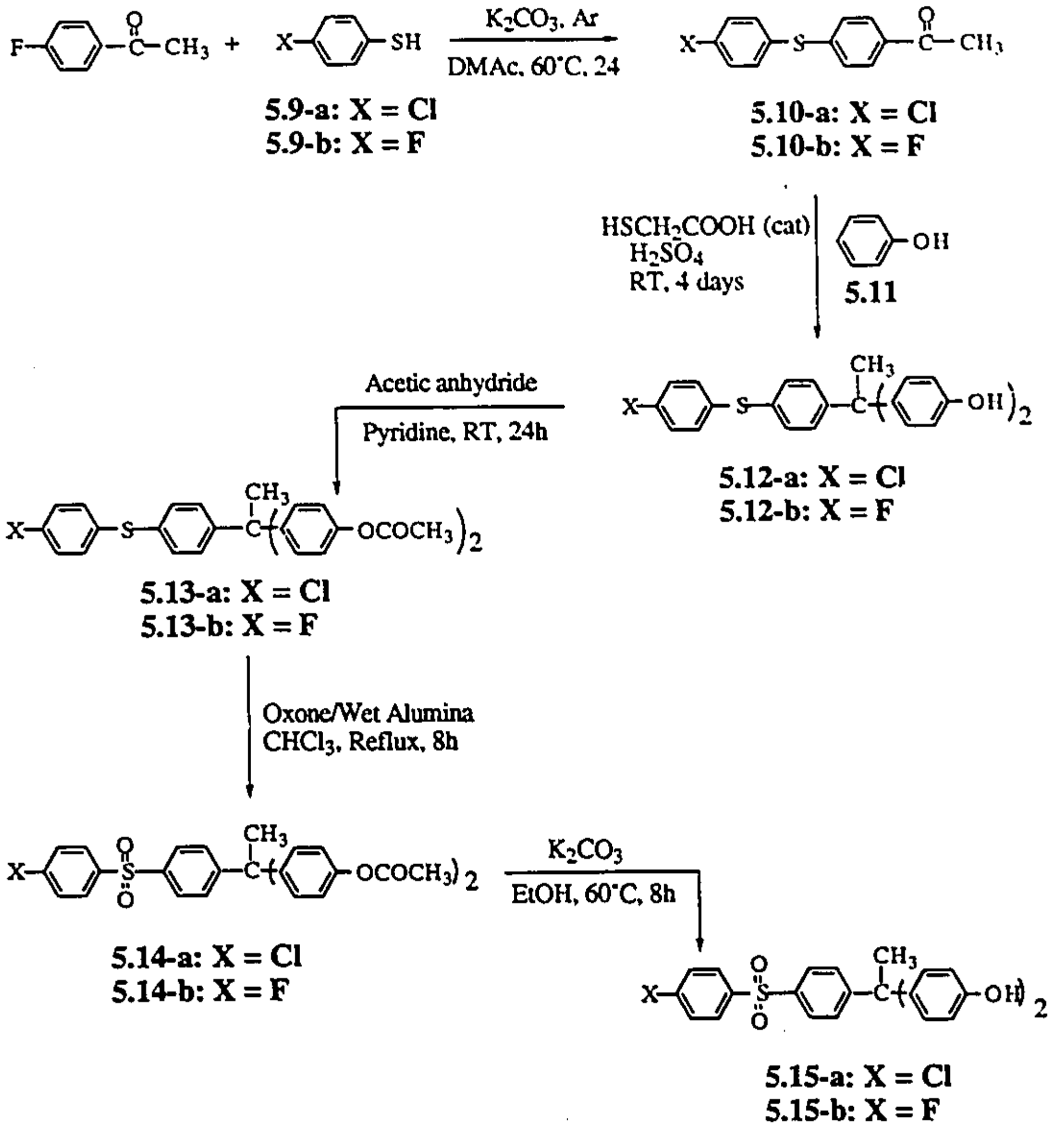
The last three reactions employed were the acetylation of the phenols, (13) to avoid their oxidation, followed by the oxidation of the aryl sulfide groups by Oxone, (14) and finally cleavage of the ester linkages (13) of **5.14** (**a** or **b**) to generate the activated monomers **5.15** (**a** or **b**) using potassium carbonate.

The overall yields of the monomer **5.15-a** and **5.15-b** from **5.8** were 27 % and 12 %, respectively. Nuclear magnetic resonance, NMR, and mass spectrometric characterization of each of those products confirmed the proposed structures (see Experimental Section).

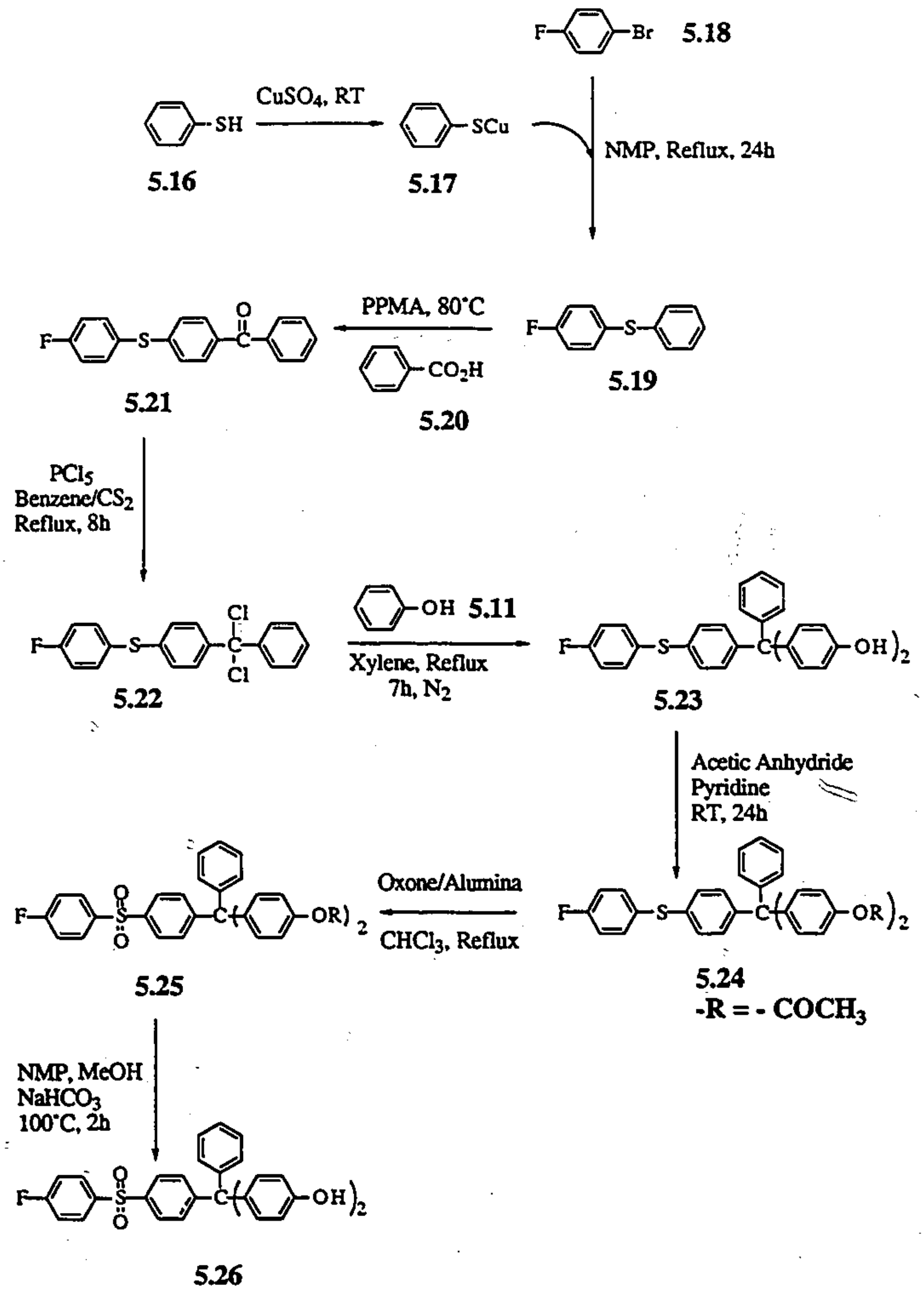
5.3.2 Preparation of activated monomer 5.26.

The synthesis of the monomer **5.26** is showed in Scheme 5.7. The reaction began with the formation of cuprous phenylmercaptide **5.17** (20) by the addition of thiophenol **5.16**, to a solution of copper sulfate at room temperature.

Scheme 5.6


F
CH3
X
SH
K2CO3, Ar
DMAc, 60°C, 24
5.9-a: X = Cl
5.9-b: X = F
5.10-a: X = Cl
5.10-b: X = F
HSCH2COOH (cat)
H2SO4
RT, 4 days
OH
5.11
Acetic anhydride
Pyridine, RT, 24h
5.12-a: X = Cl
5.12-b: X = F
OCOCH3
5.13-a: X = Cl
5.13-b: X = F
Oxone/Wet Alumina
CHCl3, Reflux, 8h
5.14-a: X = Cl
5.14-b: X = F
K2CO3
EtOH, 60°C, 8h
5.15-a: X = Cl
5.15-b: X = F

Scheme 5.7


5.18
CuSO4, RT
5.16
5.17
NMP, Reflux, 24h
PPMA, 80°C
5.21
5.20
5.19
PCl5
Benzene/CS2
Reflux, 8h
5.11
Xylene, Reflux
7h, N2
5.22
5.23
Acetic Anhydride
Pyridine
RT, 24h
Oxone/Alumina
CHCl3, Reflux
5.25
5.24
-R = - COCH3
NMP, MeOH
NaHCO3
100°C, 2h
5.26

The displacement of the fluoride of p-bromofluorobenzene **5.18** (21), by a molecule of cuprous phenylmercaptide **5.17**, gave 4-fluorodiphenylsulfide **5.19**, in an Ullman type reaction. The condensation product of this reaction **5.19**, in a Fridel-Craft reaction with benzoic acid **5.20**, employing phosphorus pentoxide/methanesulfonic acid, PPMA, as the condensing agent and solvent for the reaction (22) gave the ketone **5.21**.

In the following step the dichloride product **5.22** was formed from the carbonyl-containing compound **5.21** using phosphorus pentachloride as the chlorinating agent in benzene/carbon disulfide under reflux.(23) The dichloride product **5.22** was then made to react with two molecules of phenol **5.11**, in the presence of xylene as the inert solvent under reflux(24) to produce the bis-phenol **5.23**.

The last three reactions were the acetylation of the phenoxy groups of **5.23** to avoid their oxidation followed by the oxidation of the aryl sulfide groups by Oxone, and the cleavage of the ester linkages of **5.25** using sodium bicarbonate to form the activated monomer **5.26**.

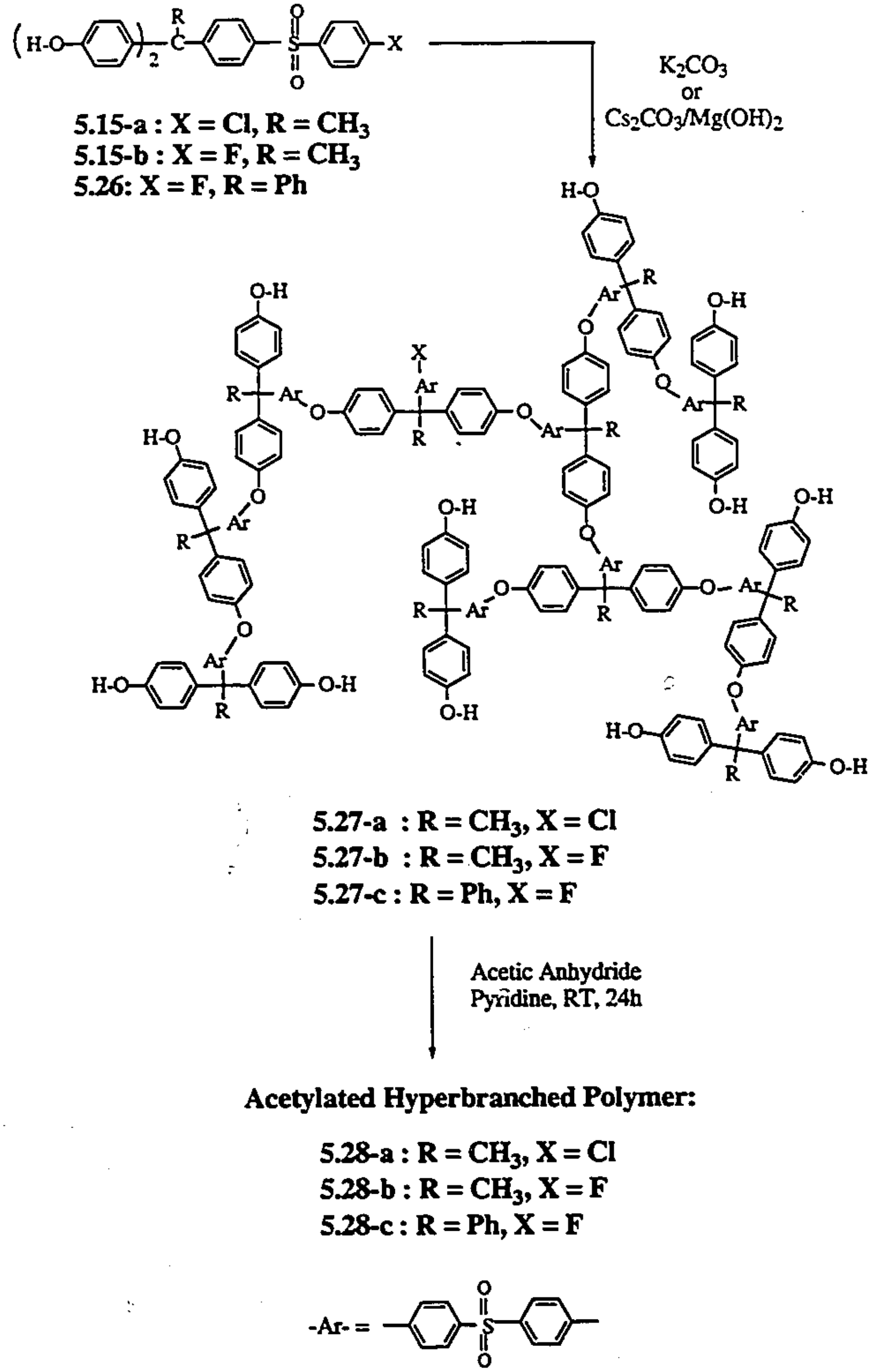
The overall yield of the monomer **5.26** from **5.15** was around 15 %. NMR and mass spectrometric characterization of each of those products confirmed the proposed structures (see Experimental Section).

5.3.3 Preparation of hyperbranched poly(aryl ether sulfone)s 5.27-a and 5.27-b.

The hyperbranched poly(aryl ether sulfone)s **5.27-a** and **5.27-b** were prepared by polycondensation of the activated monomers **5.15-a** and **5.15-b**, respectively.

The monomer **5.15-a** was polymerized using K_2CO_3 in NMP/toluene under nitrogen atmosphere, and the monomer **5.15-b** employing a mixture of Cs_2CO_3:$Mg(OH)_2$, DMAc/Toluene, and argon according to the general procedure described in Scheme 5.8.

Scheme 5.8



5.15-a : X = Cl, R = CH$_3$
5.15-b : X = F, R = CH$_3$
5.26: X = F, R = Ph

5.27-a : R = CH$_3$, X = Cl
5.27-b : R = CH$_3$, X = F
5.27-c : R = Ph, X = F

Acetylated Hyperbranched Polymer:

5.28-a : R = CH$_3$, X = Cl
5.28-b : R = CH$_3$, X = F
5.28-c : R = Ph, X = F

The resulting mixture was heated at 130°C and the water formed in the reaction was removed by azeotropic distillation. The toluene was distilled and the reaction mixture was heated at 150°C -180°C for 0.5 - 3.0 hours according to the procedure described in the Experimental Section. The mixture was cooled, poured into water acidified with a few drops of HCl, and the polymer filtered and dried. The yield in the reactions for **5.27-a** and **5.27-b** were 78% and 99%, respectively.

5.3.4 Preparation of hyperbranched poly(aryl ether sulfone) 5.27-c.

The hyperbranched poly(aryl ether sulfone) **5.27-c** was prepared by polycondensation of the activated monomer **5.26** using K_2CO_3 and DMAc/toluene under nitrogen atmosphere, (Method A) or a mixture of Cs_2CO_3:$Mg(OH)_2$, DMAc/Toluene, and argon (Method B) according to the general procedure shown in Scheme 5.8 and previously described for the syntheses of **5.27-a** and **5.27-b**. The yield of the reaction for both methods was about 92 %.

5.3.5 Nuclear magnetic resonance.

The structures of hyperbranched polymers **5.27-a**, **5.27-b**, and **5.27-c** consist of terminal units (T), lineal units (L), and branching points (R), as shown in Scheme 5.9. However, due to the complexity of these systems only a general assignation of the absorption to the different protons or carbons in these molecules was possible. The broad molecular size distribution of these polymers led to significant peak broadening in their ^{1}H NMR spectra. To simplify this study we chose the lineal block "L" to describe the NMR spectra. This is the only block that can generate all the different possible signals in the polymer.

The ^{1}H NMR spectra of monomers **5.15-a**, **5.15-b**, and **5.26** and those of the hyperbranched poly(aryl ether sulfone)s **5.27-a**, **5.27-b**, and **5.27-c** confirm their general structures (Figs. 5.9, 5.10a, 5.11a, and 5.12a).

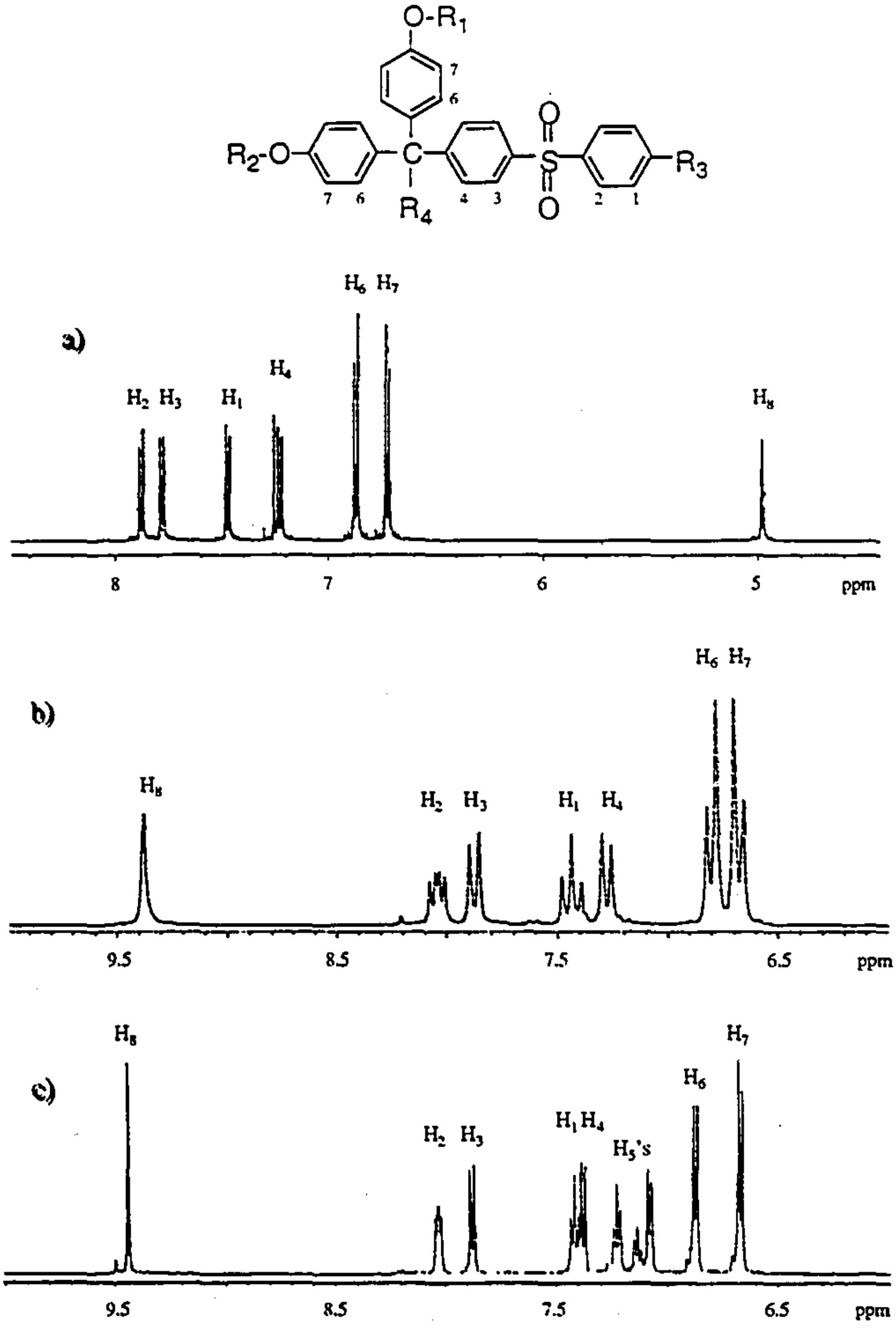


Figure 5.9. ^{1}H NMR spectra of monomers ($R_1 = R_2 = H$): a) **5.15-a:** $R_3 = Cl$, $R_4 = CH_3$, b) **5.15-b:** $R_3 = F$, $R_4 = CH_3$, and c) **5.26:** $R_3 = F$, R_4 = Phenyl (H_5's).

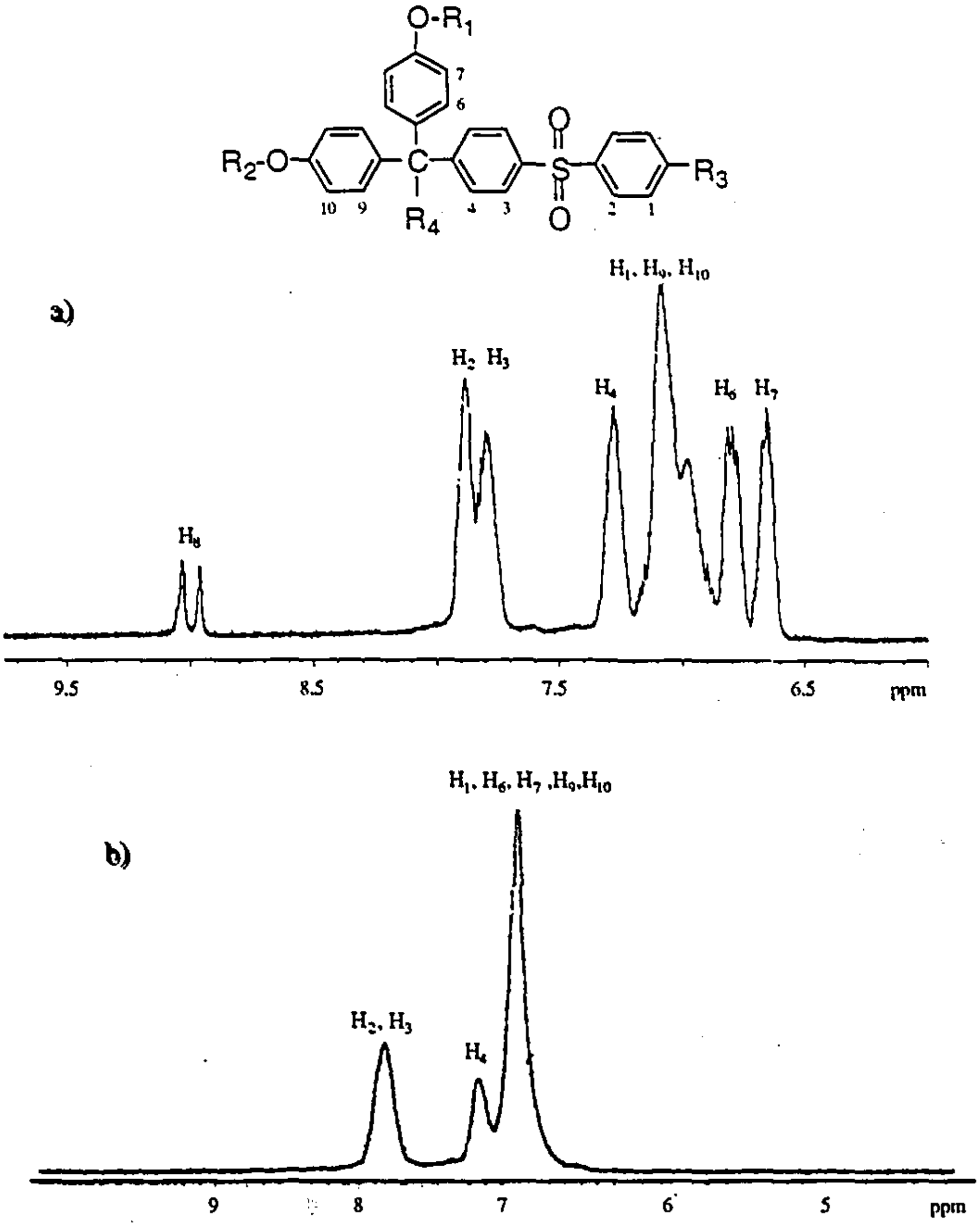


Figure 5.10. ^{1}H NMR spectra of hyperbranched poly(aryl ether sulfone)s (R_2 = P, R_3 = OP', R_4 = CH_3): a) **5.27-a** (R_1 = H_8), b) **5.28-a** (R_1 = $COCH_3$). P and P' are segments of hyperbranched polymers.

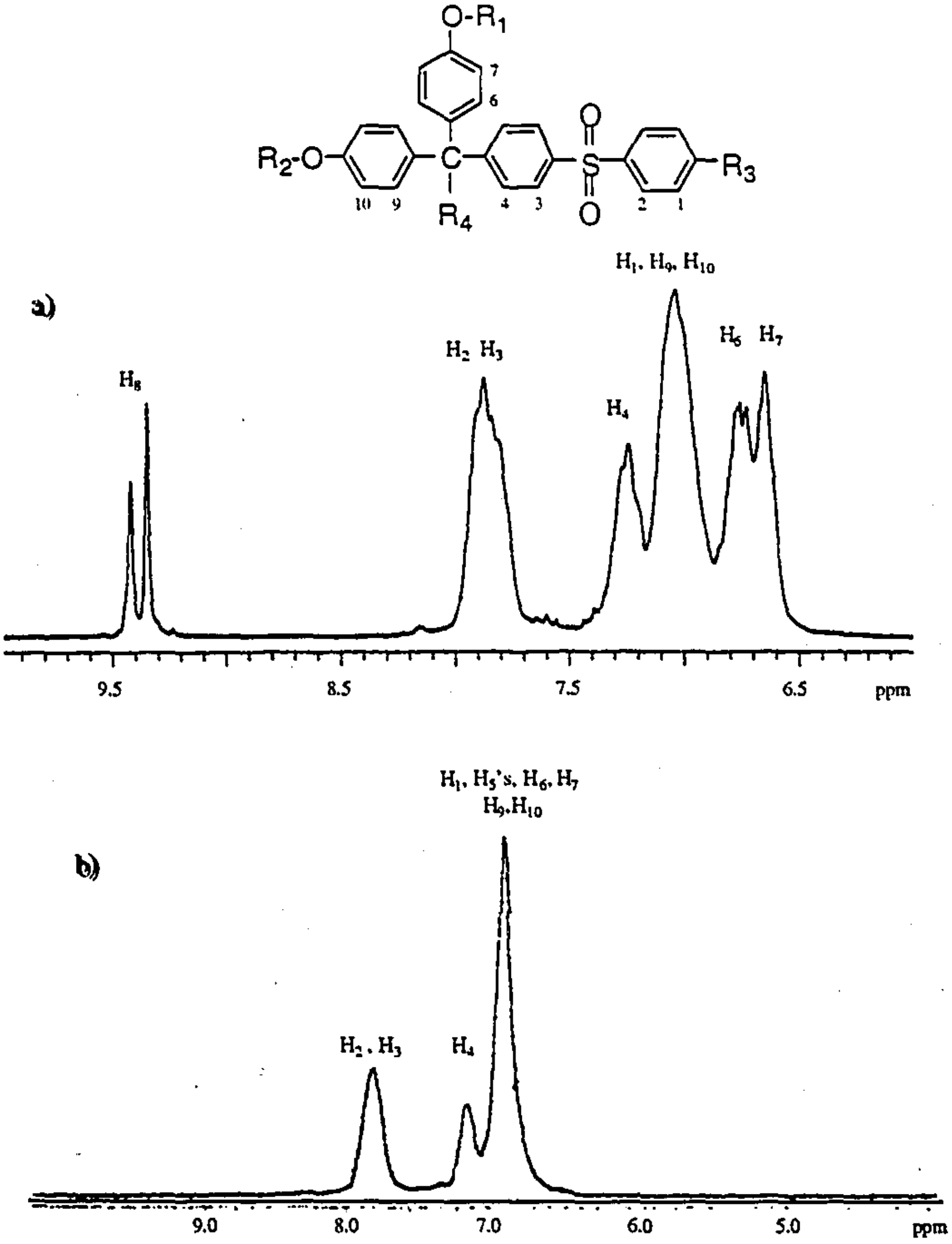


Figure 5.11. ^{1}H NMR spectra of hyperbranched poly(aryl ether sulfone)s (R_2 = P, R_3 = OP', $R_4 = CH_3$): a) **5.27-b** (R_1 = H_8), b) **5.28-b** ($R_1 = COCH_3$). P and P' are segments of hyperbranched polymers.

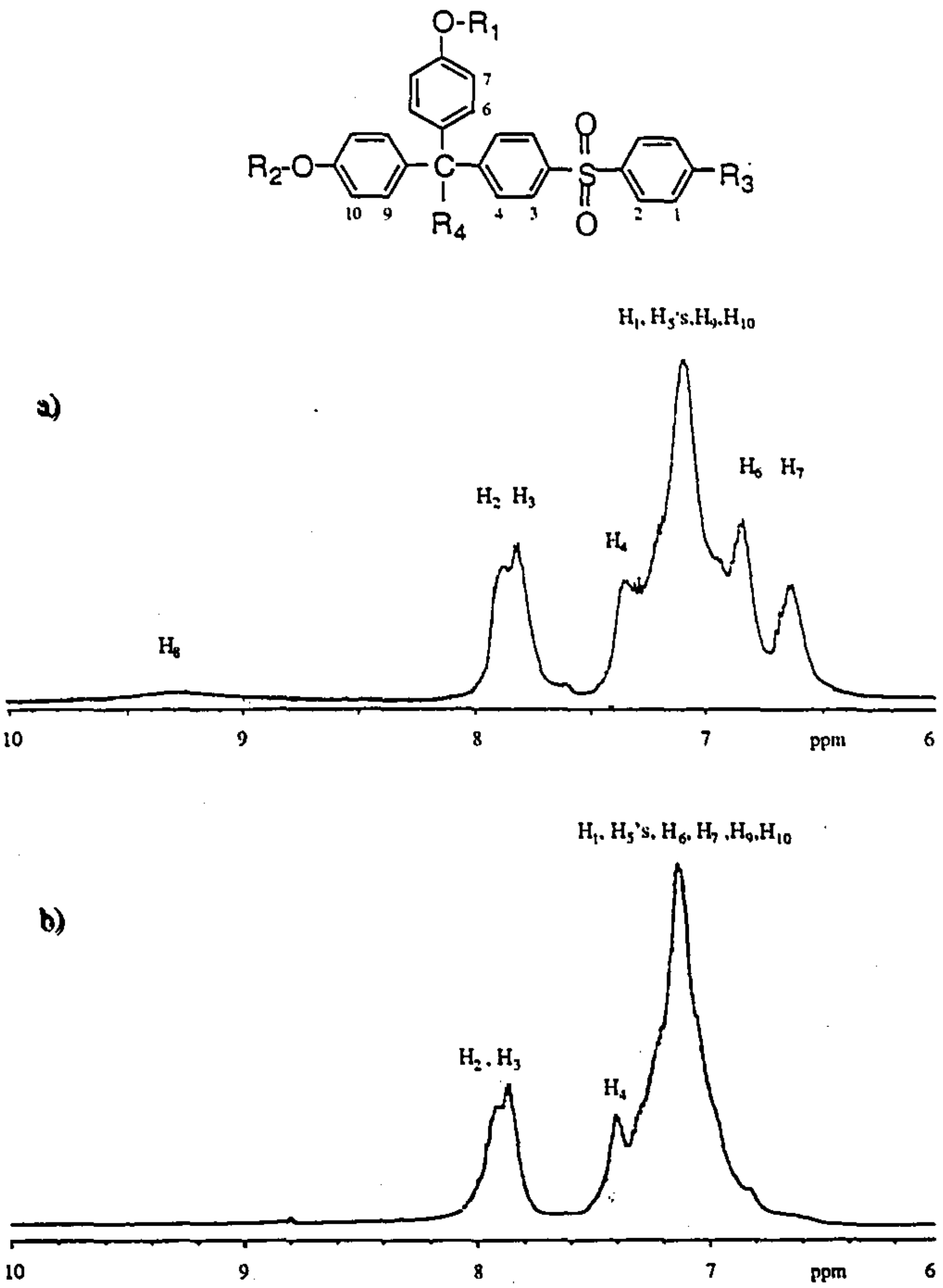
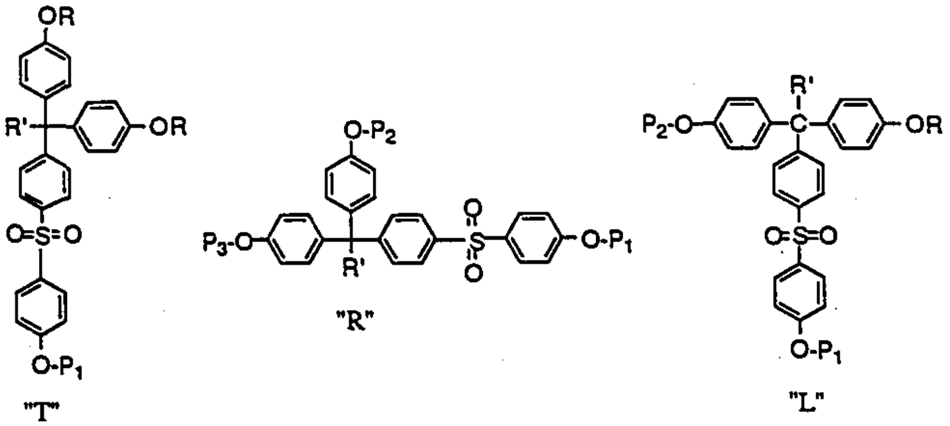


Figure 5.12. ^{1}H NMR spectra of hyperbranched poly(aryl ether sulfone)s (R_2 = P, R_3 = OP', R_4 = Phenyl (H_5's)): a) **5.27-c** ($R_1 = H_8$), and b) **5.28-c** ($R_1 = COCH_3$). P and P' are segments of hyperbranched polymers.

The spectra of the monomers show resonances corresponding to $HO-C_6H_4$- terminal groups (H_6, H_7). The fact that the resonance of the aromatic protons ortho to the chlorides and fluorides, H_1, present in the monomers (7.4 - 7.5 ppm) disappeared in the polymers and that the resonances of the aromatic protons close to the ether bonds in the polymers (H_1, H_2, H_9, H_{10}) are intense suggest that the displacement of the chloride and fluorides took place and that ether linkages were formed.

Scheme 5.9



P = polymer segment; R = H, acetyl; R' = methyl, phenyl.

Polymers **5.27-a** and **5.27-b** have the same repeat and terminal units; they only differ in the method of synthesis. Consequently, the NMR results are very similar.

5.3.5.1 Functionalization.

The self-condensation of monomers **5.15-a**, **5.15-b**, and **5.26** described above results in the formation of hyperbranched polymers **5.27-a**, **5.27-b**, and **5.27-c** with phenolic chain ends. These multiple chain ends have a high reactivity and can be converted into the corresponding acetyl esters. This modification changes the solubility of these polymers and may be useful in their characterization.

Acetylation of phenol-terminated poly(aryl ether sulfone)s **5.27-a**, **5.27-b**, and **5.27-c** with acetic anhydride and pyridine (13) gave the acetyl-terminated poly(aryl ether sulfone)s **5.28-a**, **5.28-b**, and **5.28-c** . The absence of the phenolic O-H stretch at 3300 cm^{-1} indicates that the functionalization was complete (Fig. 5.13). In contrast to the phenol-terminated poly(aryl ether sulfone)s which were soluble in alcohols, aqueous base, or highly polar aprotic solvents such as THF and DMF, the functionalized poly(aryl ether sulfone)s **5.28-a**, **5.28-b**, and **5.28-c** were soluble in a variety of organic solvents such as chloroform or toluene.

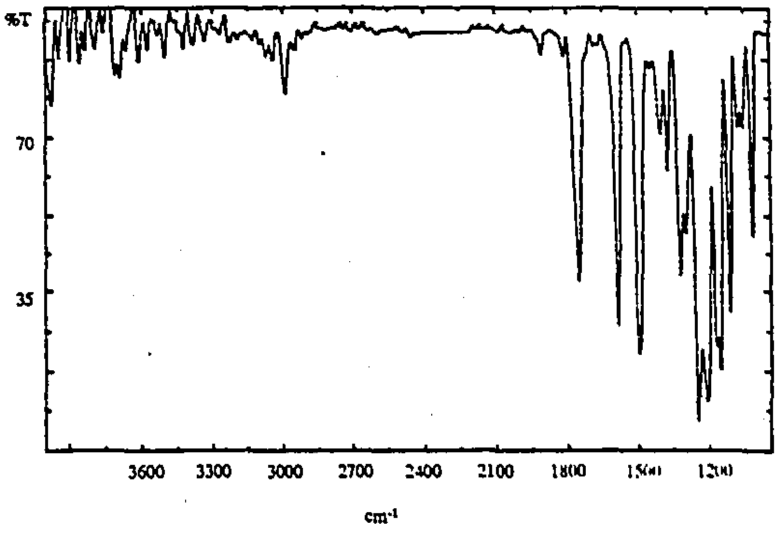


Figure 5.13. FTIR spectrum of acetylated hyperbranched poly(aryl ether sulfone) **5.28-a** in $CDCl_3$.

The ^1H NMR spectra of **5.28-a**, **5.28-b**, and **5.28-c** (Figs. 5.10b, 5.11b, and 5.12b) and Cosy experiments are in agreement with the proposed structures. The signals for the aromatic protons closer to the sulfone groups (H_2, H_3) resonated at about 7.8 ppm. The aromatic protons closer to the oxygen (H_1, H_7, H_{10}) and to the quaternary carbons (H_4, H_6, H_9) range from 7.5 ppm - 6.7 ppm, while the resonances for the methyl protons are seen near 2.1 ppm.

The same general conclusions are obtained from the ^{13}C NMR spectra of these poly (aryl ether sulfone)s. For example, there are three signals for C's at ß positions from oxygen atoms (C_2, C_{12}, C_{17}) in the acetylated products of the hyperbranched polymers which resonate at about 120 ppm, 122 ppm, and 118 ppm but there is only a single signal for that type of carbons in the monomers. This carbon, C_{12}, resonates at about 115 ppm (Figs. 5.14, 5.15, and 5.16), very close to the C at the ß position from the fluoro atom in the monomers **5.15-b** and **5.26** (C_2).

5.3.6 MALDI mass spectrometric characterization.

Matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF-MS) was used for the mass determination of these hyperbranched polymers.

The analyses was carried out on a Kratos Compact MALDI III instrument in the reflectron mode using dithranol as the matrix. Silver trifluoroacetate was added to stabilize the system. The MALDI mass results of the hyperbranched polymers **5.27-a**, **5.27-b**, and **5.27-c** and those of their respective acetylated products **5.28-a**, **5.28-b**, and **5.28-c** are given in figures 5.17 and 5.18 and in Tables 5.4 and 5.5. We see evidence for the formation of oligomers with degree of polymerization between 2 and 14; however by this method we can not exclude the possibility that higher molecular weight materials have been formed.

The values of mass/charge found correspond to the oligomeric molecular ion (a silver cation is complexed with the oligomeric molecules). The molecular masses, M's, of the hyperbranched poly(aryl ether sulfone)s **5.27-a**, **5.27-b**, and **5.27-c** were calculated using the following general equation:

$$M(n) = n\,(A - B)\ \mathrm{Da}$$

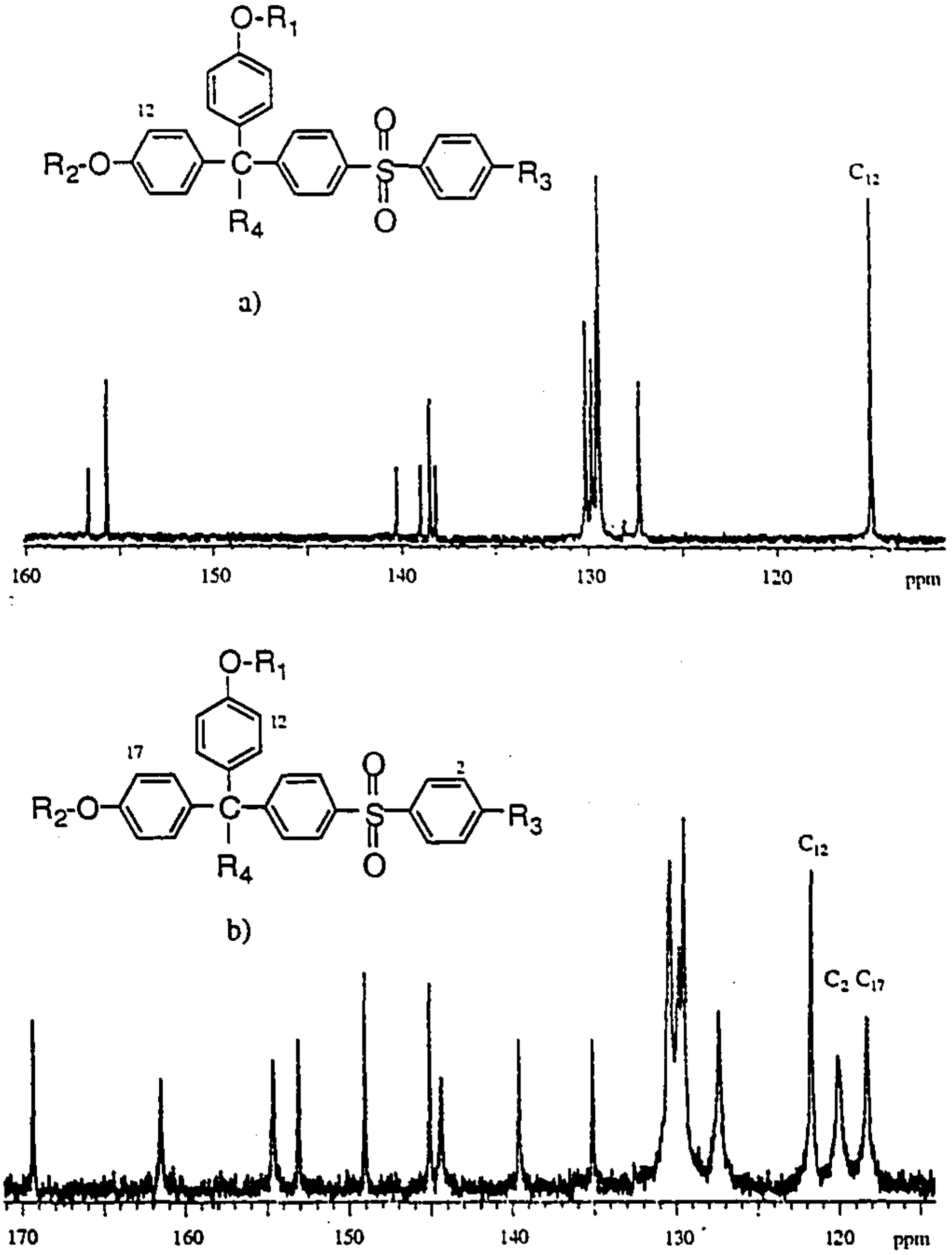


Figure 5.14. ^{13}C NMR spectra of: a) monomer **5.15-a** ($R_1 = R_2 = H$, $R_3 = Cl$) and b) hyperbranched poly(aryl ether sulfone) **5.28-a** ($R_1 = COCH_3$, $R_2 = P$, $R_3 = OP'$). P and P' are segments of hyperbranched polymers, and $R_4 = CH_3$.

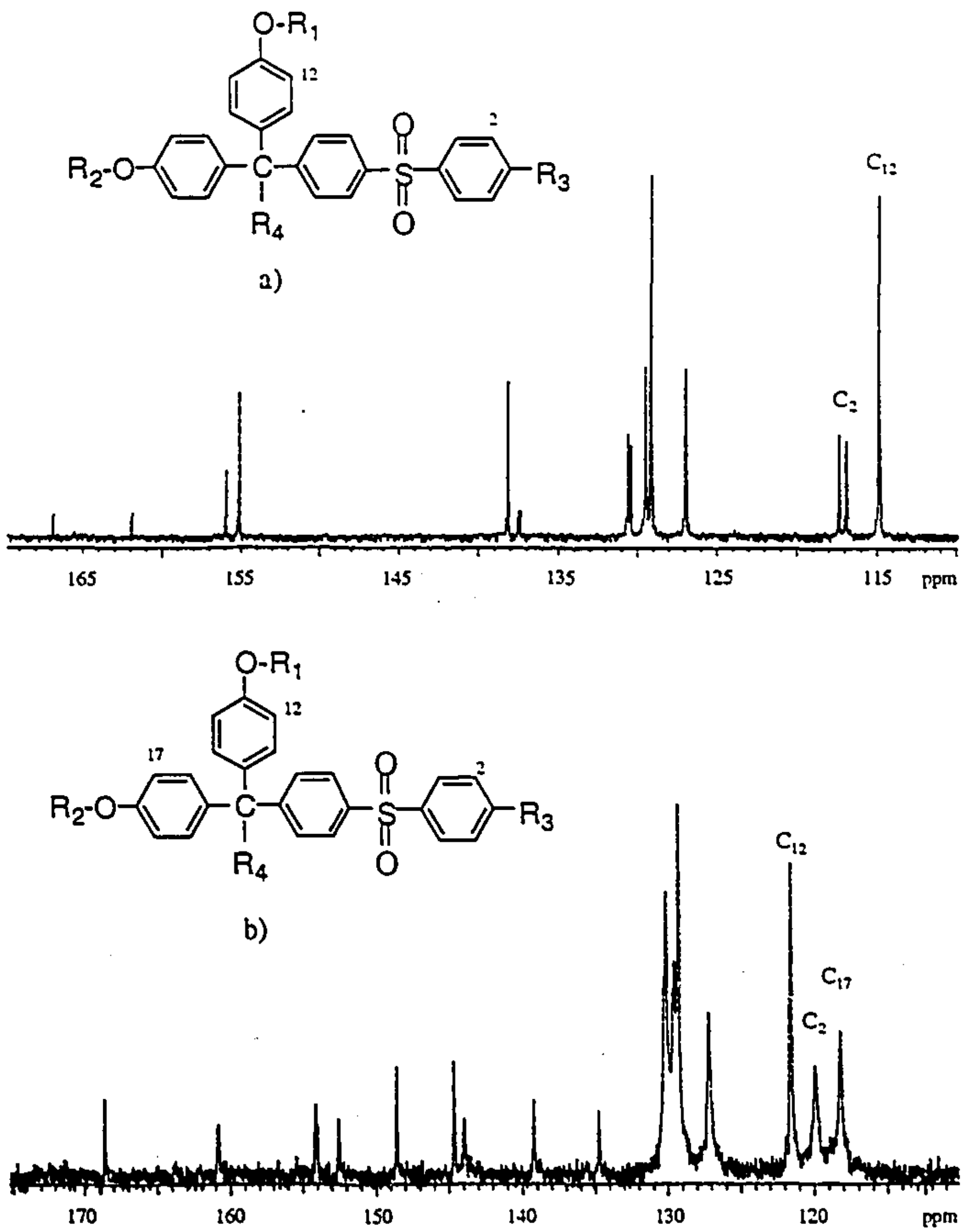


Figure 5.15. ^{13}C NMR spectra of: a) monomer **5.15-b** ($R_1 = R_2 = H$, $R_3 = F$) and b) hyperbranched poly(aryl ether sulfone) **5.28-b** ($R_1 = COCH_3$, $R_2 = P$, $R_3 = OP'$). P and P' are segments of hyperbranched polymers, and $R_4 = CH_3$.

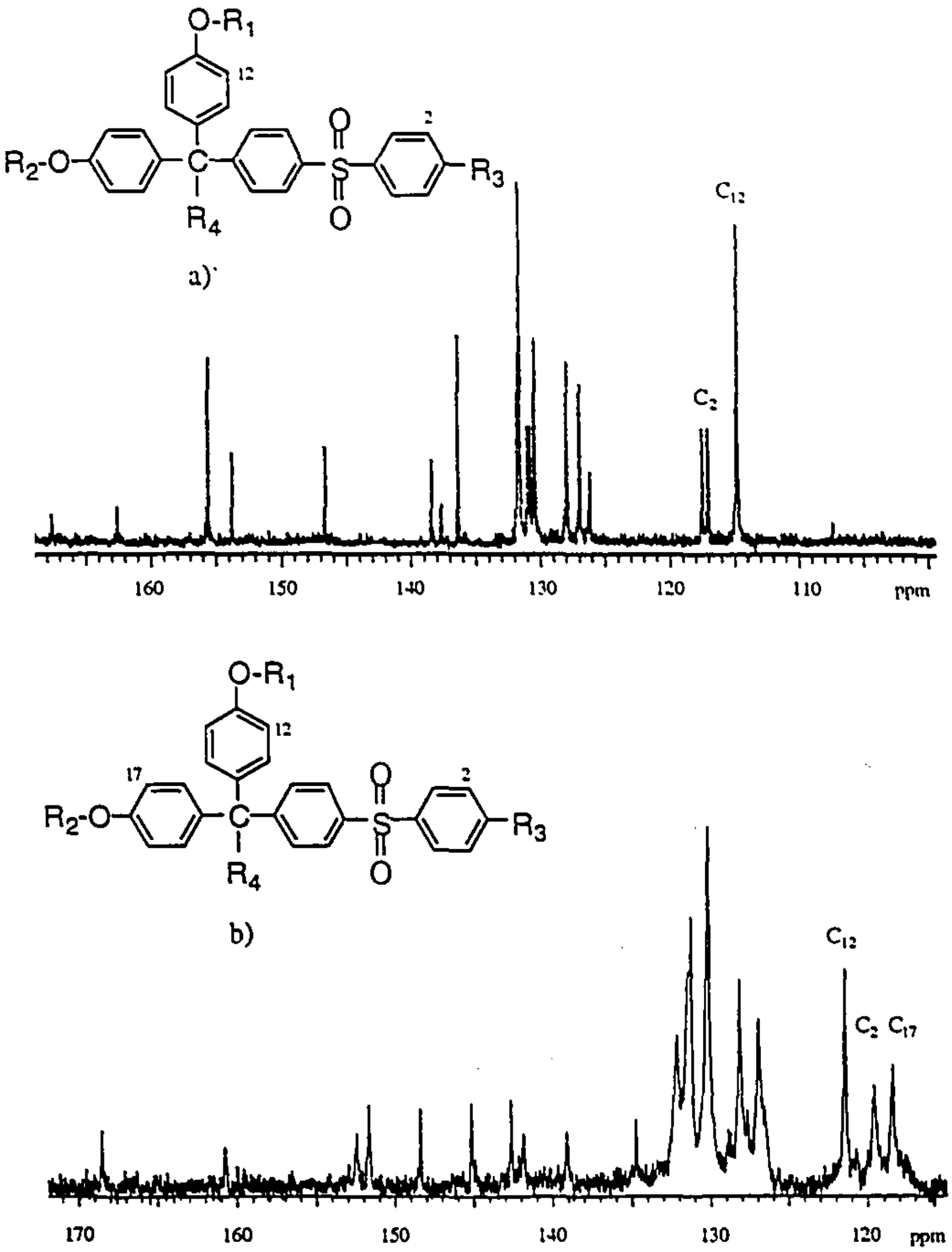


Figure 5.16. ^{13}C NMR spectra of: a) monomer **5.26** ($R_1 = R_2 = H$, $R_3 = F$) and b) hyperbranched poly(aryl ether sulfone) **5.28-c** ($R_1 = COCH_3$, $R_2 = P$, $R_3 = OP'$). P and P' are segments of hyperbranched polymers, and R_4 = Phenyl.

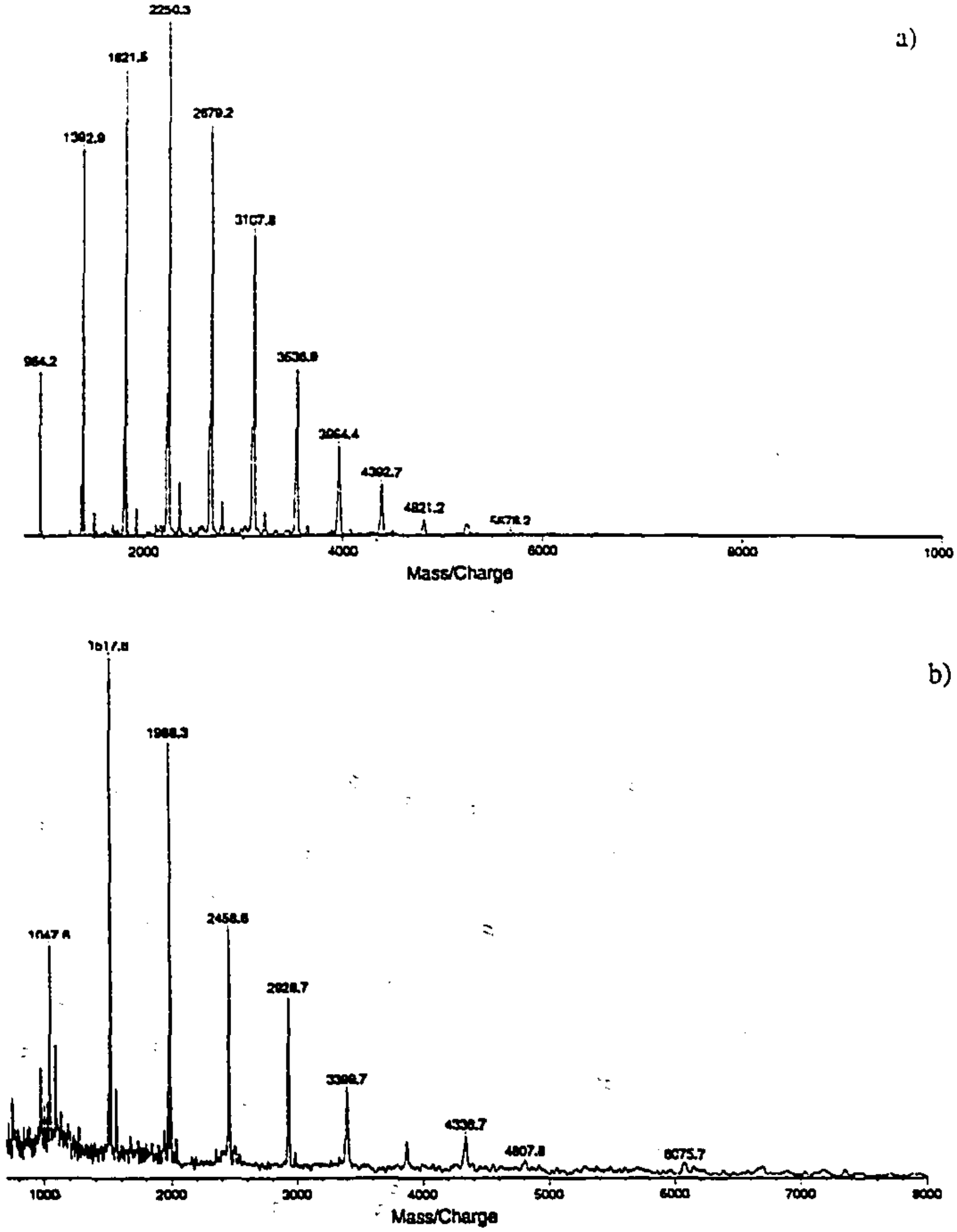


Figure 5.17. MALDI mass spectra of hyperbranched poly(aryl ether sulfone)s: a) **5.27-b** and b) **5.28-b**.

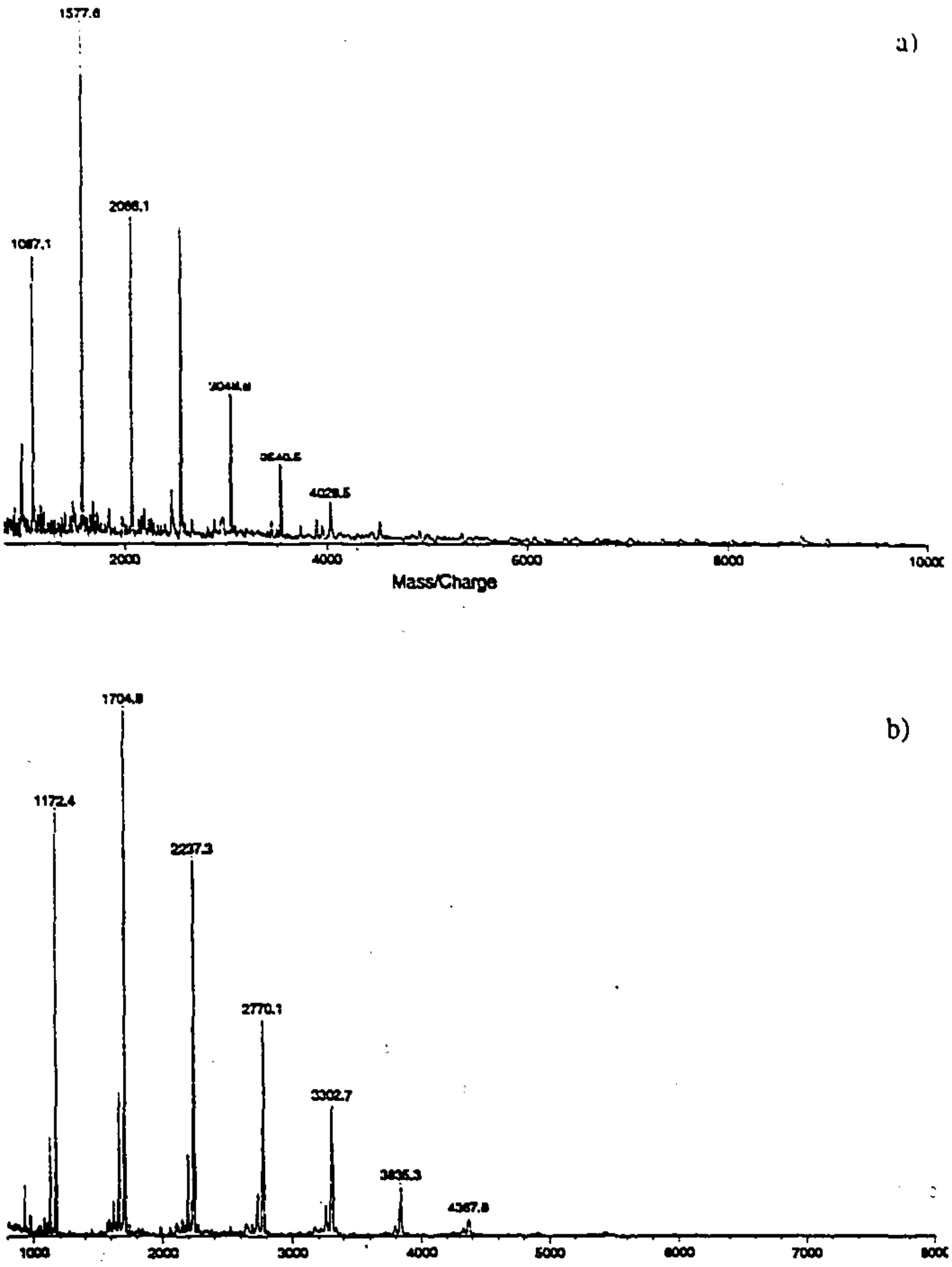


Figure 5.18. MALDI mass spectra of hyperbranched poly(aryl ether sulfone)s: a) **5.27-c** and b) **5.28-c**.

Table 5.4. MALDI mass spectrometric analyses of hyperbranched poly(aryl ether sulfone)s 5.27-a, 5.27-b, 5.28-a, and 5.28 a)

Polymer n b)	5.27 $(M+Ag)^+$ c)	5.27-a Mass/Charge	5.27-b Mass/Charge	5.28 $(M+Ag)^+$ c)	5.28-a Mass/Charge	5.28-b Mass/Charge
2	965	966.1	964.2	1049	1049.2	1047.6
3	1393.5	1394.7	1392.6	1519.5	1520.8	1517.8
4	1822	1822.9	1821.5	1990	1991	1988.3
5	2250.5	2251.8	2250.3	2460.5	2461.5	2458.6
6	2679	2680.1	2679.2	2931	2931.9	2928.7
7	3107.5	3109	3107.8	3401.5	3402	3399.7
8	3536	3536.2	3536.9	3872	3872.6	3868.8
9	3964.5	-	3964.4	4342.5	4343	4338.7
10	4393	-	4392.7	4813	4813	4807.8
11	4821.5	-	4821.2	5283.5	5283.3	-
12	5250	-	5248.2	5754	5750	-
13	5678.5	-	5678.2	-	-	-
14	6107	-	6102.7	-	-	-

a) Dithranol:Sample:CF_3CO_2Ag = 40:4:2. b) n = degree of polymerization. c) M= molecular mass, Da; Ag = silver atomic mass, Da.

In this equation n represents the degree of polymerization of the oligomer, A the molecular mass of the respective monomer (**5.15-a**: 465.0 Da, **5.15-b**: 448.5 Da, **5.26**: 510.6), and B the molecular mass of the small molecule eliminated during the condensation reaction (HCl for the hyperbranched polymer **5.27-a** and HF for the hyperbranched polymers **5.27-b** and **5.27-c**). For example, the molecular masses for the hyperbranched polymer **5.27-a** were obtained using A = 465.0 Da, B = 36.45 Da.

Due to the fact that polymers **5.27-a** and **5.27-b** (and **5.28-a** and **5.28-b**) have the same repeat and terminal units the MALDI results are almost identical.

The MALDI results for phenol-terminated hyperbranched poly(aryl ether sulfone)s are similar to those found previously for aryl halide-terminated hyperbranched poly(aryl ether sulfone)s. These systems lost n and not n-1 molecules of HCl or HF, as expected according to the stiochiometry of the reaction. A termination reaction in which a halide (Cl^- or F^-) is displaced by a hydroxyl group present in the molecule (internal cyclization) can be the explanation for that.

Table 5.5. MALDI mass spectrometric analyses of hyperbranched poly(aryl ether sulfone)s 5.27-c and 5.28-c a)

Polymer	**5.27-c**	**5.27-c-1** d)	**5.27-c-2** e)	**5.28-c**	**5.28-c-1**	**5.28-c-2**
n b)	$(MI+Ag)^+$ c)	Mass/Charge	Mass/Charge	$(MI+Ag)^+$ c)	Mass/Charge	Mass/Charge
2	1089.2	1088.4	1087.1	1173.2	1174.5	1172.4
3	1579.8	1578.7	1577.6	1705.8	1707.8	1704.8
4	2070.4	2069.6	2068.1	2238.4	2240.3	2237.3
5	2561	2560.6	2558.6	2771	2773.7	2770.1
6	3051.6	3051	3048.8	3303.6	3306.8	3302.7
7	3542.2	3541.2	3540.5	3836.2	3836.8	3835.3
8	4032.8	4031.0	4029.5	4368.8	-	4367.8
9	4523.4	-	4518.5	-	-	-

d) Synthesized by Method A. e) Synthesized by Method B. More detail in **Table 5.4.**

As we mentioned in Part 5.2.3, reductive dechlorination can be another possible termination reaction in the synthesis of **5.27-a**, since if an atom of chlorine is displaced by an atom of hydrogen the differences between the calculated molecular ion masses and the experimental values of mass/charge are still reasonable. However, since reductive defluorination is a less probable reaction, the displacement of the fluoride by a hydroxyl group present in the molecule becomes the most probable termination reaction in the synthesis of the hyperbranched polymers **5.27-b** and **5.27-c**.

The results of the analysis of the MALDI data for the respective acetylated products (**5.28**) of these polymers are also similar to those found previously (Tables 5.4 and 5.5). The values of mass/charge found correspond to the oligomeric molecular ion (a silver cation is complexed with the oligomeric molecules) and n instead of n-1 molecules of HCl or HF were lost. The molecular masses, M's, of the hyperbranched polymers were calculated using the following equation:

$$M(n) = n\,(A - B + C)\ \mathrm{Da}$$

where C = 42 Da. This value, as expected, corresponds to the mass difference between the acetate group (59 Da) and the hydroxyl group (17 Da). The small peak that accompanies each of the intense signals present in the MALDI mass spectra of **5.28-c** could be a consequence of an incomplete acetylation of the polymer or fragmentation of the molecule with loss of an acetyl group.

For all these systems, the differences between the calculated values (M + Ag) and the experimental values (Mass/Charge) were about 0.1 % . The MALDI mass spectrometric data accumulated was very useful in the identification of the termination reaction and characterization of the lower molecular weight species formed in the polymerization reaction. Unfortunately, it was not possible to correlate any special effects related to the nature of the monomers, condensation agent, or conditions employed in the polymerization reaction. The differences observed in the n maximum values detected for these samples are probably due to the technique itself. Even though the general mass spectra of these samples were all similar, we observed differences in the peak intensities and in the maximum molecular weight reached for a single sample analyzed several times. It is known that the way the sample, matrix, and stabilizer interact and coprecipitate affects the characteristics of the mass spectra, as well as other conditions such as beam power, shot number, area analyzed, and nature of the sample.

5.3.7 Effect of the conditions of the polymerization reaction on the characteristics and properties of the hyperbranched poly(aryl ether sulfone)s.

The influence of factors such as monomer concentration and reaction temperature was explored (Table 5.6 and 5.7). As we will show below, the molecular weights were controlled by the combinations of these factors. We observed that an increase in temperature or monomer concentration can cause a corresponding increase in molecular weight and viscosity of the polymer, under certain conditions.

In the synthesis of phenol-terminated hyperbranched polymer **5.27-b**, concentrations of 0.50, 0.60, 0.70, and 0.80 mol/L were employed. Insoluble materials were formed when the higher concentrations where used in combination with the higher temperatures. For example: a) reflux conditions and 0.70 mol/L or b) 150°C and 0.80 mol/L. However, the polymers were totally soluble when the concentrations were decreased to 0.50 mol/L and 0.70 mol/L, respectively. As we discussed previously, a lower concentration produces lower molecular weight polymers and consequently totally soluble materials.

The same general results are valid for the phenol-terminated hyperbranched polymer **5.27-a**. At 180°C and concentrations higher than 0.50 mol/L insoluble material were formed. The maximum concentration used was lower, probably due to the higher reaction temperature employed or relatively lower rate of the termination reaction.

The weight average molecular weight and the polydispersities of the respective acetyl-terminated hyperbranched polyethers **5.28-a** and **5.28-b** are given also in Table 5.6. Their molecular masses were measured by SEC relative to polystyrene narrow molecular mass standards. The shape of the SEC chromatograms (Figs. 5.19 and 5.20) showed overlay peaks which indicated that species with very different molecular weight and size were present in these samples.

Table 5.6. Effect of the polymerization conditions on the molecular weight and viscosity of the hyperbranched poly(aryl ether sulfone)s 5.27-a, 5.27-b, 5.28-a, and 5.28-b

Polymer	R a)	C (mol/L) b)	T (°C)	Mw(g/mol)c)	PD c)	n_{inh} (dL/g)d)
5.27-a-1	OH	0.20	180	-	-	0.13
5.27-a-2	OH	0.50	180	-	-	0.25
5.28-a-2	Acetyl	-	-	20223	4.6	0.22
5.27-b-1	OH	0.50	164	-	-	0.26
5.28-b-1	Acetyl	-	-	31333	5.5	0.22
5.27-b-2	OH	0.60	150	-	-	0.21
5.28-b-2	Acetyl	-	-	27393	6.1	0.20
5.27-b-3	OH	0.70	150	-	-	0.19
5.28-b-3	Acetyl	-	-	28453	5.2	0.18

a) R = terminal functionality of the hyperbranched polymer. b) C = monomer concentration. c) Mw = weight average molecular weight and PD = index of polydispersity measured by SEC, based on polystyrene standards, chloroform, 1mL/min, UV-Detector. d) Inherent viscosity, NMP, 0.5 g/dL, 25°C.

An increase in the concentration of monomer **5.15-b** fron 0.60 to 0.70 mol/L did not produce the expected increase in molecular weight. It was probably due to the higher viscosity of the reaction mixture which made the stirring of the system difficult. The higher Mw was obtained when a concentration of 0.5 mol/L was used under reflux conditions. It again suggests that temperatures lower than 164°C are not favorable.

Inherent viscosities of **5.27-a**, **5.28-a**, **5.27-b**, and **5.28-b** are given in Table 5.6. Most of the values were around 0.20 dL/g. Slightly higher values were obtained for the polymers **5.27-a-2** and **5.27-b-1** which were synthesized using a monomer concentration of 0.50 mol/L and temperature of 180°C (NMP) and 164°C (DMAc), respectively. The lowest viscosity (0.13 dL/g) was also found when the lowest concentration (0.20 mol/L) was employed.

The reaction seems to be more efficient when the condensation agent was a mixture of Cs_2CO_3 and $Mg(OH)_2$, and the displaced halide was a fluoride. For example, the reaction yield was higher for the hyperbranched polymers **5.27-b** respect to **5.27-a** (almost quantitative reaction vs 78%). The shape of the chromatograms also suggest that polymer **5.28-a** (Fig. 5.19) contains a higher amount of low molecular weight species compared to polymer **5.28-b** (Fig. 5.20a).

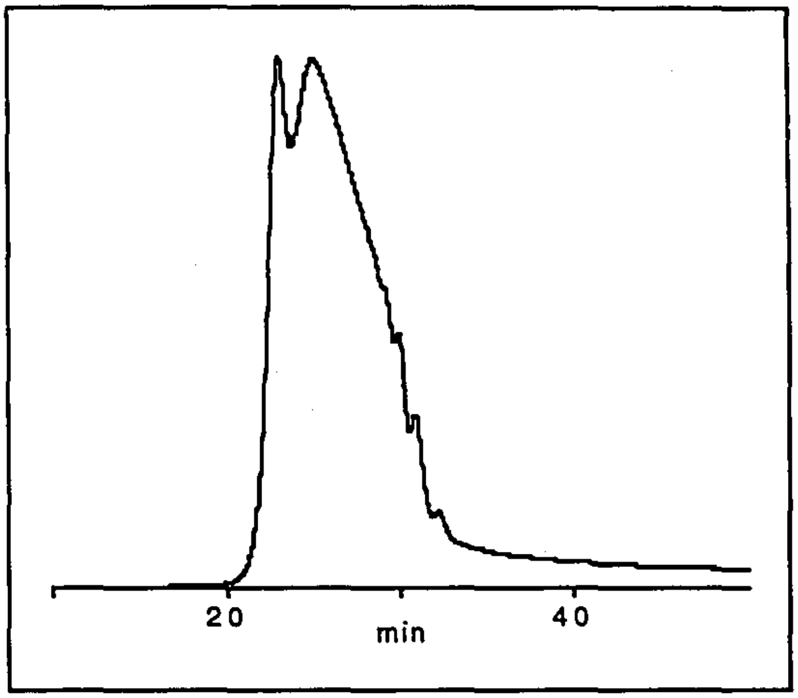


Figure 5.19. SEC chromatogram of hyperbranched poly(aryl ether sulfone) **5.28-a-2.** Analysis conditions in **Table 5.6.**

Very similar results were obtained for hyperbranched polymers **5.27-c** and **5.28-c** (Table 5.7 and Fig. 5.21). The lowest (0.10 dL/g) and highest (0.24 dL/g) viscosities, molecular weight, and polydispersity were obtained for the lowest (0.25 mol/L) and highest (0.70 mol/L) concentrations, respectively. The dependency of molecular characteristics on the monomer concentration was very clear in this case.

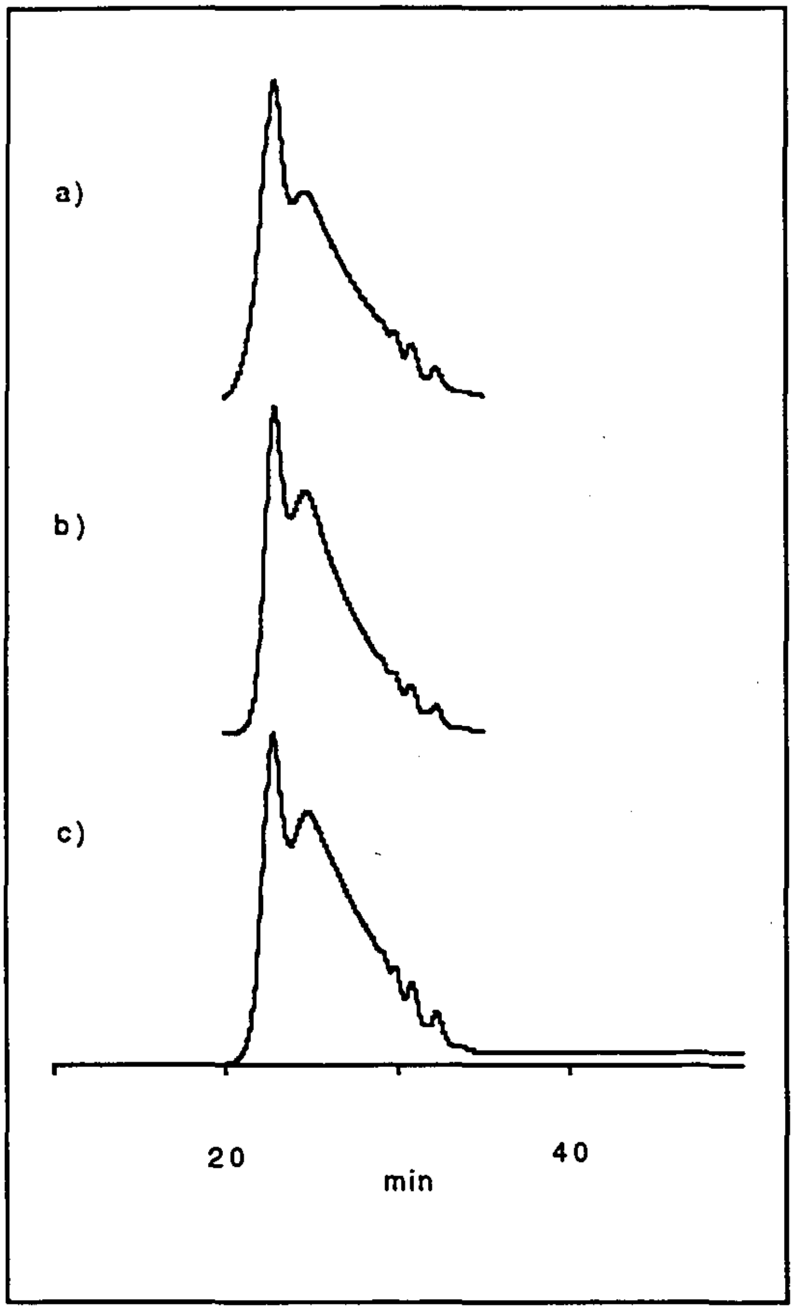


Figure 5.20. SEC chromatograms of hyperbranched poly(aryl ether sulfone) **5.28-b**: a) **1**, b) **3**, and c) **2**. Analysis conditions in **Table 5.6.**

Table 5.7. Effect of the polymerization conditions on the molecular weight and viscosity of hyperbranched poly(aryl ether sulfone)s 5.27-c and 5.28-c

Polymer	R a)	C (mol/L) b)	T (°C)	Mw (g/mol) c)	PD c)	η_{inh} (dL/g) d)
5.27-c-1 e)	OH	0.36	164	-	-	0.17
5.28-c-1	Acetyl	-	-	12308	5.4	0.14
5.27-c-2 f)	OH	0.25	164	-	-	0.12
5.28-c-2	Acetyl	-	-	10341	3.7	0.10
5.27-c-3 f)	OH	0.70	150	-	-	0.24
5.28-c-3	Acetyl	-	-	27686	6.1	0.24

Details in **Table 5.6.** e) Synthesized by Method A. f) Synthesized by Method B.

We did not detect differences in the yields of **5.27-c** using potassium carbonate (Methods A) or cesium carbonate:magnesium hydroxide (Method B). In both case the yield was around 92%. However, the shape of the chromatograms suggests that the proportion of low molecular weight species in the polymer is higher when Method A was used (compare Figures 5.21c and 5.21b).

As was expected, the lowest yield was obtained for polymer **5.27-a** in what the condensation agent was potassium carbonate and the displaced halide was a chloride.

According to the MALDI spectrometry analyses unimolecular termination reactions have apparently occurred. At lower concentration, cyclization of an activated aryl chloride or fluoride with one of the many phenolates surrounding it in the same molecule would be expected to be favored. Insoluble materials are formed at higher concentrations since bimolecular reactions are favored, yielding high molecular weight hyperbranched polymers before termination and high viscosity reaction mixtures.

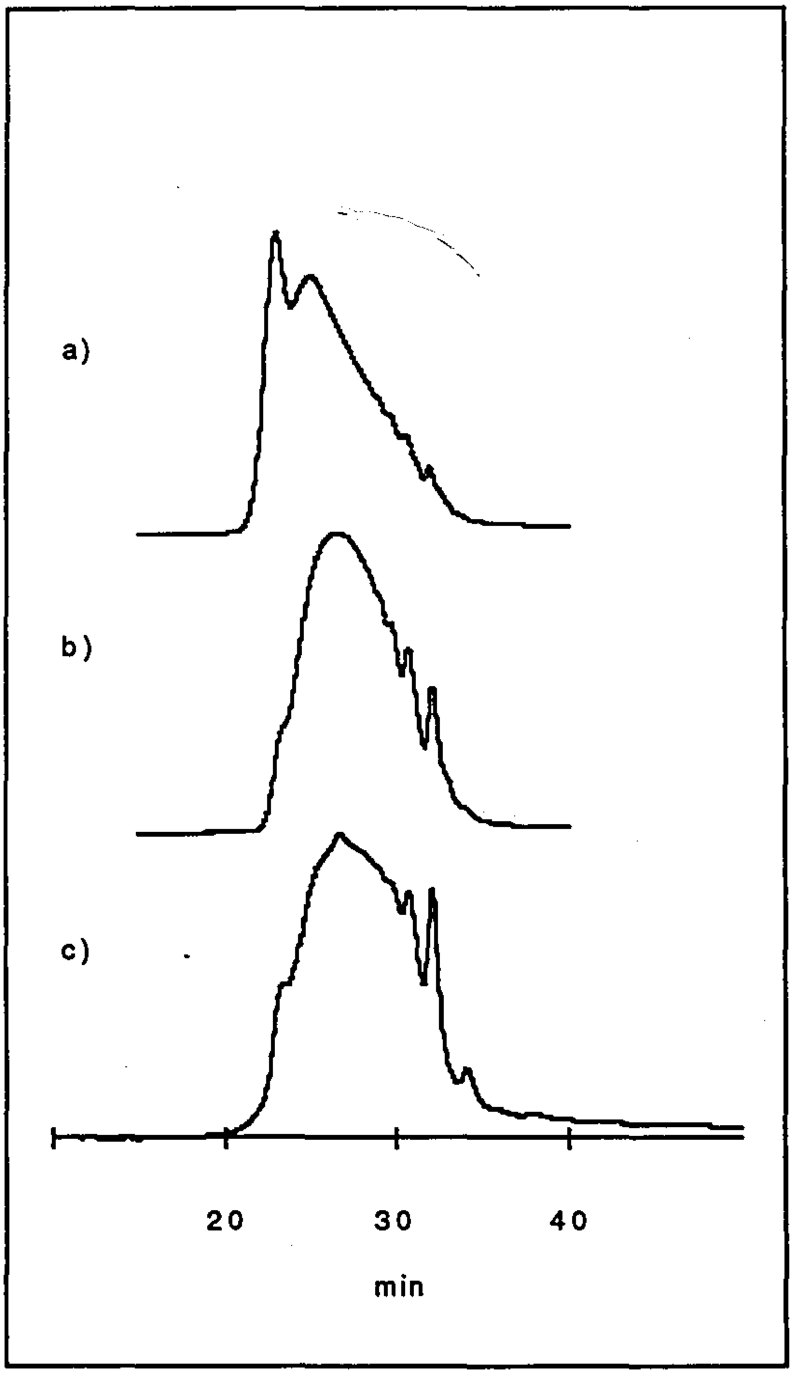


Figure 5.21. SEC chromatograms of hyperbranched poly(aryl ether sulfone) **5.28-c**: a) **3**, b) **2**, and c) **1**. Analysis conditions in **Table 5.6.**

5.3.8 Properties.

The phenol-terminated hyperbranched poly(aryl ether sulfone)s synthesized showed low inherent viscosities. The maximum values obtained were about 0.25 dL/g. Their thermal properties were studied by differential scanning calorimetry (DSC) and thermogravimetric analyses (TGA), (Table 5.8). Thermal analyses under nitrogen at 10°C/min showed that they retain 95 % of their masses up to about 340°C - 420°C . The presence of traces of F^- and Cs^+ could affect the thermal stability of the hyperbranched polymers (**5.27-b** and **5.27-c-3**) synthesized using cesium carbonate since relatively lower TGA temperatures were obtained for them. The thermal stability of the phenol-terminated poly(aryl ether sulfone)s is lower than those of their respective acetylated products and those of aryl halide-terminated hyperbranched polymers. It can be a consequence of the higher reactivity of the terminal phenol groups.

Table 5.8. Some properties and characteristics of phenol-terminated hyperbranched poly(aryl ether sulfone)s

Polymer	5.27-a	5.28-a	5.27-b	5.28-b	5.27-c-1	5.28-c-1	5.27-c-3	5.28-c-3
η_{inh} (dL/g) a)	0.25	0.22	0.26	0.22	0.17	0.14	0.24	0.24
Tg (°C) b)	261	242	253	240	276	254	277	253
Td (°C) c)	395	420	345	377	397	417	355	365
Mw (g/mol) d)	-	20223	-	31333	-	12308	-	27686
PD d)	-	4.6	-	5.5	-	5.5	-	6.1

a) Inherent viscosity, NMP, 0.5 g/dL, 25°C. b) Nitrogen, 10 °C/min. c) 5% loss weight, 10 °C/min. d) SEC, based on polystyrene standards, chloroform, 1mL/min, UV-Detector.

We observe Tg's at about 250°C with no evidence for melting or crystallization. The stronger intermolecular interactions between the terminal -OH groups in the phenol-terminated hyperbranched polymers probably cause their relatively higher Tg's compared with those obtained for aryl halide-terminated or acetylated hyperbranched polymers.

5.4 Conclusions.

The polycondensation of A_2B monomers **5.4-a, 5.4-b, 5.15-a, 5.15-b**, and **5.26**, via a one-pot approach has been shown to be a route for the formation of hyperbranched poly(ether sulfone)s possessing high thermal stability and aryl halide and hydroxyl terminal functionality. The main advantage of this one-pot method is its simplicity, which allows rapid access to large amounts of these materials.

MALDI-TOF-MS allowed to determine the polymerization grade of the oligomeric species present in these samples and suggests that the termination reaction in these systems is an internal cyclization. We also found that molecular weights and viscosities are controlled by the concentration of the monomer and temperature of the reaction. This observation in combination with the mass results indicates that relatively low monomer concentrations are favorable for intramolecular cyclizations which cause the termination of the polymerization reaction with the consequent generation of a low molecular weight hyperbranched polymer. Relatively high monomer concentrations favored bimolecular reaction which produces insoluble materials. The condensation reaction was more efficient when the condensation agent was a mixture of Cs_2CO_3 and $Mg(OH)_2$ and the displaced halide was a fluoride. The formation of insoluble magnesium fluoride and the use of the more active nucleophilic polycondensation agent, Cs_2CO_3, can explain those results. In addition, the best conditions were found when the monomer concentrations were around 0.5-0.7 mol/L and the reaction was carried out at 150°C-164°C using DMAc as the solvent of the reaction.

Halide-terminated hyperbranched polymers have a slightly lower glass transitions but higher thermal stabilities than those of the phenol-terminated hyperbranched polymers. Both of them had similar inherent viscosities when the polymerization conditions were the same. The terminal phenolic groups of the poly(aryl ether sulfone)s were readily functionalized in almost quantitative fashion, confirming the accessibility of the chain ends.

5.5 Experimental.

Materials. In experiments requiring dry solvent, N-methylpyrrolidinone, NMP (Aldrich) and N,N-dimethyl acetamide, DMAc (Aldrich), were dried over calcium hydride and distilled under vacuum; ethyl ether, DEE (BDH) was dried over sodium and distilled under nitrogen. Acetic anhydride (BDH), benzene (A&C), benzoic acid (Aldrich), p-bromofluorobenzene (Lancaster), carbon disulfide (Aldrich), copper (II) sulphate pentahydrate (Aldrich), 4-fluoroacetophenone (Aldrich), mercaptoacetic acid (Aldrich), methanesulfonic acid (Omega), phosphorous pentachloride (A&C), phosphorous pentoxide (Anachemia), sodium carbonate (BDH), sodium bicarbonate (BDH), thiophenol (Lancaster) were used as obtained. For more detaild see Chapter 2-4.

General methods and polymer characterization. For details see Chapter 2, Part 2.8.

Synthesis of activated monomer p-[4,4'-Bis(4-chlorophenylsulfonyl)] triphenylmethyl phenol 5.4-a.

Synthesis of 5.2. To 18.65 g (30 mmol) of **5.1-a** in pyridine (80 g) at 0°C was added acetic anhydride (102 g), dropwise. The ice bath was removed and the reaction was allowed to continue for 24 h at room temperature. The contents were poured into a beaker containing 200 mL of 10-15% aqueous HCl at 0°C. A gum was obtained, which was dissolved in ethyl ether, and the solution extracted with water. The ethereal phase was separated, dried with magnesium sulfate, filtered and rotoevaporated. The separated gum was dried under vacuum at 70°C, overnight, to obtain 19.51 g of **5.2** (yield = 98%, purity of the isolated product by HPLC = 99%): ^{1}H NMR (50 MHz, DMSO-d_6) δ 7.5-7.2 (m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 169.1, 148.9, 146.0, 145.5, 143.7, 133.8 (d), 133.2, 132.1, 131.1, 129.7, 128.1, 126.7, 121.0, 65.1, 22.8; MS (EI) m/e calc'd for $C_{39}H_{28}S_2Cl_2O_2$:

662.09077, found 662.09077; 662, 585, 554, 543, 527, 477, 443, 435, 401, 257, 241, 228, 181, 165, 152, 144, 112, 97, 84; Analysis calc'd for $C_{39}H_{28}S_2Cl_2O_2$: C, 70.58%; H, 4.25%; S, 9.66%; Cl, 10.68%; found: C, 70.18%; H, 4.36%; S, 9.84%; Cl, 10.49%.

Synthesis of 5.3. Wet alumina was prepared by adding water (10 mL) to the alumina (50 g; Brockman grade I, 200 mesh) and shaking until a free flowing homogeneous powder was obtained.

Product **5.2** (16.59 g, 25 mmol) was added to a vigorously stirred suspension of wet alumina (50.0 g) and Oxone (92.50 g, 150 mmol) in chloroform (250 mL). The mixture was heated at reflux for 24 h. When the reaction finished, it was cooled, filtered and the solid washed thoroughly with chloroform. The solution was concentrated and coagulated in methanol (200 mL). The precipitate (15.46 g) was dissolved in 15 mL of acetone and coagulated in 30 mL of methanol to afford 10.67 g of **5.3** (yield = 59%). The purity was checked by TLC (aluminium sheet of silica gel 60 F_{254}, hexanes:ethyl acetate, 6:4): ^1H NMR (200 MHz, DMSO-d_6) δ 8.40-7.60 (m, 8H), 7.76-7.64 (d, J = 8.6 Hz, 4H), 7.50-7.40 (d, J = 8.5 Hz, 4H), 7.40-7.00 (m, 9H), 2.25 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 169.1, 151.6, 149.2, 144.4, 142.1, 140.3, 139.9, 139.5, 132.0, 131.9, 130.8, 130.0, 129.6, 129.5, 128.6, 127.5, 127.3, 121.6, 65.9, 22.8; Analysis calc'd for $C_{39}H_{28}S_2Cl_2O_6$: C, 64.37%; H, 3.88%; S, 8.81%; Cl, 9.74%; found: C, 64.02%; H, 3.98%; S, 9.03%; Cl, 9.18%.

Synthesis of 5.4-a. To product **5.3** (14.55 g, 20 mmol) was added ethanol (150 mL), DMAc (50 mL) and potassium carbonate (2.76 g, 20 mmol). The mixture was stirred at 100°C for 1 h. Then, it was cooled and poured into 10% aqueous HCl. The precipitate was separated by filtration, washed with water, dried at 100°C under reduced pressure to afford 13.15 g of a light brown solid (isolated yield = 96%). The purity of the product was checked by TLC (aluminium sheet of silica gel 60 F_{254}, hexane:ethyl acetate, 6:4):

^{1}H NMR (500 MHz, DMSO-d_6) δ 9.50 (s, 1H), 7.90-7.98 (d, 4H), 7.90-7.82 (d, 4H), 7.70-7.60 (d, 4H), 7.40-7.35 (d, 4H), 7.30-7.20 (t, 2H), 7.10-7.20 (t, 1H), 7.10-7.05 (d, 2H), 6.90-6.80 (d, J = 7.8 Hz, 2H), 6.70-6.60 (d, J = 7.8 Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 154.9, 152.3, 144.9, 140.3, 139.8, 139.1, 136.2, 132.1, 132.0, 130.8, 130.1, 129.6, 128.5, 127.4, 127.1, 115.6, 65.7; MS (MALDI(Ag)) m/e 795.2 (MI).

Synthesis of p-[[4,4'-Bis(4-fluorophenylsulfonyl)]triphenylmethyl]phenyl carbonate 5.6

Synthesis of p-[[4,4'-Bis(4-fluorophenylthio)]triphenylmethyl]phenyl carbonate 5.5. A mixture of phenol **5.1-b** (40 mmol, 23.55 g), pyridine (100 mL) and toluene (150 mL) was stirred under argon for 0.5 h at 40°C. Then, a solution of bis(trichloromethyl) carbonate (triphosgene, 10 mmol, 2.97 g) in toluene (50 mL) was added, under the same conditions, for a period of 1.0 h. When the reaction finished, it was poured into methanol (1000 mL) and filtered. The solid recovered was dissolved in DMAc (150 mL), and the solution poured into 1% aqueous hydrochloric acid, filtered and dried. The solid was purified by fractional precipitation dissolving the sample in chloroform (15 mL/g) and using methanol as the nonsolvent. After the workup 15.40 g of a white solid was obtained (isolated = 64%). The purity of the isolated product by HPLC was 85% (Column: C8, THF:H_2O, 85:15): ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.49-7.42 (m, 8H), 7.31-7.04 (m, 42H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 165.0-160.1 (d, J = 245.7 Hz), 149.1, 146.0, 144.7, 144.5, 135.4-135.2 (d, J = 8.0Hz), 132.3, 131.9, 131.1, 129.4-129.30 (d, J = 3.1 Hz), 128.3, 128.1, 126.7, 120.3, 117.2-116.8 (d, J = 21.8 Hz), 65.0; MS (EI) m/e 1202, 999, 495, 460, 303, 154, 137; MS(MALDI(Ag)) m/e 1312.9 (MI), 1420.1.

Synthesis of 5.6. The method is similar to that employed for the synthesis of **5.3**. Product **5.5** (3.61 g, 3 mmol) was added to a vigorously stirred suspension of wet alumina (12.54 g) and Oxone (23.22 g, 36 mmol) in chloroform (30 mL). The mixture was heated at reflux for 8 h. When the reaction finished, it was cooled, filtered and the solids washed thoroughly with chloroform. The solution was concentrated and coagulated in methanol (60 mL) to afford 3.91 g of a white solid (isolated yield = 98%): ^{1}H NMR (200 MHz, DMSO-d_6) δ 8.10-8.00 (m, 8H), 7.98-7.88 (d, 8H), 7.54-7.40 (m, 16H), 7.40-7.10 (m, 18H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 167.0-162.1 (J = 250.5 Hz), 151.1, 148.6, 144.4, 142.8, 138.8, 137.1-137.0 (J = 2.7 Hz), 131.4, 130.9-130.7 (J = 9.7 Hz), 130.1, 128.5, 127.4, 126.7, 121.1, 117.5-117.0 (J = 22.5 Hz), 65.3; MS (MALDI(Ag)) m/e 1441.3 (MI), 1580.9 (MI); Analysis calc'd for $C_{75}H_{50}S_4O_{11}F_4$: H, 3.79%; S, 9.63%; F, 5.71%; found: H, 3.70%; S, 9.75%; F, 5.55%.

Synthesis of activated monomer 1,1,1-[4-(4-chloro phenylsulfonyl)-4',4"-dihydroxi]triphenylethane 5.15-a.

Synthesis of 4-(4-chlorophenylthio)phenyl methyl ketone 5.10-a. A mixture of 4-chlorothiophenol **5.9-a** (47.73 g, 0.33 mol), 4-fluoroacetophenone (41.44 g, 0.30 mol), anhydrous potassium carbonate (24.88 g, 0.18 mol) and DMAc (1000 ml) was mechanically stirred under argon for 0.5 h at room temperature. After that, the temperature was increased to 60°C (no higher since by-products make the purification of the product difficult), and the reaction was allowed to go for 24 h (the reaction was followed by HPLC). When the reaction finished, the reaction mixture was poured into 2000 mL of water. The precipitate was filtered (isolated yield = 100%, purity of the isolated product = 95%), recrystallized in methanol: water (6:1), (15 mL CH_3OH/g) and dried to obtain 52.03 g of **5.10-a** (yield = 66%, purity of the isolated product by HPLC = 98%): m.p. 52-54°C; ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.96-7.84 (m, 2H), 7.60-7.42 (bs, 4H), 7.36-7.24 (m, 2H), 2.55 (s, 3H); ^{1}C NMR (50 MHz, CDC_3) δ 196.5, 144.1, 135.2, 135.1, 135.0, 131.2, 130.2, 129.3, 128.1, 28.0; MS (EI) m/e calc'd for C_{14} H_{11} S Cl 0: 262.02191, found 262.02191; 262, 247, 184; Analysis calc'd for C_{14} H_{11} S Cl 0: C, 64.00%; H, 4.22%; S, 12.20%; Cl, 13.49%; found: C, 63.82%; H, 4.25%; S, 12.48%; Cl, 13.34%.

Synthesis of 1,1,1-[4-(4-chlorophenylthio)-4',4"-dihydroxi]triphenylethane 5.12-a. To a mixture of phenol **5.11** (56.46 g, 0.60 mol), **5.10-a** (26.28 g, 0.10 mol) and a catalytic amount of mercaptoacetic acid ($HSCH_2COOH$) kept a room temperature was added 96% concentrated sulfuric acid (30.08 g). After 4 days (the reaction was followed by HPLC), 400 mL of water were added to the reaction mixture (the color changed from red to blue), stirred for a few minutes and left overnight. A white solid precipitated which was filtered, washed with water and dried for 3 h at 70°C under vacuum to obtain 35.94 g of **5.12-a** (yield = 83%, purity of the isolated product by HPLC = 93%): m.p. 156-158°C; ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.45-7.20 (m, 6H), 7.10-7.00 (d, 2H), 6.88-6.78 (d, J = 8.7 Hz, 4H), 6.72-6.64 (d, J = 8.8 Hz, 4H), 2.55 (s, 3H); 13C NMR (50 MHz, DMSO-d_6)) δ 155.0, 149.7, 138.9, 134.7, 131.7, 130.7, 130.0, 129.6, 129.5, 129.2, 128.0, 114.8, 51.5, 31.4; MS (IE) m/e calc'd for C_{26} H_{21} S Cl O_2: 432.09507, found 432.09507; 432, 417, 323, 247, 195, 184, 165, 152, 144, 119, 108, 94, 77.

Synthesis of 5.13-a. The method is similar to that employed for the synthesis of **5.2.** To 32.48 g (75 mmol) of **5.12-a** in pyridine (75 g) at 0°C was added acetic anhydride (110 g) dropwise. The ice bath was removed and the reaction was allowed to go for 24 h at room temperature. The contents were poured into a beaker containing 750 mL of 20 % aqueous HCl at 0°C. The yellow viscous liquid separated by decantation was dissolved in ethyl ether and the solution extracted with water. The ethereal phase was separated, dried with magnesium sulfate, filtered, concentrated and left overnight in a covered beaker.

The precipitate was separated by filtration and washed with cold ethyl ether. After the workup 26.37 g of **5.13-a** (yield = 68%, purity of the isolated product by HPLC = 98%) was obtained: m.p. 153-155°C; ^{1}H NMR (200 MHz, DMSO-d_6)) δ 7.50-7.25 (m, 8H), 7.14-7.06 (m, 8H), 2.27 (s, 6H), 2.14 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 169.3, 149.0, 148.0, 146.0, 134.4, 113.3, 132.7, 130.7, 129.9, 129.7, 121.4, 52.9, 32.1, 22.8; MS (IE) m/e calc'd for $C_{30}\ H_{25}\ S\ Cl\ 0_4$: 516.11620, found 516.11620; 516, 501, 459, 417; Analysis calc'd for $C_{30}\ H_{25}\ S\ Cl\ 0_4$: C, 69.69%; H, 4.87%; S, 6.20%; Cl, 6.86% found: C, 69.60%; H, 5.01%; S, 6.46%; Cl, 6.79%.

Synthesis of 5.14-a.

The method is similar to that employed for the synthesis of **5.3.** Product **5.13-a** (18.10 g, 35 mmol) was added to a vigorously stirred suspension of wet alumina (35.00 g) and Oxone (64.79 g, 105 mmol) in chloroform (90 mL). The mixture was heated at reflux for 8 h. When the reaction finished, it was cooled, filtered and the solids washed thoroughly with chloroform. The solution was concentrated and poured into methanol (150 mL). The precipitate was separated by filtration and washed with methanol to afford 14.60 g of **5.14-a** (isolated yield = 76%). Some times it was necessary to leave the chloroform-methanol solution overnight in a covered beaker to obtain the solid. The purity of the solid was checked by TLC (aluminium sheet of silica gel 60 F_{254} , hexanes:ethyl acetate, 6:4): m.p. 167-169°C; ^{1}H NMR (200 MHz, DMSO-d_6) δ 8.05-7.97 (d, J = 8.7 Hz, 2H), 7.97-7.90 (d, J = 8.5 Hz, 2H), 7.75-7.65 (d, J = 8.8 Hz, 2H), 7.37-7.30 (d, J = 8.7 Hz, 2H), 7.08 (s, 8H), 2.27 (s, 6H), 2.14 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 169.2, 154.8, 149.2, 145.0, 140.3, 140.0, 139.2, 130.1, 129.9, 129.8, 129.5, 127.7, 121.6, 53.4, 32.0, 22.8; MS (EI) m/e calc'd for $C_{30}\ H_{25}\ S\ Cl\ 0_6$: 548.10603, found 548.10603; 548, 506, 491, 464, 449, 279, 213, 112, 43; Analysis calc'd for $C_{30}\ H_{25}\ S\ Cl\ 0_6$: C, 65.63%; H, 4.59%; S, 5.84%; Cl, 6.49%; found: C, 65.18%; H, 4.68%; S, 6.08%; Cl, 6.88%.

Synthesis of 5.15-a. The method is similar to that employed for the synthesis of **5.4.** To product **5.14-a** (5.49 g, 10 mmol) was added ethanol (75 mL) and potassium carbonate (1.38 g, 10 mmol). The reaction mixture was stirred at 60°C for 8 h. When the reaction finished, the mixture was poured into 75 mL of water and acidified slowly to pH = 2-4 using concentrated HCl . A gum was formed which was separated by decantation, dissolved in ethyl ether (75 mL), and the solution washed with water, dried with magnesium sulfate, filtered and concentrated under reduced pressure. The concentrated solution was treated with petroleum ether with stirring until a solid came out. The beige solid was separated by filtration and dried to afford 4.42 g of **5.15-a** (isolated yield = 95%). The purity was checked by TLC (aluminium sheet of silica gel 60 F_{254}, hexanes:ethyl acetate, 5:5): m.p. 228-230°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90-7.86 (d, J = 8.8 Hz, 2H), 7.80-7.76 (d, J = 8.8 Hz, 2H), 7.50-7.46 (d, J = 8.8 Hz, 2H), 7.24-7.20 (d, J = 8.8 Hz, 2H), 6.88-6.84 (d, J = 8.8 Hz, 4H), 6.74-6.70 (d, J = 8.8 Hz, 4H), 5.00 (s, 2H), 2.05 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 156.7, 155.7, 140.3, 139.0, 138.5, 138.2, 130.1, 129.8, 129.5, 129.4, 127.3, 115.0, 51.3, 30.3; MS (EI) m/e calc'd for $C_{26}H_{21}SClO_4$: 464.08490, found 464.08490; 464, 449, 294, 279, 159, 111.

Synthesis of activated monomer 1,1,1-[4-(4-fluorophenylsulfonyl)-4',4"-dihydroxi]triphenylethane 5.15-b.

Synthesis of 4-(4-fluorophenylthio)phenyl methyl ketone 5.10-b. The method is similar to that employed for the synthesis of **5.10-a.** A mixture of 4-fluorothiophenol **5.9-b** (42.30 g, 0.33 mol), 4-fluoroacetophenone (41.44 g, 0.30 mol), anhydrous potassium carbonate (24.87 g, 0.18 mol) and DMAc (600 ml) was mechanical stirred under argon for 0.5 h at room temperature. After that, the temperature was increased to 60°C (not higher since by-products make the purification of the product difficult), and the reaction mixture was allowed to react for 24 h (the reaction was followed by HPLC).

When the reaction finished, the reaction mixture was poured into 2000 mL of water. The precipitate was filtered (isolated yield = 100 %, purity of the isolated product = 92%), recrystallized in methanol: water (5:1), (10 mL CH_3OH / g) and dried to obtain 47.29 g of **5.10-b** (yield = 64%, purity of the isolated product by HPLC = 97 %): m.p. 68-70°C; ^1H NMR (200 MHz, DMSO-d_6) δ 7.93-7.85 (d, J = 8.47 Hz, 2H), 7.66-7.55 (m, 2H), 7.42-7.30 (m, 2H), 7.25-7.18 (d, J = 8.39 Hz, 2H), 2.54 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 199.5, 165.6-160.7 (J = 247.1 Hz), 145.2, 136.8-136.6 (J = 8.2 Hz), 134.6, 129.2, 127.1, 117.6-117.2 (J = 21.6 Hz), 28.0; MS (EI) m/e 246, 231, 202; Analysis calc'd for C_{14} H_{11} S F 0: C, 68.27%; H, 4.50%; S, 13.02%; found: C, 68.23%; H, 4.51%; S, 13.17%.

Synthesis of 1,1,1-[4-(4-fluorophenylthio)-4',4"-dihydroxi]triphenylethane 5.12-b. The method is similar to that employed for the synthesis of **5.12-a.** To a mixture of phenol **5.11** (84.69 g, 0.90 mol) **5.10-b** (24.63 g, 0.10 mol) and a catalytic amount of mercaptoacetic acid ($HSCH_2COOH$) kept a room temperature was added 96% concentrated sulfuric acid (44.89 g). After 2 weeks (the reaction was followed by HPLC), 300 mL of water was added to the reaction mixture (the color changed from red to blue), stirred for a few minutes, and then the blue solid separated by decantation. The procedure was repeated, but this time the mixture was left overnight. A blue-grey solid came out. It was filtered (previous separation of a phenol gel formed), washed several times with water, and dissolved in ethyl ether. The solution was dried with magnesium sulfate, filtered, and concentrated under vacuum. The concentrated solution was treated with petroleum ether:ethyl ether (95:5) under stirring until a solid came out. The precipitate was filtered and dried to obtain 16.57 g of **5.12-b** (yield = 40%, purity by HPLC of the isolated product = 93%): m.p. 132-134°C; 1H NMR (200 MHz, DMSO-d6) δ 9.3, 7.48-7.38 (m, 2H), 7.30-7.22 (d, 2H), 7.22-7.13 (d, 2H), 7.06-6.96 (d, 2H), 6.86-6.76 (d, J = 8.7 Hz, 4H), 6.70-6.62 (d, J = 8.7 Hz, 4H), 2.53 (s, 3H); 13C NMR (50

MHz, DMSO-d6) δ 163.8-159.0 (J = 245.4 Hz), 155.0, 148.9, 139.0, 133.9-133.7 (J = 8.3 Hz), 132.4, 129.9-129.8 (J = 3.7 Hz), 129.4, 129.3, 129.2, 117.1-116.6 (J = 21.8 Hz), 114.7, 51.4, 31.4; MS (IE) m/e calc'd for $C_{26} H_{21} S O_2 F$: 416.12463, found 416.12462; 416, 401, 322, 307, 231, 195, 165, 129, 94.

Synthesis of 5.13-b. The method is similar to that employed for the synthesis of **5.2.** To 31.24 g (75 mmol) of **5.12-b** in pyridine (75 g) at 0°C was added acetic anhydride (110 g), dropwise. The ice bath was removed and the reaction was allowed to go for 24 h at room temperature. The contents were poured into a beaker containing 750 mL of 20% aqueous HCl at 0°C. The yellow viscous liquid separated by decantation was dissolved in ethyl ether and the solution extracted with water. The ethereal phase was separated, dried with magnesium sulfate, filtered, concentrated and coagulated in methanol. The light yellow precipitate was separated by filtration and washed with methanol. After the workup 20.27 g of **5.13-b** (yield = 54%, purity of the isolated product by HPLC = 96%) was obtained: m.p. 138-140°C; ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.53-7.41 (m, 2H), 7.33-7.15 (m, 4H), 7.13-6.95 (m, 10H), 2.27 (s, 6H), 2.12 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 169.2, 164.8-159.9 (J = 245.4 Hz), 149.0, 147.3, 146.0, 134.8-134.6 (J = 8.3 Hz), 129.9, 129.8, 129.3, 121.3, 117.1-116.7 (J = 21.8 Hz), 52.9, 32.1, 22.8; MS (IE) m/e calc'd for $C_{30} H_{25} S O_4 F$: 500.14575, found 500.14575; 500, 485, 443, 401, 43; Analysis calc'd for $C_{30} H_{25} S O_4 F$: C, 71.98%; H, 5.03%; S, 6.4%; F, 3.8%; found: C, 71.79%; H, 5.13%; S, 6.71%; F, 3.71%.

Synthesis of 5.14-b. The method is similar to that employed for the synthesis of **5.3.** Product **5.13-b** (17.52 g, 35 mmol) was added to a vigorously stirred suspension of wet alumina (35.00 g) and Oxone (64.75 g, 105 mmol) in chloroform (350 mL). The mixture was heated at reflux for 8 h. When the reaction finished, it was cooled, filtered and the solids washed thoroughly with chloroform. The solution was concentrated and poured into methanol (175 mL). The precipitate was separated by filtration and washed with methanol to afford 16.59 g of **5.14-b** (isolated yield = 89%). The purity of the white solid was checked by TLC (aluminium sheet of silica gel 60 F_{254}, hexanes:ethyl acetate, 6:4): m.p. 148-150°C; ^{1}H NMR (200 MHz, DMSO-d_6) δ 8.12-8.02 (m, 2H), 7.98-7.90 (d, 2H), 7.54-7.40 (m, 2H), 7.38-7.28 (d, 2H), 7.10-7.02 (s, 8H), 2.25 (s, 6H), 2.15 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 169.2, 167.8-162.8 (J = 252.7 Hz), 154.6, 149.2, 145.0, 139.5, 137.8, 130.9-130.7 (J = 9.4 Hz), 129.9, 129.8, 127.6, 121.6, 117.3-116.9 (J = 22.1 Hz), 53.4, 32.0, 22.7; MS (EI) m/e calc'd for $C_{30}H_{25}SFO_6$: 532.13557, found 532.13557; 532, 490, 475, 448, 433, 213, 43; Analysis calc'd for $C_{30}H_{25}SFO_6$: C, 67.66%; H, 4.73%; S, 6.02%; F, 3.57%; found: C, 67.27%; H, 4.81%; S, 6.09%; F, 3.70%.

Synthesis of 5.15-b. The method is similar to that employed for the synthesis of **5.15-a.** To product **5.14-b** (5.33 g, 10 mmol) was added ethanol (75 mL) and potassium carbonate (1.38 g, 10 mmol). The reaction mixture was stirred at 60°C for 24 h. After the workup a the beige solid was separated by filtration and dried to afford 4.26 g of **5.15-b** (isolated yield = 95%). The purity was checked by TLC (aluminium sheet of silica gel 60 F254 , hexanes:ethyl acetate, 5:5): m.p. 213-215°C; ^{1}H NMR (200 MHz, DMSO-d_6) δ 9.38 (s, 2H), 8.10-7.98 (m, 2H), 7.92-7.82 (d, J = 8.4 Hz, 2H), 7.50-7.34 (m, 2H), 7.34-7.20 (d, J = 8.4 Hz, 2H), 6.84-6.74 (d, J = 8.8 Hz, 4H), 6.74-6.62 (d, J = 8.5 Hz, 4H), 2.01 (s, 3H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 166.9-161.9 (J = 250.2 Hz), 156.0, 155.2, 138.2, 137.5 (d, J = 2.8 Hz), 130.7-130.5 (J = 9.6 Hz), 129.5, 129.2, 127.0, 117.4-116.9 (J = 22.6 Hz), 114.9, 52.0, 31.3; MS (EI) m/e calc'd for $C_{26}H_{21}SFO_4$: 448.11445, found 448.11445; 448, 433, 418, 274, 213, 105; MS (MALDI(Ag)) m/e 558.7 (MI), 556.7; Analysis calc'd for $C_{26}H_{21}SFO_4$: C, 69.63%; H, 4.72%; S, 7.15%; F, 4.24%; found: C, 69.35%; H, 5.09%; S, 7.24%; F, 4.20%.

Synthesis of activated monomer [4(4-fluorodiphenylsulfonyl)-4',4''-dihydroxi] tetraphenylmethane 5.26.

Synthesis of 4-fluorodiphenyl sulfide 5.19. Cuprous phenylmercaptide **5.17** was precipitated as a yellow solid by addition of thiophenol **5.16** (100.26 g, 0.91 mol) to $5H_2O.CuSO_4$ (114.85 g, 0.46 mol) in 800 mL of water at roon temperature. The product was filtered off, washed with benzene (to remove the by-product diphenyldisulfide) and dried to obtain 67.00 g of the thiolate (isolated yield = 43%).

p-Bromofluorobenzene **5.18** (78.77 g, 0.45 mol) was dissolved in 600 mL NMP and heated for 15 min at 180°C. The thiolate **5.17** was added (74.22 g, 0.43 mol) to the hot solution and the mixture was stirred and reflux for 24 h. The hot reaction mixture was quenched by pouring into a mixture of 400 g ice and 250 mL concentrated hydrochloric acid. This solution was extracted twice with 200 mL portions of ethyl ether. The ether extract was dried over anhydrous magnesium sulfate. The extract was then filtered and the crude product was isolated from the filtrate by removal of the ether. After the workup, 92 g of a brown liquid was obtained. It was purified by two vacuum distillations. After the purification, 56.21 g of 4-fluorodiphenylsulphide **5.19**, was obtained (yield = 64%, purity of the isolated product by HPLC = 99%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43-7.39 (m, 2H), 7.36-7.32 (m, 2H), 7.28-7.20 (m, 5H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 163.9-159.0 (J = 242.6 Hz), 135.6, 134.1-133.9 (J = 8.4 Hz), 129.8, 129.5, 127.1, 117.1, 116.6 (J = 21.6 Hz); MS (EI) m/e calc'd for $C_{12}H_9SF$: 204.04090, found 204.04090; 204, 184, 109, 77.

Synthesis of 4(4-fluorophenylthio)diphenyl ketone 5.21. The reagent PPMA, 1:10 solution by weight of phosphorus pentoxide in methanesulfonic acid, was prepared according to the reported procedure (22).

A mixture of benzoic acid **5.20** (4.88 g, 40 mmol) and 4-fluorodiphenylsulfide **5.19** (8.17 g, 40 mmol) in PPMA (60 mL) was stirred at 80°C for 24 h. The red solution was poured into 400 mL water and neutralized with sodium carbonate. The white product was filtered, washed with water and dried to obtain an isolated yield of 100 %. After recrystallization from petroleum ether, 10.13 g of **5.21** was obtained (yield = 82 %, purity of the isolated product by HPLC = 98%) : m.p. 96-98°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.70-7.56 (m, 7H), 7.54-7.48 (t, 2H), 7.36-7.28 (t, 2H), 7.24-7.19 (d, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 195.0, 165.6-160.7 (J = 247.3 Hz), 144.6, 137.8, 136.8-136.6 (J = 8.3 Hz), 135.0, 132.6, 131.1, 130.1, 128.6, 127.0, 117.6-117.2 (J = 21.9 Hz); MS (EI) m/e calc'd for $C_{19}H_{13}SOF$: 308.06711, found 308.06711; 308, 231, 202, 181, 170, 152, 105, 77; Analysis calc'd for $C_{19}H_{13}SOF$: H, 4.25%; F, 6.16%; found: H, 4.18%; F, 6.15%.

Synthesis of 5.22. Product **5.21** (6.18 g, 20 mmol) and phosphorous pentachloride (6.25 g, 30 mmol) were added to a dried mixture of 40 mL of benzene and 8 mL of carbon disulfide. After refluxing the mixture for 24 h, the solvent was removed by slow distillation. The remaining material (an orange liquid) was purified by distillation of byproduct $POCl_3$ using the Kugelrohr equipment at 100°C for 0.5 h. After that, 6.83 g of **5.22** was obtained (yield = 94%, purity of the isolated product by HPLC = 97%): ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.69-7.60 (m, 2H), 7.55-4.43 (m, 4H), 7.43-7.32 (m, 3H), 7.19-7.04 (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 165.3-160.4 (J = 246.7 Hz), 143.8, 142.2, 139.6, 136.2-136.0 (J = 8.3 Hz), 129.4, 128.5, 128.4, 127.8, 127.7, 117.5-117.0 (J = 21.6 Hz), 92.3.

Synthesis of [4(4-fluorodiphenylthio)-4',4"-dihydroxi]tetraphenylmethane 5.23. Freshly distilled phenol **5.11** (8.47 g, 90 mmol) was mixed with distilled xylene (11 mL) under nitrogen while stirred vigorously and **5.22** (6.54 g, 18 mmol) was added. The resulting mixture was slowly heated up to the boiling point of the xylene. Evolution of HCl then occurred. The mixture was stirred and heated for 7 h. When **5.22** was added, the reaction mixture took on an intense violet color which later changed to orange. The reaction mixture was extracted with ethyl ether and the ethereal phase washed with water, dried with magnesium sulfate and concentrated by rotoevaporation of the ether. The concentrated orange solution was poured into petroleum ether under stirring for 0.5 h. An orange solid came out, which was dried overnight under vacuum at 70°C to obtain 8.53 g of **5.23** (yield = 99%, purity of the isolated product by HPLC = 88%) : m.p. 116-118° (C); ^{1}H NMR (200 MHz, DMSO-d_6) δ 9.40-9.34 (d, 2H), 7.52-7.42 (m, 2H), 7.35-7.02 (m, 10H), 6.95-6.60 (m, 9H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 153.4, 147.0, 145.9, 139.3, 135.0-134.9 (J = 8.2 Hz), 134.5, 132.5, 132.1, 131.2, 128.5, 127.9, 126.3, 117.2-116.7 (J = 21.6 Hz), 114.9, 64.4; MS (EI) m/e calc'd for $C_{31}H_{23}SO_2F$: 478.14027, found 478.14027; 478, 401, 384, 309, 275, 229, 181.

Synthesis of 5.24. The method is similar to that employed for the synthesis of **5.2.** To 8.14 g (17 mmol) of **5.23** in pyridine (24 mL) at 0°C was added acetic anhydride (32 mL) dropwise. The ice bath was removed and the reaction was let to go for 24h at room temperature. The contents were poured into a beaker containing 180 mL of 20% aqueous HCl at 0°C. A yellow gum was obtained which was washed with water and separated by decantation. The gum was then dissolved in 180 mL of ethyl ether, the solution dried with magnesium sulphate, filtered, and concentrated. The concentrated solution was poured into 50 mL of methanol. The precipitate was separated by filtration and the solid dried overnight under vacuum at 70°C to obtain 5.36 g of **5.24** (yield = 56%, purity of the isolated product by HPLC = 97%): m.p. 164-166°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48-7.44 (m, 2H), 7.30-7.07 (m, 15H), 7.07-7.03 (d, 4H), 2.22 (s, 6H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 168.6, 164.1-159.3 (J = 243.4 Hz), 148.3, 145.7, 144.6, 143.2, 134.9-134.8 (J = 8.3 Hz), 133.9, 131.4, 131.3, 130.2, 128.6, 128.2, 128.0, 126.3, 121.2, 117.2-116.8 (J

= 21.7 Hz), 64.2, 21.2; MS (EI) m/e calc'd for $C_{35}H_{27}SO_4F$: 562.16140, found 562.16140; 562, 520, 485, 443, 427, 401, 385, 275, 181, 43; Analysis calc'd for $C_{35}H_{27}SO_4F$: C, 74.71%; H, 4.84%; S, 5.70%; F, 3.38%; found: C, 74.58%; H, 4.94%; S, 5.80%; F, 3.15%.

Synthesis of 5.25. The method is similar to that employed for the synthesis of **5.3**. Product **5.24** (11.25 g, 20 mmol) was added to a vigorously stirred suspension of wet alumina (20.00 g) and Oxone (37.00 g, 60 mmol) in chloroform (100 mL). The mixture was heated at reflux for 24 h. When the reaction finished, it was cooled, filtered and the solids washed thoroughly with chloroform. The solution was concentrated by rotoevaporation and poured in 50 mL of methanol. The new solution was left overnight in a covered beaker. A solid was separated. After the workup, 9.40 g of **5.25** was obtained (isolated yield = 79%). The purity of the isolated product was checked by TLC (TLC aluminium sheets of silica gel 60 F_{254}, hexanes:ethyl acetate, 5:5): m.p. 103-105°C; ^{1}H NMR (200 MHz, DMSO-d_6) δ 8.12-8.00 (m, 2H), 8.00-7.90, (d, 2H), 7.54-7.40 (m, 4H), 7.40-7.02 (m, 13H), 2.26 (s, 6H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 169.6, 167.0-162.0 (J = 250.4 Hz), 152.0, 148.4, 145.2, 142.6, 138.6, 137.2, 131.5, 131.3, 130.8-130.7 (J = 9.7 Hz), 130.2, 128.2, 127.2, 126.5, 121.5, 117.5-117.0 (J = 22.4 Hz), 64.7, 21.1; MS (EI) m/e calc'd for $C_{35}H_{27}SO_6F$: 594.15122, found 594.15122; 594, 552, 510, 433, 416, 275, 228, 199, 181, 43.

Synthesis of 5.26. The method is similar to that employed for the synthesis of **5.4**. To product **5.25** (1.78 g, 3 mmol) was added methanol (25 mL), a saturated solution of sodium bicarbonate in water (25 mL), and NMP (30 mL). The mixture was stirred at 100°C for 2 h. When the reaction was finished, it was cooled to room temperature and acidified slowly to pH = 2-4 using 10% aqueous HCl. Then, water (25 mL) was added and a gum was formed. The gum was separated, dissolved in ethyl ether (75 mL), and the solution washed with water, dried with magnesium sulphate, filtered and evaporated under reduced pressure to afford 1.04 g of a yellow solid (isolated yield = 68%). The purity was checked by TLC (hexanes:ethyl acetate, 6:4): ^1H NMR (500 MHz, DMSO-d_6) δ 9.44 (s, 2H), 8.05-7.98 (m, 2H), 7.90-7.84 (d, J = 8.3 Hz, 2H), 7.48-7.40 (t, 2H), 7.40-7.30 (d, J = 8.3 Hz, 2H), 7.30-7.20 (t, 2H), 7.20-7.10 (t, 1H), 7.10-7.00 (d, 2H), 6.80-6.90 (d, J = 8.3 Hz, 4H), 6.60-6.70 (d, J = 8.3 Hz, 4H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 167.0-162.0 (J = 250.6 Hz), 155.1, 153.3, 146.2, 138.1, 137.4-137.3 (J = 2.8 Hz), 136.1, 131.5, 131.4, 130.7-130.5 (J = 9.7 Hz), 130.2, 127.8, 126.8, 126.0, 117.4-117.0 (J = 22.4 Hz), 114.8, 64.0; MS (MALDI (Ag)) m/e 620.6(MI), 618.7; MS (EI) m/e calc'd for $C_{31}H_{23}SO_4F$: 510.13010, found 510.13010; 510, 416, 257, 228, 183, 94.

Preparation of hyperbranched polymers.

Synthesis of hyperbranched polymer 5.7. The sodium salt of **5.4-a** was prepared by treating **5.4-a** in ethyl ether with excess of NaH; the solution was filtered to removed excess NaH and the ether was removed in vacuum.

To a 25 mL round bottomed flask, fitted with a condenser and a nitrogen inlet, there was added the sodium salt of **5.4-a** (1.415 g, 2 mmol) and NMP (10 mL).The reaction mixture was stirred vigorously and maintained under reflux (2 h, 6 h, or 15 h). After that, it was cooled, poured into methanol (440 mL) acidified with a few drops of HCl, and filtered. The solid recovered was dissolved in DMAc (10 mL), and the solution was filtered and coagulated in an aqueous 2% HCl (40 mL). The precipitate was filtered and dried overnight at 100°C under vacuum to obtain 1.07 g of **5.7** . Assuming that all the n monomer molecules reacted and that n molecules of HCl were lost during the reaction, the isolated yield was 82%: ^1H NMR (500 MHz, DMSO-d_6) δ 8.00-7.78, 7.70-7.54, 7.44-7.34, 7.34-7.18, 7.18-7.04, 7.04-6.92, 6.92-6.88; ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 161.4, 153.4, 151.4, 150.9, 144.2, 141.2, 140.0 (d), 139.5, 139.3, 134.9, 132.3, 131.5, 131.4, 130.3, 130.1, 129.6, 129.2, 128.3, 127.0 (d), 119.5, 118.0, 64.5; MS (MALDI(Ag)) m/e 1407.8, 2056.9, 2706.5, 3355.7, 4004.6, 4652.6, 5301.5, 5950.0; Tg = 226°C (10°C/min, N_2), 5% weight loss = 462°C (10°C/min, N_2), 5% weight loss = 461°C (10°C/min, O_2); n_{inh} = 0.10 dL/g (NMP, 0.5 g/dL, 25°C).

Synthesis of hyperbranched polymer 5.8. A 25 mL, Pyrex, three-necked round bottom flask equipped with condenser, argon inlet-outlet, magnetic stirrer, and thermometer was charged with **5.6** (0.832 g, 0.625 mmol), **Cs_2CO_3** (0.107 g, 0.328 mmol), **$Mg(OH)_2$** (0.025 g, 0.422 mmol), and DMAc. Argon was sparged through the reaction mixture with stirring for 30 min at RT. After that, the reaction was allow to go for 1 h at 150°C (monomer concentration: 0.63 mol/L) or 1 - 2 h under reflux conditions (monomer concentrations: 0.13, 0.22, and 0.42 mol/L). When the reaction finished, the reaction mixture was diluted with 5 mL DMAc and allowed to cool. Then, the solution was poured into 5% aqueous hydrocloric acid, filtered, washed with methanol, and the solid dried overnight at 100°C under vacuum to obtain 0.75 g of the product. Assuming that all the n monomer molecules reacted and that n molecules of HF were lost during the reaction, the reaction yield was 95%: ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.3-7.7 (m, 8H), 7.6-6.6 (m, 17H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 167.0-162.0 (J = 250.8 Hz), 160.6, 152.6, 151.2, 150.9, 144.4, 141.2, 139.3, 138.8, 137.0, 134.7, 132.2, 131.5, 130.8-130.6 (J = 10 Hz), 130.1, 128.4, 127.3, 119.7, 118.5, 117.5-117.0 (J = 22.7 Hz), 65.2; MS (MALDI(Ag)) m/e 1372.0, 2004.3, 2637.3, 3270.0, 3902.5, 4535.4, 5167.9, 5802.2; Tg = 239°C (10°C/min, N_2), 5% weight loss = 467C (10°C/min, N_2); n_{inh} = 0.18 dL/g (NMP, 0.5 g/dL, 25°C).

Synthesis of hyperbranched polymer 5.27-a. A 25 mL, Pyrex, three-necked round bottom flask equipped with a Dean-Stark trap filled with toluene, condenser, nitrogen inlet-outlet, magnetic stirrer, and thermometer was charged with **5.15-a** (0.581 g, 1.25

mmol), anhydrous K_2CO_3 (0.190 g, 1.375 mmol), and NMP:toluene (1:1). Monomer concentrations in NMP of 0.2, 0.5 and 0.7 mol/L were employed. Nitrogen was sparged through the reaction mixture with stirring for 30 min, and then the mixture was heated to 130°C until no further water formed by azeotropic distillation was collected. After that, toluene was removed slowly while the reaction mixture was heated. The bath temperature was maintained at 180-190°C for 3 h under nitrogen. Heating was accomplished with a silicone oil bath and hot plate. The reaction mixture was allowed to cool, diluted with 5-10 mL DMAc, poured into 20-40 mL methanol containing a few drops of hydrochloric acid, filtered, and the solid dried overnight at 100°C under vacuum. After the workup 0.42 g of the product was obtained. Assuming that all the n monomer molecules reacted and that n molecules of HCl were lost during the reaction, the isolated yield was 78%: ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.10-8.90 (d), 7.96-7.70 (m), 7.36-7.18 (m), 7.18-6.86 (m), 6.86-6.72 (m), 6.72-6.60 (m), 2.40-1.90 (m); MS (MALDI(Ag)) m/e 966.1, 1394.7, 1822.9, 2251.8, 2680.1, 3109.0, 3536.2. Tg = 261°C (10°C/min, N_2), 5% weight loss = 395C (10°C/min, N_2); η_{inh} = 0.25 dL/g (NMP, 0.5 g/dL, 25°C).

Synthesis of hyperbranched polymer 5.27-b. The method is similar to that employed for the synthesis of **5.27-a.** The flask was charged with **5.15-b** (0.561 g, 1.25 mmol), Cs_2CO_3 (0.214 g, 0.656 mmol), $Mg(OH)_2$ (0.049 g, 0.844 mmol), and DMAc:toluene (1:1). Monomer concentrations in DMAc of 0.5, 0.6, 0.7 and 0.8 mol / L were employed. The bath temperature was maintained at 150°C for 0.5 h (0.6, 0.7 and 0.8 mol/L) or 160°C - 170°C for 1.0 h (0.5 and 07 mol/L) under argon. When the reaction finished, the mixture was diluted with 5 mL DMAc and allowed to cool. Then, the solution was poured into 5% aqueous hydrocloric acid (20 mL), filtered, and the solid washed with methanol, and dried overnight at 100°C under vacuum (0.54 g). Assuming that all the n monomer molecules reacted and that n molecules of HF were lost during the reaction, the reaction was almost quantitative: ^{1}H-NMR (500 MHz, DMSO-d_6) δ 9.43 (s), 9.35 (s), 8.10-7.70

(m), 7.45-6.50 (m), 2.30-1.80 (m); ^{13}C NMR (50 MHz, DMSO-d_6) δ 160.9, 155.7, 155.4, 155.2, 154.9, 152.3, 144.7, 138.9, 138.7, 138.2, 137.5, 134.7, 130.1, 129.5, 129.1, 127.0, 126.8, 119.8, 118.0, 115.1, 114.9, 52.3, 31.3; MS (MALDI(Ag)) m/e 964.2, 1392.6, 1821.5, 2250.3, 2679.2, 3107.8, 3536.9, 3964.4, 4392.7, 4821.2, 5248.2, 5678.2, 6102.7; Tg = 253°C (10°C/min, N_2), 5% weight loss = 345°C (10°C/min, N_2); n_{inh} = 0.26 dL/g (NMP, 0.5 g/dL, 25°C).

Synthesis of hyperbranched polymer 5.27-c.

Method A. The method is similar to that employed for the synthesis of **5.27-a.** The flask was charged with **5.26** (0.638 g, 1.25 mmol), anhydrous **K_2CO_3** (0.190 g, 1.375 mmol), DMAc (3.5 mL), and toluene (3.5 mL). The reaction temperature was maintained at 164°C for 3 h under nitrogen. Then, the solution was poured into methanol containing a few drops of hydrochloric acid, filtered, and the solid dried overnight at 100°C under vacuum to obtain 0.57 g of the product. Assuming that all the n monomer molecules reacted and that n molecules of HF were lost during the reaction, the isolated yield was 93%: ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.69-9.35 (bd), 8.05-7.65 (bs), 7.50-6.50 (m); ^{13}C NMR (50 MHz, DMSO-d_6) δ 160.7, 155.3, 155.1, 152.2, 146.2, 145.7, 138.9, 136.1, 135.5, 134.8, 132.2, 131.4, 130.2, 127.9, 127.7, 126.7, 119.5, 118.3, 114.9, 114.7, 35.6; MS (MALDI (Ag)) m/e 1088.4, 1578.7, 2069.6, 2560.6, 3051.0, 3541.2, 4031.0; Tg: 276°C (10°C/min, N_2), 5% weight loss = 397°C (10°C/min, N_2); n_{inh} = 0.17 dL/g (NMP, 0.5 g/dL, 25°C).

Method B. The method is similar to that employed for the synthesis of **5.27-a.** The flask was charged with **5.26** (0.64 g, 1.25 mmol), **Cs_2CO_3** (0.214 g, 0.657 mmol), **$Mg(OH)_2$** (0.050 g, 0.844 mmol), and DMAc/Toluene (1:1). Monomer concentrations in DMAc of 0.25 and 0.70 mol/L were employed. The temperature was maintained at 164°C for 1 h under argon. The reaction mixture was diluted with 5-10 mL DMAc and allowed to cool. Then, the solution was poured into 5% aqueous hydrochloric acid (20-40 mL), filtered, and the solid washed with methanol, and dried overnight at 100°C under vacuum. After the workup 0.56 g of the product was obtained. Assuming that all the n monomer molecules reacted and that n molecules of HF were lost during the reaction, the isolated yield was 91%: MS (MALDI (Ag)) m/e 1087.1, 1577.6, 2068.1, 2558.6, 3048.8, 3540.5, 4029.5, 4518.5; Tg = 277°C (10°C/min, N_2), 5% weight loss = 355°C (10°C/min, N_2); n_{inh} = 0.24 dL/g (NMP, 0.5 g/dL, 25°C).

Preparation of the acetylated hyperbranched polymers.

General procedure for the synthesis of hyperbranched polymers 5.28. To 0.33 g of polymer **5.27** in pyridine (6 mL) at 0°C was added acetic anhydride (6 mL) dropwise. The ice bath was removed and the reaction was allowed to go for 24 h at room temperature. The contents were poured into a beaker containing 50 mL of 10-15% aqueous HCl at 0°C. After filtration, the solid obtained was dried at 100°C overnight under vacuum.

Hyperbranched polymer 5.28-a. It was obtained 0.30 g of **5.28-a**: ^{1}H NMR (200 MHz, DMSO-d_6) δ 8.00-7.70 (bs), 7.36-7.16 (bs), 7.16-6.80 (bs), 2.30-1.90 (m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 169.3, 161.5, 154.7, 153.1, 149.1, 145.1, 144.4, 139.6, 135.1, 130.4, 129.8, 129.5, 127.3, 121.7, 120.0, 118.3, 52.0, 30.2, 21.1; IR ($CDCl_3$) 1014.14, 1110.49, 1153.58, 1169.22, 1208.57, 1247.22, 1295.45, 1320.15, 1500.17, 1587.40, 1753.93 cm^{-1}; MS (MALDI (Ag)) m/e 1049.2, 1520.8, 1991.0, 2461.5, 2931.9, 3402.0, 3872.6, 4343.0, 4813.0, 5283.3; Tg = 242°C (10°C/min, N_2), 5% weight loss = 420C (10°C/min, N_2); n_{inh} = 0.22 dL/g (NMP, 0.5 g/dL, 25°C).

Hyperbranched polymer 5.28-b. It was obtained 0.29 g of **5.28-b**: ^{1}H NMR (200 MHz, DMSO-d_6) δ 8.10-7.70 (bs), 7.50-6.60 (m), 2.40-1.90 (m); ^{13}C NMR (50 MHz, DMSO-d_6) δ 168.6, 160.8, 154.1, 152.5, 148.6, 144.7, 143.9, 139.2, 134.8, 130.1, 129.5, 129.2, 127.1, 121.6, 119.9, 118.2, 52.7, 31.2, 22.1; MS (MALDI(Ag)) m/e 1047.6, 1517.8, 1988.3, 2458.6, 2928.7, 3399.7, 3868.8, 4338.7, 4807.8; Tg = 240°C (10°C/min, N_2), 5% weight loss = 377C (10°C/min, N_2); n_{inh} = 0.22 dL/g (NMP, 0.5 g/dL, 25°C).

Hyperbranched polymer 5.28-c-1. It was obtained 0.29 g of **5.28-c-1**: ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.10-7.70 (m), 7.60-6.60 (m), 2.35-2.05 (bs); ^{13}C NMR (50 MHz, DMSO-d_6) δ 168.5, 160.8, 152.5, 151.7, 148.4, 145.2, 142.6, 141.8, 139.1, 134.7, 132.2, 131.3, 130.2, 128.1, 126.8, 121.4, 119.6, 118.4, 64.7, 22.1; MS (MALDI (Ag)) m/e 1174.5, 1707.8, 2240.3, 2773.7, 3306.8, 3836.8; Tg = 254°C (10°C/min, N_2), 5% weight loss = 417°C (10°C/min, N_2); n_{inh} = 0.14 dL/g (NMP, 0.5 g/dL, 25°C).

Hyperbranched polymer 5.28-c-3. It was obtained 0.29 g of **5.28-c-3**: Tg = 253°C (10°C/min, N_2), 5% weight loss = 365°C (10°C/min, N_2); n_{inh} = 0.24 dL/g (NMP, 0.5 g/dL, 25°C). For data of molecular characterization see synthesis of hyperbranched polymer **5.28-c-1.**

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